### Systemic Therapy for Diffuse Large B-cell Lymphoma

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

#### First-Line Therapy

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| **R-CHOP (category 1)**<sup>2-4</sup> | 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, and vincristine 1.4mg/m² IV bolus (max dose 2mg)  
**Days 3, 24, and 45:** Prednisone 100mg PO 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)**<sup>5,6</sup> | **Day 1:** Cyclophosphamide 750mg/m² IV, doxorubicin 50mg/m² IV, and vincristine 2mg IV  
**Days 1-5:** Prednisone 100mg PO.  
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)**<sup>7-9</sup> | **Day 1:** Rituximab 375mg/m² IV day 1  
**Days 1-4:** Etoposide 50mg/m² IV, doxorubicin 10mg/m², and vincristine 0.4mg/m²  
**Day 5:** Cyclophosphamide 750mg/m² IV  
**Days 1-5:** Prednisone 60mg/m² PO BID.  
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**<sup>**†**</sup> | **RCEPP**<sup>10</sup>  
**Days 1 and 8:** Cyclophosphamide 600mg/m² IV  
**Day 1:** Etoposide IV 70mg/m² IV (or days 1–3 if not giving PO etoposide)  
**Days 2 and 3:** Etoposide 140 mg/m² PO (rounded to the nearest 50mg capsule)  
**Days 1–10:** Procarbazine 60mg/m² PO and prednisone 60mg/m² PO.  
Repeat every 28 days until disease progression, or unacceptable toxicity. |
| **RCDOP**<sup>11,12</sup> | **Day 1:** Cyclophosphamide 750mg/m² IV, liposomal doxorubicin 30mg/m² IV, and 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. |
| **RCNOP**<sup>13-15</sup> | **Day 1:** Rituximab 375mg/m² IV  
**Day 1:** Cyclophosphamide 750mg/m² IV, mitoxantrone 10mg/m² IV, and vincristine 1.4mg/m² IV (max dose 2mg)  
**Days 1-5:** Prednisone 50mg/m² PO.  
Repeat cycle every 3 weeks for 6 cycles (max 8 cycles). |
| **DA-EPOCH + rituximab**<sup>16</sup> | **Day 1:** Rituximab 275mg/m²  
**Days 1-4:** Doxorubicin 10mg/m² IV, etoposide 50mg/m² IV, and vincristine 0.4mg/m² IV  
**Day 5:** Cyclophosphamide 750mg/m² IV  
**Days 1-5:** Prednisone 60mg/m² PO.  
Administer G-CSF on day 6 until ANC exceeds nadir.  
Repeat cycle every 3 weeks. |
Systemic Therapy for Diffuse Large B-cell Lymphoma\(^1\) (continued)

### First-Line Therapy for Patients with Poor Left Ventricular Function or Very Frail\(^{*\dagger}\) (continued)

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| **RCEOP\(^1\)** | Day 1: Rituximab 375mg/m\(^2\) IV  
Day 1: Cyclophosphamide 750mg/m\(^2\) IV, etoposide 50mg/m\(^2\) IV, and vincristine 1.4mg/m\(^2\) IV (max dose 2mg)  
Days 1–5: Prednisone 100mg PO  
Days 2–3: Etoposide 100mg/m\(^2\) PO.  
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. |
| **Patients >80 Years of Age with Comorbidities** | Day 1: Rituximab 375mg/m\(^2\)  
Day 1: Cyclophosphamide 400mg/m\(^2\), doxorubicin 25mg/m\(^2\), and vincristine 1mg  
Days 1–5: Prednisone 40mg/m\(^2\).  
Repeat every 3 weeks for 6 cycles. |
| **First-Line Consolidation (optional)** | 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. |
| **High-dose therapy with autologous stem cell rescue in patients with age-adjusted IPI high-risk disease (Category 2B)** | 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. |
| **Concurrent Presentation with CNS Disease** | Systemic methotrexate 3g/m\(^2\) or more on day 15 of a 21-day R-CHOP cycle that has been supported by growth factors. |
| **Leptomeningeal** | Methotrexate/cytarabine IT. Consider Ommaya reservoir placement and/or systemic methotrexate 3–3.5g/m\(^2\). |

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

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| **DHAP ± rituximab\(^{20-22}\)** | Days 1–4: Cisplatin 100mg/m\(^2\) IV via 24-hour infusion, cytosine 2g/m\(^2\) in 2 pulses each given 12 hours apart, and dexamethasone 40mg PO or IV ± rituximab 375mg/m\(^2\) IV prior to DHAP.  
Repeat in 3–4 weeks for 6-10 cycles. |
| **ESHAP ± rituximab\(^{23,24}\)** | Days 1–4: Etoposide 40–60mg/m\(^2\)  
Days 1–5: Methylprednisolone 250–500mg IV  
Day 5: Cytarabine 2g/m\(^2\) IV over 2–3 hours  
Days 1–4: Cisplatin 25mg/m\(^2\) IV via 24-hour infusion, ±  
Day 1 or 5: Rituximab 375mg/m\(^2\) IV.  
Repeat every 3–4 weeks for 3 cycles. |
| **GDP ± rituximab\(^{25,26}\)** | Days 1 and 8: Gemcitabine 1000mg/m\(^2\) IV over 30 minutes  
Days 1–4: Dexamethasone 40mg PO  
Day 1: Cisplatin 75mg/m\(^2\) IV OR carboplatin at AUC = 5 IV over 30 minutes, ±  
Day 8: Rituximab 375mg/m\(^2\) slow IV infusion for CD20-positive disease.  
Repeat every 3 weeks for up to 6 cycles. |
| **GEMOX ± rituximab\(^{27}\)** | Day 1: Gemcitabine 1000mg/m\(^2\) and oxaliplatin 100mg/m\(^2\) ± rituximab 375mg/m\(^2\) IV.  
Repeat every 15 days if ANC >1 × 10\(^9\)/L and platelet count >100 × 10\(^9\)/L; if not, then every 3 weeks. |
### Second-Line Therapy (for patients with intention to proceed to high-dose therapy with autologous stem cell rescue) (continued)

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| ICE ± rituximab28-30           | **Days 1-3**: Etoposide 100mg/m² IV bolus  
**Day 2**: Carboplatin AUC = 5 (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 5mcg/kg/day for cycles 1-2, increased to 10mcg/kg/day following cycle 3 until completion of peripheral blood stem cell collection,  
|                               | ± **Days 1 and 3**: Rituximab 375mg/m² IV bolus and on cycle 1, give additional dose rituximab 375mg/m² on Day 2. Repeat every 14 days or when ANC >1000 cells/mcL and platelet count >50000/mcL. |
| MINE ± rituximab31,32‡         | **Days 1-3**: Mesna 13g/m² and ifosfamide 1.3g/m²  
**Day 1**: Mitoxantrone 12mg/m²  
**Days 1-3**: Etoposide 65mg/m²,  
|                               | ± **Days 1, 6, and 8**: Rituximab 400mg/m² for 3 weeks. Repeat every 3 weeks for 2 cycles.                                                                                                              |

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

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| Bendamustine ± rituximab33-35§ | **Days 1-2**: Bendamustine 120mg/m²,  
|                               | ± **Day 1**: Rituximab 375mg/m². Repeat every 28 days for up to 6 cycles.                                                                                                                                |
| Brentuximab vedotin for CD30+ disease (Category 2B)36 | **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.                                                                                                    |
| CEPP ± rituximab (PO and IV)10 | **Days 1 and 8**: Cyclophosphamide 600mg/m² IV  
**Day 1**: Etoposide 70mg/m² IV (or on days 1-3 if not giving PO etoposide)  
**Days 2 and 3**: Etoposide 140mg/m² PO (rounded to the nearest 50 mg capsule)  
**Days 1-10**: Procarbazine 60mg/m² PO and prednisone 60mg/m² PO,  
|                               | ± **Day 1**: Rituximab 375mg/m² IV. Repeat every 28 days until disease progression or unacceptable toxicity.                                                                                       |
| CEOP ± rituximab37            | **Day 1**: Cyclophosphamide 750mg/m² IV, vincristine 1.4mg/m² IV, and epirubicin 60mg/m² IV  
**Days 1-5**: Prednisone 100mg/day PO,  
**Day 0**: Rituximab 375mg/m² IV. Repeat every 3 weeks for at least 6 cycles.                                                                                                         |
| DA-EPOCH ± rituximab38,39     | **Days 2-4**: Doxorubicin 15mg/m² via continuous IV infusion, etoposide 65mg/m² via continuous IV infusion, and vincristine 0.5mg via continuous IV infusion  
**Day 5**: Cyclophosphamide 750mg/m² IV  
**Days 1-14**: Prednisone 60mg/m² PO,  
|                               | ± **Day 1**: Rituximab 375mg/m² IV. Repeat every 21 days for 4-6 cycles.                                                                                                                               |
| GDP ± rituximab40,41           | **Days 1 and 8**: Gemcitabine 1000mg/m² IV  
**Days 1-4**: Dexamethasone 40mg IV  
**Days 1-3**: Cisplatin 25mg/m² IV OR carboplatin AUC = 5 on day 1,  
|                               | ± **Day 1**: Rituximab 375mg/m² IV. Repeat every 21 days for 2-6 cycles (max of 4 cycles if using carboplatin).                                                                                     |
| GemOx ± rituximab42,43         | **Days 1 and 8**: Gemcitabine 1200mg/m² 30-minute IV infusion  
**Day 2**: Oxaliplatin 120mg/m² 2-hour IV infusion,  
|                               | ± **Day 1**: Rituximab 375mg/m² IV. Repeat every 21 days for 6 cycles.                                                                                                                               |
| Lenalidomide ± rituximab44-46  | **Days 1-21**: Lenalidomide 20mg PO ± rituximab 375mg/m² IV weekly during cycle 1. Repeat every 28 days until complete response.                                                                            |
| Rituximab47                   | **Day 1**: Rituximab 375mg/m² 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.
NON-HODGKIN LYMPHOMA TREATMENT REGIMENS:
Diffuse Large B-Cell Lymphoma (Part 4 of 5)

References


References (continued)


