

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS:

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) (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 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.

CLL without del (11q) or del (17p)¹

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

First-line therapy for patients age ≥70 or younger with comorbidities

REGIMEN	DOSING
Obinutuzumab + chlorambucil (Category 1)²	<p>Day 1: Obinutuzumab 100mg IV and chlorambucil 0.5mg/kg orally</p> <p>Day 2: Obinutuzumab 900mg IV</p> <p>Day 8: Obinutuzumab 1000mg IV</p> <p>Day 15: Obinutuzumab 1000mg IV and chlorambucil 0.5mg/kg orally.</p> <p>Repeat cycle every 28 days for 6 cycles with obinutuzumab given at a dose of 1,000mg IV on day 1 of subsequent cycles.</p>
Ofatumumab + chlorambucil³	<p>Cycle 1</p> <p>Day 1: Ofatumumab 300mg IV</p> <p>Days 1-7: Chlorambucil 10mg/m² PO</p> <p>Day 8: Ofatumumab 1,000mg IV</p> <p>Subsequent Cycles</p> <p>Day 1: Ofatumumab 1,000mg IV</p> <p>Days 1-7: Chlorambucil 10mg/m² PO.</p> <p>Repeat cycle every 28 days for a maximum of 12 cycles.</p>
Rituximab + chlorambucil⁴	<p>Cycle 1</p> <p>Days 1-7: Chlorambucil 8mg/m²/day orally</p> <p>Cycle 3</p> <p>Day 1: Rituximab 375mg/m² IV</p> <p>Days 1-7: Chlorambucil 8mg/m²/day orally</p> <p>Cycle 4-8</p> <p>Day 1: Rituximab 500mg/m² IV</p> <p>Days 1-7: Chlorambucil 8mg/m²/day orally.</p> <p>Repeat cycle every 28 days; Administer rituximab at dose of 375mg/m² IV every 2 months for 2 years as maintenance therapy.</p>
Bendamustine ± rituximab⁵⁻⁷	<p>Day 0: Rituximab 375mg/m² IV</p> <p>Days 1 and 2: Bendamustine 70mg/m² IV.</p> <p>Repeat cycle every 28 days for 6 cycles with rituximab given at a dose of 500mg/m² on day 1 and bendamustine at a dose of 90mg/m² of subsequent cycles.</p>
Obinutuzumab (Category 2B)⁸	<p>Cycle 1</p> <p>Day 1: Obinutuzumab 100mg IV</p> <p>Day 2: Obinutuzumab 900mg IV</p> <p>Day 3: Obinutuzumab 1,000mg IV</p> <p>Days 8 and 15: Obinutuzumab 2,000mg IV</p> <p>Cycles 2-8</p> <p>Day 1: Obinutuzumab 2,000mg IV.</p> <p>Repeat cycle every 21 days.</p>
Rituximab (Category 3)⁹	<p>Day 1, 8, 15, and 22: Rituximab 375mg/m²/day IV.</p>
Fludarabine ± rituximab (FR) (Category 2B)^{10*}	<p>Days 1-5: Fludarabine 25mg/m² IV, ±</p> <p>Day 1: Rituximab 50mg/m² IV</p> <p>Day 3: Rituximab 325mg/m² IV</p> <p>Day 5: Rituximab 375mg/m² IV.</p> <p>Repeat cycle every 28 days for 6 cycles with rituximab given at a dose of 375mg/m² on day 1 of subsequent cycles.</p>

continued

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) (Part 2 of 4)

CLL without del (11q) or del (17p)¹ (continued)

First-line therapy for patients age ≥70 or younger with comorbidities (continued)

REGIMEN	DOSING
Cladribine (Category 3)¹¹	Days 1–5: Cladribine 0.12mg/kg/day IV. OR Days 1–5 OR Days 1–7: Cladribine 0.1mg/kg/day IV continuous infusion over 24 hours daily. Repeat cycle every 28 days for 6 cycles.
Chlorambucil (Category 2B)^{12,13}	Days 1–28: Chlorambucil 0.4mg/kg/day with an increase to 0.8mg/kg orally daily. Repeat cycle every 28 days for 12 cycles.

First-line therapy for patients age <70 or older without significant comorbidities

Fludarabine + cyclophosphamide + rituximab (FCR) (Category 1)¹⁴⁻¹⁶	Day 1: Rituximab 375mg/m ² IV Days 1–3: Fludarabine 25mg/m ² /day IV plus cyclophosphamide 250mg/m ² /day IV. Repeat cycle every 28 days for 6 cycles with rituximab given at a dose of 500mg/m ² on day 1 of subsequent cycles.
Fludarabine + rituximab (FR)¹⁰	Days 1–5: Fludarabine 25mg/m ² IV Day 1: Rituximab 50mg/m ² IV Day 3: Rituximab 325mg/m ² IV Day 5: Rituximab 375mg/m ² IV. Repeat cycle every 28 days for 6 cycles with rituximab given at a dose of 375mg/m ² on day 1 of subsequent cycles.
Pentostatin + cyclophosphamide + rituximab (PCR)¹⁷	Day 1: Pentostatin 2mg/m ² IV plus cyclophosphamide 600mg/m ² IV, and rituximab 375mg/m ² IV. Repeat cycle every 21 days for 6 cycles; administer rituximab thrice weekly at a dose of 100mg/m ² on day 1, followed by 375mg/m ² on days 3 and 5 of the first week only.
Bendamustine ± rituximab⁵⁻⁷	Day 1: Rituximab 375mg/m ² IV Days 1 and 2: Bendamustine 90mg/m ² IV. Repeat cycle every 28 days for 6 cycles with rituximab given at a dose of 500mg/m ² on day 1 of subsequent cycles.

CLL with del (17p)¹

First-line therapy

Alemtuzumab ± rituximab¹⁸	Day 1: Alemtuzumab 3mg IV Day 2: Alemtuzumab 10mg IV Day 3, 10, 12, 17, 19, 24, and 26: Alemtuzumab 30mg IV Days 1, 8, 15, and 22: Rituximab 375mg/m ² IV. Repeat cycle once depending on response and toxicity.
Fludarabine + cyclophosphamide + rituximab (FCR)¹⁴⁻¹⁶	Day 0: Rituximab 375mg/m ² IV Days 1–3: Fludarabine 25mg/m ² /day IV plus cyclophosphamide 250mg/m ² /day IV. Repeat cycle every 28 days for 6 cycles with rituximab given at a dose of 500mg/m ² on day 1 of subsequent cycles.
Fludarabine + rituximab (FR)¹⁰	Days 1–5: Fludarabine 25mg/m ² IV Day 1: Rituximab 50mg/m ² IV Day 3: Rituximab 325mg/m ² IV Day 5: Rituximab 375mg/m ² IV. Repeat cycle every 28 days for 6 cycles with rituximab given at a dose of 375mg/m ² on day 1 of subsequent cycles.
High-dose methylprednisolone + rituximab^{19,20}	Days 1–3: Methylprednisolone 1g/m ² IV Days 1, 8, 15, and 22: Rituximab 375mg/m ² IV. Repeat cycle every 28 days for 3 cycles.
Ibrutinib²¹	Ibrutinib 420mg orally once daily until the onset of disease progression or unacceptable toxicity.

continued

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) (Part 3 of 4)

CLL with del (17p)¹ (continued)

First-line therapy (continued)

REGIMEN	DOSING
Obinutuzumab + chlorambucil (Category 1)²	Day 1: Obinutuzumab 100mg IV and chlorambucil 0.5mg/kg orally Day 2: Obinutuzumab 900mg IV Day 8: Obinutuzumab 1000mg IV Day 15: Obinutuzumab 1000mg IV and chlorambucil 0.5mg/kg orally. Repeat cycle every 28 days for 6 cycles with obinutuzumab given at a dose of 1,000mg on day 1.

CLL with del (11q)¹

First-line therapy

Obinutuzumab + chlorambucil (Category 1)²	Day 1: Obinutuzumab 100mg IV and chlorambucil 0.5mg/kg orally Day 2: Obinutuzumab 900mg IV Day 8: Obinutuzumab 1000mg IV Day 15: Obinutuzumab 1000mg IV and chlorambucil 0.5mg/kg orally. Repeat cycle every 28 days for 6 cycles with obinutuzumab given at a dose of 1,000mg on day 1.
Ofatumumab + chlorambucil³	Cycle 1 Day 1: Ofatumumab 300mg IV Days 1-7: Chlorambucil 10mg/m ² PO Day 8: Ofatumumab 1,000mg IV Subsequent Cycles Day 1: Ofatumumab 1,000mg IV Days 1-7: Chlorambucil 10mg/m ² PO. Repeat cycle every 28 days for a maximum of 12 cycles.
Rituximab + chlorambucil²²	Day 1: Rituximab 375mg/m ² IV Days 1-7: Chlorambucil 10mg/m ² orally. Repeat cycle every 28 days for 6 cycles with rituximab given at a dose of 500mg/m ² .
Bendamustine ± rituximab⁵⁻⁷	Day 0: Rituximab 375mg/m ² IV Days 1 and 2: Bendamustine 90mg/m ² IV. Repeat cycle every 28 days for 6 cycles with rituximab given at a dose of 500mg/m ² on day 1 of subsequent cycles.
Cyclophosphamide, prednisone ± rituximab²³	Day 1: Cyclophosphamide 750mg/m ² IV ± rituximab 375mg/m ² IV Days 1-5: Prednisone 100mg orally daily. Repeat cycle every 21 days until maximal response, disease progression, or unacceptable toxicity.
Reduced-dose FCR²⁴	Day 1: Rituximab 375mg/m ² IV Days 2-4: Fludarabine 20mg/m ² /day IV plus cyclophosphamide 150mg/m ² /day IV Day 14: Rituximab 500mg/m ² IV. Repeat cycle every 28 days for 6 cycles with rituximab given at a dose of 500mg/m ² on days 1 and 14 and fludarabine and cyclophosphamide given on days 1-3 of subsequent cycles; then, administer rituximab at a dose of 500mg/m ² on day 1 every 3 months until disease progression.
Rituximab (Category 3)⁹	Day 1, 8, 15, and 22: Rituximab 375mg/m ² /day IV.
Chlorambucil^{12,13}	Days 1-28: Chlorambucil 40mg/m ² orally daily. Repeat cycle every 28 days for 12 cycles.

* In patients ≥ 70 years of age, fludarabine does not appear to have a benefit for first-line therapy over other therapies including chlorambucil.

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) (Part 4 of 4)

References

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