

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS:

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) (Part 1 of 3)

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 + chlorambucil²	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 IV on day 1 of subsequent cycles.
Rituximab + chlorambucil³	Cycle 1 Days 1–7: Chlorambucil 8mg/m ² /day orally Cycle 3 Day 1: Rituximab 375mg/m ² IV Days 1–7: Chlorambucil 8mg/m ² /day orally Cycle 4–8 Day 1: Rituximab 500mg/m ² IV Days 1–7: Chlorambucil 8mg/m ² /day orally. Repeat cycle every 28 days; Administer rituximab at dose of 375mg/m ² IV every 2 months for 2 years as maintenance therapy.
Bendamustine ± rituximab^{4,6}	Day 0: Rituximab 375mg/m ² IV Days 1 and 2: Bendamustine 70mg/m ² IV. Repeat cycle every 28 days for 6 cycles with rituximab given at a dose of 500mg/m ² on day 1 and bendamustine at a dose of 90mg/m ² of subsequent cycles.
Cyclophosphamide, prednisone ± rituximab⁷	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.
Rituximab⁸	Day 1, 8, 15, and 22: Rituximab 375mg/m ² /day IV.
Fludarabine ± rituximab^{9*}	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.
Cladribine¹⁰	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^{11,12}	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.

CLL without del (11q) or del (17p)¹

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

Fludarabine + cyclophosphamide + rituximab (FCR)¹³⁻¹⁵	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)⁹	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.

continued

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) (Part 2 of 3)

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

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

REGIMEN	DOSING
Pentostatin + cyclophosphamide + rituximab (PCR)¹⁶	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 ± rituximab^{4,6}	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.
Obinutuzumab + chlorambucil²	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 (17p)¹

First-line therapy

Alemtuzumab ± rituximab^{17,18}	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)¹³⁻¹⁵	Day 0: Rituximab 375mg/m ² IV Days 1-3: Fludarabine 25mg/m ² /day IV plus cyclophosphamide 250mg/m ² /day. 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)⁹	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^{17,18}	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.
Ibrutinib¹⁹	Ibrutinib 420mg orally once daily until the onset of disease progression or unacceptable toxicity.
Obinutuzumab + chlorambucil²	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 + chlorambucil²	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.
Rituximab + chlorambucil²⁰	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 ± rituximab^{4,6}	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.

continued

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

CLL with del (11q)¹ (continued)

First-line therapy (continued)

REGIMEN	DOSING
Cyclophosphamide, prednisone ± rituximab⁷	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 FCR²¹	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.
Rituximab⁸	Day 1, 8, 15, and 22: Rituximab 375mg/m ² /day IV.
Chlorambucil^{11,12}	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.

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