Tailoring CLL Treatment: Navigating Comorbidities

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CLL, chronic lymphocytic leukemia.

Learning Objectives

Understand the factors that may impact care and treatment choices in patients with CLL with underlying comorbidities and concomitant conditions

Integrate a multidisciplinary team approach and shared decision making with treatment planning, communication with patients, and effective patient monitoring

CLL, chronic lymphocytic leukemia.

1

Overview of Comorbidities and Concomitant Conditions in Patients With CLL

Patients With CLL Are Typically Elderly and Present With Comorbidities[1,2]

The median age at CLL diagnosis is 70 years, and the age at first treatment is even higher as many patients do not require immediate treatment[1,2]

Elderly patients often present with comorbidities, including cardiac disease[2-5]

- For instance, the prevalence of AF in patients with newly diagnosed CLL is 6.1%

Studies have shown that a majority of patients with CLL (>90%) present with at least 1 comorbid health condition at the time of diagnosis[6,7]

Polypharmacy (≥5 drugs) is frequent in patients with CLL, even in those without comorbidities, making management of CLL challenging for many patients[8,9]

Comorbidities are prevalent in patients with CLL and contribute to inferior outcomes, including reduced treatment tolerance and shorter survival[6,10,11]

AF, atrial fibrillation; CLL, chronic lymphocytic leukemia.

1. Hallek M, et al. *Am J Hematol.* 2021;96(12):1679-1705. 2. Stauder R, et al. *Ann Oncol.* 2017;28(2):218-227. 3. Rigolin GM, et al. *Blood.* 2017;139(26):3495-3498. 4. Dzeshka MS, et al. *Am J Hypertens.* 2017;30(8):733-755. 5. Shanafelt TD, et al. *Leuk Lymphoma.* 2017;58(7):1630-1639. 6. Strati P, et al. *Br J Haematol.* 2017;178(3):394-402. 7. Villavicencio A, et al. *Int J Environ Res Public Health.* 2021;18(2):701. 8. Brieghel C, et al. *Hemasphere.* 2025;9(7):e70172. 9. Rotbain EC, et al. *Clin Epidemiol.* 2021;13:1155-1165. 10. Tedeschi A, et al. *Blood Adv.* 2021;5(24):5490-5500. 11. Rotbain EC, et al. *Blood Adv.* 2022;6(8):2701-2706.

Overview of Common Comorbidities and Concomitant Conditions in CLL

Concomitant condition/comorbidity	Proportion of patients affected	Manifestation and considerations for CLL patients
Polypharmacy[1-4] (eg, anticoagulants, antiplatelet agents)	• In a cohort of patients diagnosed with CLL 1997-2018, **93%** had a median number of 6 prescription medications within 1 year of CLL diagnosis[1] – In a study of patients treated with a cBTKi, **11%** and **34%** used a concomitant anticoagulant and antiplatelet agent, respectively[2]	• Polypharmacy is defined as concurrent use of multiple drugs (≥5) for 1 or more conditions[3,4] – Frequent in CLL population, even in patients without comorbidities[1] – Increases risk of DDIs, drug-food interactions, prescribing cascade, unnecessary treatment changes, and increased healthcare costs[1,3,4]
Renal function[5]	• **7.5%** of patients with CLL at diagnosis have impaired renal function	• Kidney disease in patients with CLL can result from acute kidney injury, glomerular disease, renal infiltration/obstruction, and TLS – May affect treatment strategies and clinical trial eligibility/outcomes • Reduced renal function is a risk factor for development of TLS with BCL-2i treatment
Hematologic conditions (disease or autoimmune related)[6-8]	• AICs affect **4%-7%** of patients with CLL, mainly consisting of AIHA and ITP[6,7] – AIHA occurs in **5%-10%** of patients with CLL – ITP presents in **2%-5%** of patients with CLL	• In patients with CLL, AICs can be preexisting or treatment emergent[6,7] – Treatment with targeted therapies may induce/exacerbate AIC[6,8] – Newer studies suggest treatment-emergent AICs may be associated with high-risk CLL[8]
CV comorbidity (eg, hypertension, AF)[9-11]	• Up to **37%** of patients with CLL have CV disease at diagnosis and treatment initiation[9-11] – **6%** of patients with CLL had prior history of AF; hypertension was associated with risk of incident AF[12-14]	• As CLL mainly affects older adults, there's a high prevalence of CV disease in this group compared with younger adults[9] • Treatment with BTKis may further elevate the risk of CV events, specifically in patients with pre-existing CV comorbidities[9,12]

AF, atrial fibrillation; AIC, autoimmune cytopenia; AIHA, autoimmune hemolytic anemia; BCL-2i, B-cell leukemia/lymphoma-2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; cBTKi, covalent Bruton's tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; CV, cardiovascular; DDI, drug-drug interaction; ITP, immune thrombocytopenia; TLS, tumor lysis syndrome.

1. Rotbain EC, et al. *Clin Epidemiol.* 2021;13:1155-1165. 2. Jones JA, et al. *Br J Haematol.* 2017;178(2):286-291. 3. Hoel RW, et al. *Mayo Clin Proc.* 2021;96(1):242-256. 4. Lymphoma Research Foundation. Accessed July 1, 2025. https://lymphoma.org/wp-content/uploads/2018/03/6609-LRF-Oral-Therapies-White-Paper-Final2-Web-03_14.pdf 5. Wanchoo R, et al. *Clin Kidney J.* 2018;11(5):670-680. 6. Vitale C, et al. *Cancers (Basel).* 2020;12(2):282. 7. Moreno C. *Blood.* 2021;137(25):3464-3465. 8. Vitale C, et al. *Blood.* 2021;137(25):3507-3517. 9. Molica S, et al. *Cancers (Basel).* 2025;17(1):119. 10. Fernandez Turizo MJ, et al. *Oncologist.* 2025;30(2). 11. Larsson K, et al. *Br J Haematol.* 2020;190(4):e245-e248. 12. Galitzia A, et al. *Cancers (Basel).* 2024;16(11):1996. 13. Shanafelt TD, et al. *Leuk Lymphoma.* 2017;58(7):1630-1639. 14. Dzeshka MS, et al. *Am J Hypertens.* 2017;30(8):733-755.

Overview of Common Comorbidities and Concomitant Conditions in CLL (cont'd)

Concomitant condition/comorbidity	Proportion of patients affected	Manifestation and considerations for CLL patients
 **Recurrent infection[1-3] (eg, pneumonia and URTI)**	• **26%** of patients have a 5-year risk of severe infections in CLL[1]	• Patients with CLL have a compromised immune system, leading to increased susceptibility to infection, and CLL treatment can further compromise immune function and increase the risk of infection[2,3]
 **Hepatic function[4]**	• **3.5%** of patients with CLL at diagnosis present with abnormal liver function[4]	• Liver disorders can result from liver infiltration by leukemic cells, immunologic manifestations associated with CLL, primary and secondary hepatic malignancies, drug-induced hepatotoxicity, infections, and Richter transformation[5] • Patients with CLL with abnormal liver function were more likely to have advanced Rai stage, and lower hemoglobin and platelet counts compared with those with normal liver tests[4] • Abnormal liver function in patients in patients with CLL was associated with shorter OS compared with those with normal liver function[4]
 **Diabetes[6]**	• **8%-24%** of newly diagnosed patients with CLL have comorbid diabetes[6,7]	• 82% of patients with CLL with diabetes received ≥6 prescription drugs[6] • In general, studies in other cancers suggest that cancer treatment and symptoms can have a negative impact on diabetes self-management[8]

CLL, chronic lymphocytic leukemia; OS, overall survival; URTI, upper respiratory tract infections.

1. Grywalska E, et al. Cells. 2020;9(11):2398. 2. Rivera D, et al. *Curr Oncol Rep.* 2022;24(8):1003-1014. 3. Molica S, et al. *Cancers (Basel).* 2025;17(1):119. 4. Hampel PJ, et al. *Am J Hematol.* 2017;92(12):1362-1369. 5. Kreiniz N, et al. *Clin Lymphoma Myeloma Leuk.* 2017;17(12):863-869. 6. Rotbain EC, et al. *Clin Epidemiol.* 2021;13:1155-1165. 7. Vainer N, et al. *Expert Rev Hematol.* 2024;17(9):617-629. 8. Hershey DS, et al. *Diabetes Educ.* 2012;38(6):779-790.

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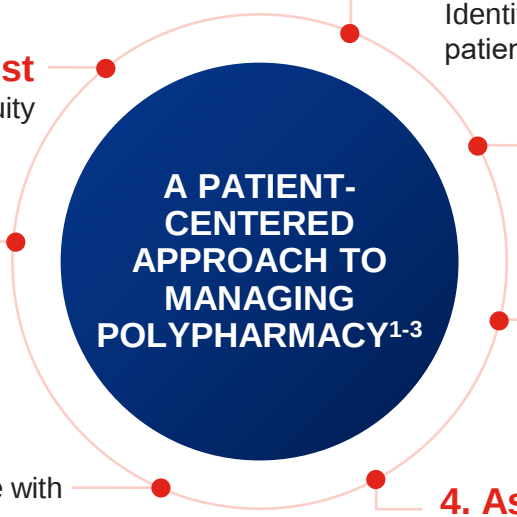
Best Practices for Managing Comorbidities/ Concomitant Conditions in Patients With CLL

Optimal Management of Polypharmacy Needs to Be Individualized for Each Patient[1]



1. Assess patient's needs
Identify drugs related to problem and establish patient's perspectives and priorities

2. Define context and goals
Find out how medicines used fit with/impact patient's overall health goals and functionality

3. Identify problematic medicines
Identify inappropriate medicines from their list of medications (eg, DDI)

4. Assess risks and benefits
Assess risks and benefits in the patient context and discuss with patient to confirm based on their individual and clinical priorities

5. Agree to actions Agree with the patient and the prescriber to interrupt, reduce dose, discontinue, or start alternative medication. Evaluate if treatment change/referral is needed

6. Communicate
Inform relevant parties to facilitate implementation (community pharmacist, social care, HCP, care home staff, etc)

7. Monitor, review and adjust
Reassess regularly to ensure continuity of care

Tips for tracking multiple medications[4]

- Access and monitor electronic medical records
- Assign 1 team member to monitor all medications and supplements
- Use mobile drug tracking apps for patients

SDM is essential for polypharmacy management by empowering patients with knowledge about their medications and potential adverse events so they can take an active role in managing their health[2,5]

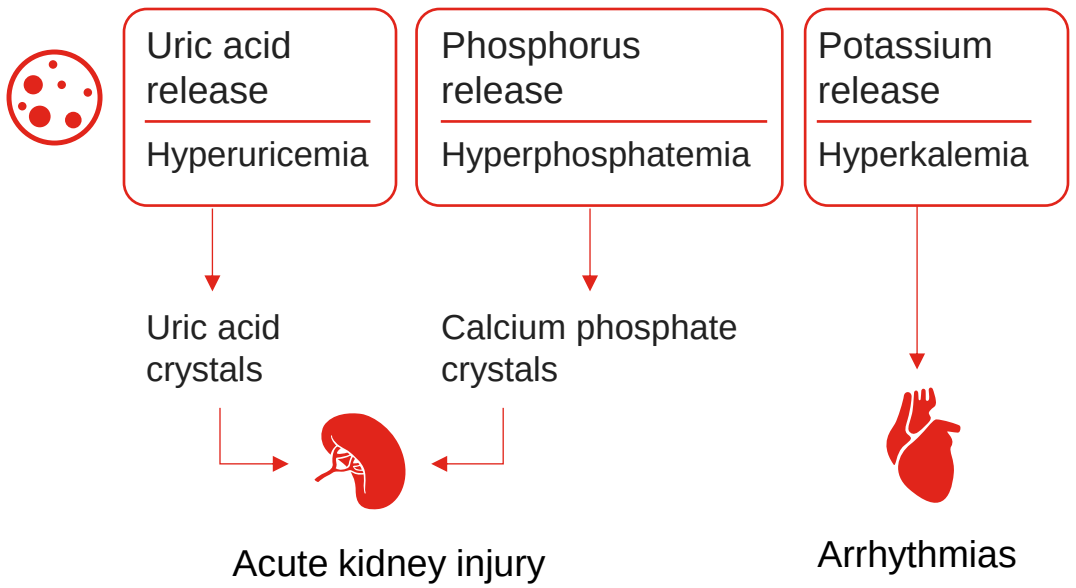
DDI, drug-drug interaction; HCP, healthcare provider; SDM, shared decision making.

1. Barnett NL, et al. *Eur J Hosp Pharm.* 2016;23(2):113-117. 2. Skaikh A. The Pharmaceutical Journal. Accessed July 1, 2025. https://pharmaceutical-journal.com/article/ld/managing-and-reducing-polypharmacy-when-prescribing 3. Hoel RW, et al. *Mayo Clin Proc.* 2021;96(1):242-256. 4. Lymphoma Research Foundation. Accessed July 1, 2025. https://lymphoma.org/wp-content/uploads/2018/03/6609-LRF-Oral-Therapies-White-Paper-Final2-Web-03_14.pdf 5. Soumerai JD, et al. *Blood Adv.* 2025;9(5):1213-1229.

Careful Observation of Kidney Health Is Crucial to Optimize CLL Outcomes

- Renal insufficiency* developed in up to 24% of patients with CLL at follow-up and was associated with advanced disease, unfavorable prognostic factors (eg, unmutated *IGHV*, del[17p] and del[11q]) and shorter OS[1]
  - Because patients rarely undergo a kidney biopsy, there is limited understanding in the prophylaxis and management of CLL-associated renal insufficiencies[2]
- Kidney dysfunction can increase the risk of TLS[3]
  - TLS is a life-threatening oncologic emergency, with incidence of 3%-6% in patients with CLL receiving BCL-2i therapy[2,4]
  - TLS prophylaxis includes adequate hydration and slow ramping up of BCL-2i for all risk groups, antihyperuricemic medication, and intensive clinical monitoring for moderate- and high-risk groups[2,†]

Clinical presentation of TLS[2]



Multidisciplinary collaboration, including nephrologists and hematologists, is critical to managing patients with CLL and renal involvement[2,5]

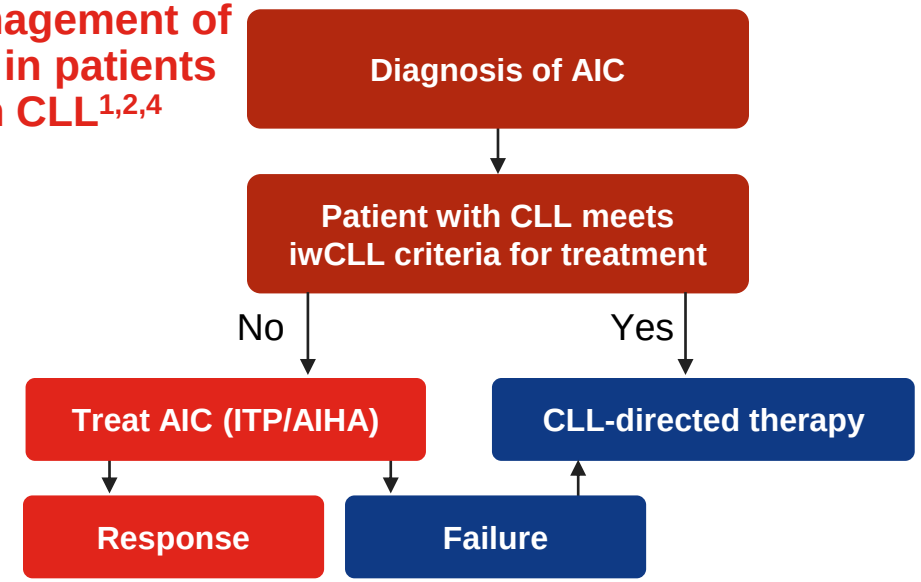
*Renal insufficiency was defined as creatinine clearance ≤45 mL/min. †TLS is not common with BTKi treatment.

BCL-2i, B-cell lymphoma-2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; del, deletion; *IGHV*, immunoglobulin heavy chain variable region gene; OS, overall survival; TLS, tumor lysis syndrome.

1. Strati P, et al. *Haematologica.* 2017;102(1):e22-e25. 2. Wanchoo R, et al. *Clin Kidney J.* 2018;11(5):670-680. 3. Soumerai JD, et al. *Blood Adv.* 2025;9(5):1213-1229. 4. Valtis YK, et al. *Blood Adv.* 2024;8(22):5806-5813. 5. Bender ST, et al. *Front Med (Lausanne).* 2023;10:1279005.

Careful Assessment of Hematologic Conditions in Patients With CLL Helps to Determine the Management Plan[1]

Management of AIC in patients with CLL[1,2,4]



Management considerations

- Initial treatment of AIHA or ITP includes steroids with or without anti-CD20 mAb and/or immunosuppressive agents[1,3,4]
- Second-line treatment options for AIHA include anti-CD20 mAb, splenectomy, IV immunoglobulins, and/or immunosuppressive therapy[1,3]
  - Some patients with ITP not responding to glucocorticoids may benefit from anti-CD20 mAb, immunosuppressive agents, or thrombopoietin analogs[1,3]
- When AIC-directed treatment is not sufficient, CLL-directed therapy is recommended[3,4]

In patients with significant cytopenia, a **bone marrow biopsy with aspirate** is useful to determine the direct **cause**, to distinguish between CLL-related causes (eg, marrow infiltration, splenic sequestration, AIHA, or ITP) vs other causes (eg, treatment-related)[5]

Management of AIC in patients with CLL should focus on the autoimmune phenomenon with CLL-directed therapy reserved for refractory cases or patients with disease progression[1-4]

AIC, autoimmune cytopenia; AIHA, autoimmune hemolytic anemia; CLL, chronic lymphocytic leukemia; ITP, immune thrombocytopenia; IV, intravenous; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; mAb, monoclonal antibody.

1. Gordon MJ, et al. *Am J Hematol.* 2022;97(Suppl 2):S26-S34. 2. Moreno C. *Blood.* 2021;137(25):3464-3465. 3. Hallek M, et al. *Blood.* 2018;131(25):2745-2760. 4. Vitale C, et al. *Cancers (Basel).* 2020;12(2):282. 5. Soumerai JD, et al. *Blood Adv.* 2025;9(5):1213-1229.

Management of CV Comorbidities in Patients With CLL Focuses on Screening, Prevention, and Monitoring[1]

- Hypertension is the leading CV risk factor for AF, and hypertension, CAD, and valvular heart disease independently increased the risk of incident AF during follow-up in patients with CLL[2,3]
- Targeting BP and optimizing its control is one of the major components of AF management and can include NOACs where appropriate[1,2]
  - The goal BP is <130/80 mm Hg to reduce the risks of hypertension-induced organ damage[1]
- Management of additional risk factors includes weight reduction, blood lipids and glucose control, sleep-disordered breathing management, and smoking and alcohol cessation[1,2]

Pretreatment workup should include comprehensive patient history, including BP assessment, ECG, concomitant medications, and assessment of CV risk (eg, diabetes, obesity, dyslipidemia, chronic renal disease, history of arrythmias, heart failure, etc)[4,5]

For more information on improving cardiac care in patients with CLL, please see medical.lilly.com

A multidisciplinary approach is optimal for concurrent management of cancer and CV disease and should include an oncologist, a cardio-oncologist, an onco-nephrologist, and a clinical pharmacist[1,4,5]

AF, atrial fibrillation; BP, blood pressure; CAD; coronary artery disease; CLL, chronic lymphocytic leukemia; CV, cardiovascular; ECG, electrocardiogram; NOAC, nonvitamin K antagonist oral anticoagulant.

1. Pandey S, et al. *Clin Kidney J.* 2023;16(12):2336-2348. 2. Dzeshka MS, et al. *Am J Hypertens.* 2017;30(8):733-755. 3. Shanafelt TD, et al. *Leuk Lymphoma.* 2017;58(7):1630-1639. 4. Awan FT, et al. *Blood Adv.* 2022;6(18):5516-5525. 5. Quartermaine C, et al. *JAAC CardioOncol.* 2023;5(5):570-590.

Vigilant Monitoring and Implementation of Prevention Strategies Are Important to Managing Infections in Patients With CLL[1]

- Because patients with CLL are more susceptible to infection, routine vaccinations are recommended, as reasonable rates of seroprotection and seroconversion are achieved in immunocompromised patients with cancer, with minimal adverse events[1,2]

Strategies for infection prevention in patients with CLL[1]

Bacterial infections

- No routine antibiotic prophylaxis
- Ig replacement therapy for severe hypogammaglobulinemia (<400 mg/dL) and/or recurrent or severe infection
- Monitor for high ANC

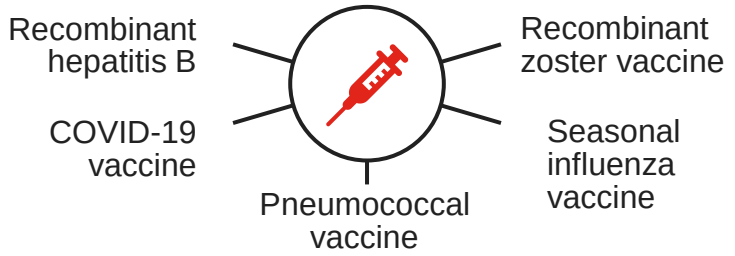
Fungal infections

- Consider prophylaxis in
  - Frail older patients with R/R CLL and/or prolonged neutropenia
  - Those with previous fungal infections
  - Patients receiving chronic, concomitant steroids

Viral infections

- Monitor for infection/ pretreatment of HBV, HCV, HIV, HSV 1/2, VZV, and CMV prior to starting CLL therapy
- If HBV reactivation detected, administer preemptive therapy with antivirals

Recommended vaccinations for patients with CLL[1]*



Increased susceptibility to infection in patients with CLL necessitates timely prevention, recognition, and treatment[1]

*As indicated by clinical practice recommendations. Live vaccines are contraindicated in patients with CLL.[2]

ANC, absolute neutrophil count; CLL, chronic lymphocytic leukemia; CMV, cytomegalovirus; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HSV, herpes simplex virus; Ig, immunoglobulin; R/R; relapsed/refractory; VZV, varicella zoster virus.

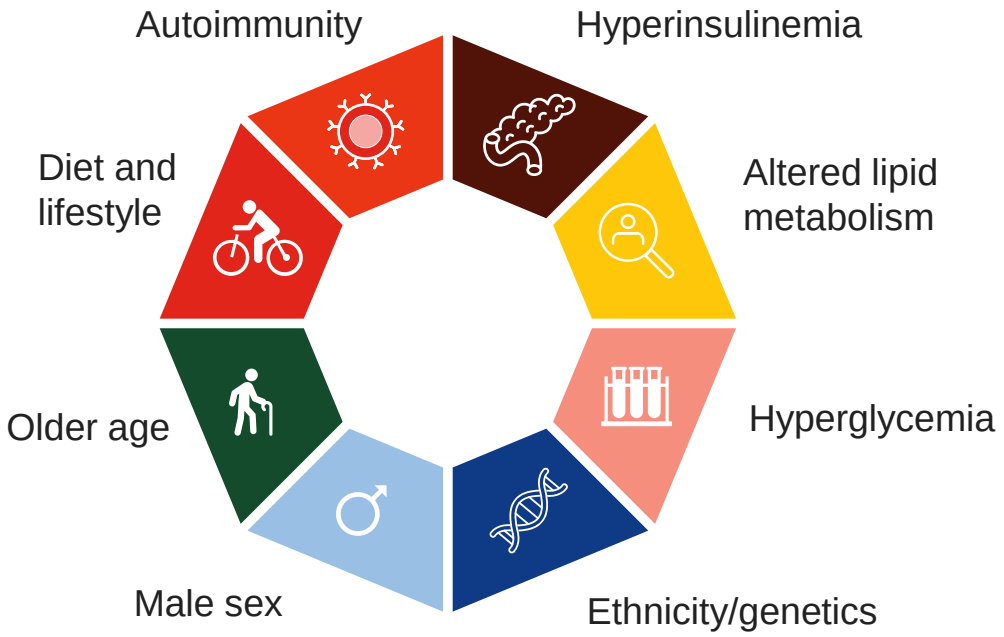
1. Rivera D, Ferrajoli A. *Curr Oncol Rep*. 2022;24(8):1003-1014. 2. Hallek M, et al. *Blood.* 2018;131(25):2745-2760.

An MDT Approach and Careful Monitoring of Infections Are Essential in Patients With CLL and Diabetes[1]

- Patients with CLL and T2D experienced poorer survival outcomes compared with patients with CLL without T2D[1,2]
  - The increased mortality was largely driven by increased risk of death due to infections
  - Patients with CLL and T2D were also less likely than patients without T2D to receive treatment for CLL
- Treatment of CLL with concomitant T2D should utilize an individualized approach that considers mortality, risk of late diabetic complications, and CLL disease severity[1]

Patients with CLL and T2D may benefit from individualized infection prophylaxis, vigilance for infections during ongoing treatment, and closer monitoring during instances of infection[1]

Common mechanism and risk factors for CLL and T2D[1]



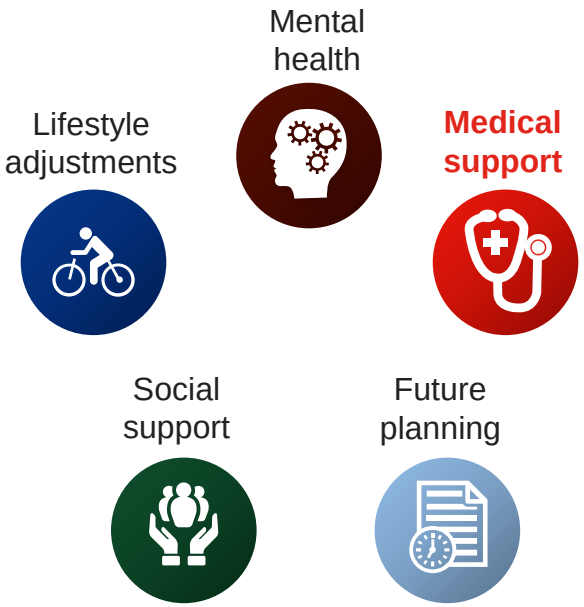
Patients with CLL and T2D often have additional comorbidities, and an MDT approach that involves multiple specialties is essential for optimal supportive care of co-occurring CLL and T2D[1]

CLL, chronic lymphocytic leukemia; MDT, multidisciplinary team; T2D, type 2 diabetes.

1. Vainer N, et al. *Expert Rev Hematol.* 2024;17(9):617-629. 2. Rotbain EC, et al. *Am J Hematol*. 2023;98(8):1236-1245.

Multidisciplinary and Holistic Approach to Survivorship Care Is Optimal for Patients With CLL and Comorbid Conditions[1]

Key domains for survivorship care



Medical support in CLL long-term care encompasses[1,2]

- Treatment management
- Secondary cancer screening and patient education
- Monitoring disease progression
- Managing frailty
- Control of modifiable CV risk factors and cardiac assessments for patients on BTKis
- Prevention and screening for bone disease
- Infection prevention

- As treatment strategies have improved survival rates in patients, CLL has been transformed into a chronic condition for the majority of patients[1]
- The number of survivors who are living with CLL is increasing and there is a growing need for a tailored, patient-centered approach to survivorship and ongoing care that combines patient education, surveillance, prevention, early intervention, and MDT care coordination[1,2]
- With increased life expectancy, long-term CLL survivors face new challenges, including risk of infections, bone disease, CV complications, and secondary malignancies[1,2]
  - Many of these conditions and their risk factors can be identified with routine screening and are potentially preventable[2]

Long-term care for patients with CLL requires an MDT approach that integrates CLL treatment with the proactive management of frailty, comorbidities, and psychosocial well-being to enhance both survival and quality of life[1]

BTKi, Bruton's tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; CV, cardiovascular; MDT, multidisciplinary team.

1. Molica S, et al. *Cancers (Basel).* 2025;17(1):119. 2. Fedele PL, et al. *J Clin Oncol*. 2024;42(17):2005-2011.

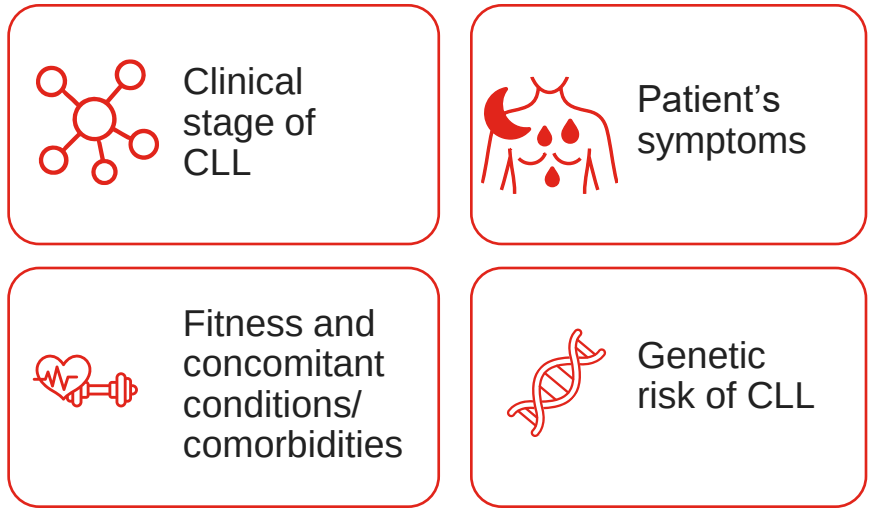
3

Considerations for Patients With CLL in the Presence of Comorbidities and Concomitant Conditions

Selecting Treatment for Patients With CLL Based on Their Comorbidities/Concomitant Conditions

- In an era of targeted therapies, concomitant disease and patient preference are important factors in CLL treatment selection[1]
- As treatment with these agents is associated with specific AEs, preexisting conditions (eg, cardiomyopathies, arrhythmia, renal failure), patient preference (continuous vs fixed-duration therapy), and comedication (eg, CYP inhibitors, anticoagulants) need to be discussed during the SDM process[1-3]
  - A detailed patient assessment at the pretreatment evaluation should be done to select a patient-tailored therapy avoiding predictable complications based on the toxicity profile of each of the available drugs[3,4]
- Additional important factors when selecting appropriate therapy include[5]
  - Drug-specific toxicity profile
  - Patient compliance to treatment
  - Goal of therapy

Parameters to be considered before recommending treatment for CLL[1]



A holistic approach to patient care involving the multidisciplinary team that considers the patient's comorbidities and other medications is necessary for optimal management and assurance that potential AEs are not being interpreted as a new medical condition[3,6]

AE, adverse event; CLL, chronic lymphocytic leukemia; CYP, Cytochrome P450; SDM, shared decision making.

1. Hallek M. *Hematol Oncol.* 2023;41(Suppl 1):129-135. 2. Hallek M, et al. *Am J Hematol.* 2021;96(12):1679-1705. 3. Soumerai JD, et al. *Blood Adv.* 2025;9(5):1213-1229. 4. Galitzia A, et al. *Cancers (Basel).* 2024;16(11):1996. 5. Fresa A, et al. *J Clin Med.* 2021;10(21):5104. 6. Lymphoma Research Foundation. Accessed July 1, 2025. https://lymphoma.org/wp-content/uploads/2018/03/6609-LRF-Oral-Therapies-White-Paper-Final2-Web-03_14.pdf

Considerations for Treatment Selection for Patients With CLL Based on Comorbidities and Concomitant Conditions

Concomitant condition/comorbidity	Considerations for CLL treatment selection
Polypharmacy (eg, anticoagulants, antiplatelet agents)[1,2]	**Non-warfarin anticoagulant and/or single antiplatelet therapy[1]** • Clarify the indication for anticoagulation/antiplatelet therapy and whether its continued use is needed • BCL-2i–based therapy or a more selective BTKi may be a preferred option **Warfarin anticoagulant[1]** • If considering BTKi, use of an alternative anticoagulant may be preferable **Dual antiplatelet therapy[1,2]** • BCL-2i–based therapy recommended over BTKi, although more selective BTKi may still be an option
Renal function[3]	• For treatment with BCL-2i, use a dose ramp-up protocol with TLS prophylaxis and monitoring[3] – For high-risk patients with tumor burden and reduced renal function (creatinine clearance <80 cc/min), the initial doses of BCL-2i should be administered in the hospital with close monitoring, early prophylaxis and aggressive IV fluids[3] – Early nephrology consultation is recommended for patients with moderate to severe risk of TLS[3]
Hematologic conditions (disease or autoimmune related)[4,5]	• Cytopenia can result from treatment, including BTKis or BCL-2i[4,5] • Growth factor support for cytopenia resulting from treatment is recommended[5] • Treatment-emergent flare of AIC can be managed with short-course corticosteroids or anti-CD20 monoclonal antibody treatment, and most patients can continue BTKi therapy[6] • Dose modifications or interruptions are recommended in patients with severe cytopenia treated with BTKis[5]
CV comorbidity (eg, hypertension, AF)[1,5,6] For more information on improving cardiac care in patients with CLL, please see medical.lilly.com	**Hypertension** • Optimize pharmacotherapy for control of baseline hypertension before treatment initiation[6] • BTKis can be appropriate for patients with well-managed CV risk[7] • More selective BTKi may be an option for patients with uncontrolled or difficult-to-manage hypertension[1] **AF history** • More selective BTKis can be appropriate with multidisciplinary team involvement[1,7] • For patients with persistent or paroxysmal AF, a more selective BTKi can be considered, although this can occasionally precipitate recurrent AF[1]

AF, atrial fibrillation; AIC, autoimmune cytopenia; BCL-2i, B-cell leukemia/lymphoma-2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; CV, cardiovascular; TLS, tumor lysis syndrome.

1. Soumerai JD, et al. *Blood Adv.* 2025;9(5):1213-1229. 2. Shah NN, et al. *Haematologica*. 2025;110(1):92-102. 3. Wanchoo R, et al. *Clin Kidney J.* 2018;11(5):670-680. 4. Hallek M, et al. *Blood.* 2018;131(25):2745-2760. 5. Galitzia A, et al. *Cancers (Basel).* 2024;16(11):1996. 6. Lipsky A, et al. *Hematology Am Soc Hematol Educ Program.* 2020(1):336-345. 7. Awan FT, et al. *Blood Adv.* 2022;6(18):5516-5525.

Considerations for Treatment Selection for Patients With CLL Based on Comorbidities and Concomitant Conditions (cont'd)

Concomitant condition/comorbidity	Considerations for CLL treatment selection
 **Recurrent infection (eg, pneumonia and URTI)[1-4]**	• Routine management of CLL may increase susceptibility to infection in patients with CLL[1] • Routine vaccinations are recommended before initiation of treatment if possible[2] • Prophylactic measures vary for targeted therapies; IgG replacement therapy can be considered in all treated patients with a history of severe infections and severe hypogammaglobulinemia (IgG level of <4 g/L)[3] • PJP prophylaxis can be considered for patients treated with BTKis and anti-CD20 mAbs[3] • Before treatment initiation, patients should be screened for HBV and HCV due to potential of reactivation following treatment with immunosuppressive therapies (eg, anti-CD20 mAbs, cellular therapy)[2,4]
 **Hepatic function[3,5-9]**	• In patients with CLL, abnormal hepatic enzymes have significant prognostic implications and are associated with more advanced Rai staging requiring earlier treatment initiation and shorter OS compared with those with normal liver tests[5,6] • Many CLL therapies have been associated with hepatotoxicity[3,7-9] – The specific PI can be referenced for possible dose adjustments or cautions in patients with severe hepatic impairment
 **Diabetes[3,10]**	• BTKis are metabolized by cytochrome P450 similar to some antidiabetic drugs. Concomitant treatment with 1 or several of these drugs may thus induce hypoglycemic events, particularly if an individual is further treated with other cytochrome P450–metabolized drugs[3,10] • Considerations of the presence of diabetes and other CV risk factors are essential when selecting treatment, particularly between different BTKis[10]

BTKi, Bruton's tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; CV, cardiovascular; HBV, hepatitis B virus; HCV, hepatitis C virus; IgG, immunoglobulin G; mAb, monoclonal antibody; OS, overall survival; PI, prescribing information; PJP, *Pneumocystis jirovecii* pneumonia; URTI, URTI, upper respiratory tract infections.

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4 Key Takeaways

Key Takeaways

Comorbidities are prevalent in patients with CLL and contribute to inferior outcomes, including reduced treatment tolerance and survival.[1-5]

Assessment and management of comorbidities/concomitant conditions in patients with CLL necessitate a holistic approach with a multidisciplinary team; this approach is optimal for management of comorbidities and polypharmacy to ensure AEs are not being interpreted as a new medical condition.[6-8]

As CLL is a chronic condition for most patients, long-term care should integrate CLL treatment with proactive management of frailty, comorbidities, and psychosocial well-being to enhance both survival and quality of life.[8,9]

Comorbidities and concomitant conditions can influence treatment selection; thus, their optimal management must be considered as part of the treatment decision-making process in CLL.[6,10,11]

AE, adverse event; CLL, chronic lymphocytic leukemia.

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