

Current Treatment Algorithm for CLL and Clinical Trial Spotlight: A Resource for Clinicians

Overview

- Chronic lymphocytic leukemia (CLL) is the most common leukemia in adults accounting for approximately 25% of all new cases of leukemia^[1]
- CLL is risk stratified based on staging and adverse or favorable prognostic factors
 - Rai staging system divides CLL into low-risk (stage 0), intermediate-risk (stage I/II), and high-risk (stage III/IV) diseases
 - Favorable prognostic factors include wild-type *TP53*, mutated *IGHV*, and del(13q)
 - Unfavorable prognostic factors include mutated *TP53*, unmutated *IGHV*, del(11q), and del(17p)
- Asymptomatic early-stage disease can be closely monitored without active treatment
- For patients with CLL requiring treatment, current options include targeted therapies inhibiting BTK, BCL-2, or PI3K and chemoimmunotherapy for select patients
- Ongoing phase III clinical trials are investigating novel agents and combination therapy regimens in both newly diagnosed and previously treated CLL
- This resource focuses on the current treatment algorithm and key ongoing phase III clinical trials in CLL as of December 2020

Table 1. iwCLL 2018 Indications for Treatment^[2]

At least 1 of the following criteria should be met
Progressive marrow failure as evidenced by development or worsening of anemia (hemoglobin < 10 g/dL) or thrombocytopenia (platelet count < 100,000/μL)
Massive or progressive or symptomatic splenomegaly
Massive lymph nodes (ie, ≥ 10 cm in longest diameter) or progressive or symptomatic lymphadenopathy
Progressive lymphocytosis as defined by an increase of $\geq 50\%$ during a 2-month period or a lymphocyte doubling time of < 6 months. Factors contributing to lymphocytosis other than CLL (eg, infection, steroid use) should be excluded
Autoimmune complications including anemia or thrombocytopenia poorly responsive to corticosteroids
Symptomatic or functional extranodal involvement (eg, skin, kidney, lung, spine)
- Disease-related symptoms as defined by any of the following: - Unintentional weight loss $\geq 10\%$ within the previous 6 months - Significant fatigue (ie, ECOG performance status ≥ 2) - Fever $\geq 100.5^{\circ}\text{F}$ or 38.0°C for ≥ 2 weeks without evidence of infection - Night sweats for ≥ 1 month without evidence of infection

iwCLL, International Workshop on Chronic Lymphocytic Leukemia.

Figure 1. Treatment algorithm for CLL without del(17p) or *TP53* mutation (December 2020).^[3]

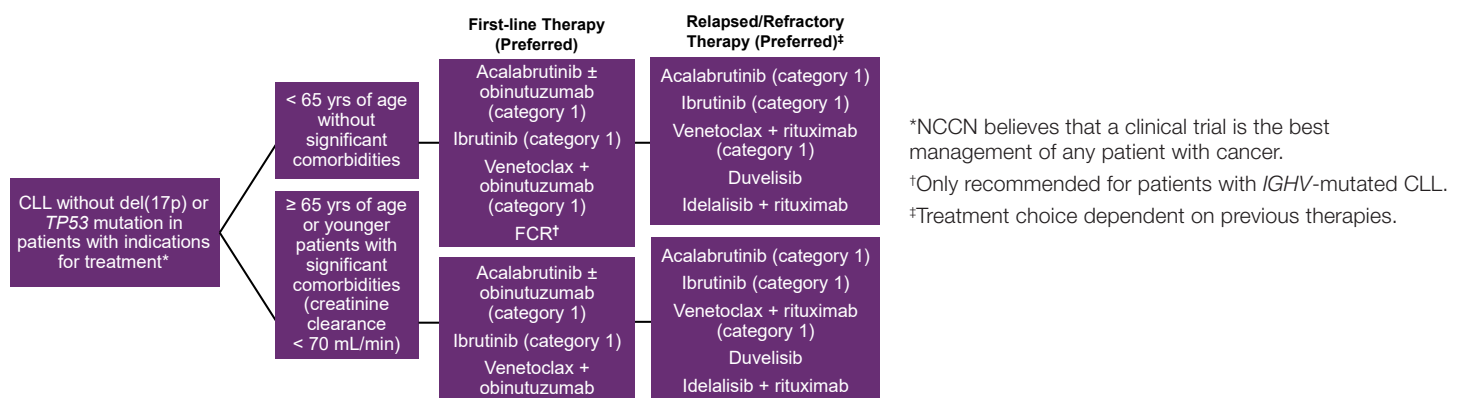
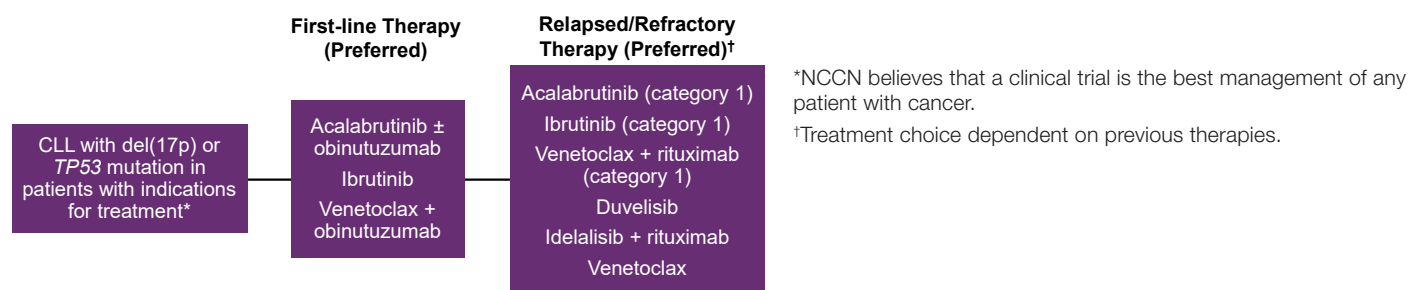


Figure 2. Treatment algorithm for CLL with del(17p) or TP53 mutation (December 2020).^[3]



Get expert guidance using an Interactive Decision Support Tool on:

- Selecting treatments for patients with CLL (available at: www.clinicaloptions.com/CLLtool)
- Assessing and managing adverse events associated with BTK inhibitors (available at: www.clinicaloptions.com/BTKtool)

Table 2. Select Ongoing Phase III Clinical Trials in Newly Diagnosed CLL^[4]

Trial	Population	Actual/ Planned N	Status	Treatment Arms
UNITY-CLL* (NCT02612311)	All patients	600	Fully accrued	Ublituximab + umbralisib vs ublituximab vs umbralisib vs obinutuzumab + chlorambucil
GAIA/CLL13 (NCT02950051)	Fit patients	920	Fully accrued	Venetoclax + rituximab vs venetoclax + obinutuzumab vs venetoclax + obinutuzumab + ibrutinib vs chemoimmunotherapy
GLOW (NCT03462719)	≥ 65 yrs of age or unfit patients	211	Fully accrued	Ibrutinib + venetoclax vs obinutuzumab + chlorambucil
SEQUOIA (NCT03336333)	All patients	680	Recruiting patients [†]	Cohort 1: zanubrutinib vs BR (no del[17p]); cohort 2: zanubrutinib (del[17p]); cohort 3: zanubrutinib + venetoclax (del[17p])
ACE-CL-311 (NCT03836261)	All patients	780	Recruiting patients [†]	Acalabrutinib + venetoclax vs acalabrutinib + venetoclax + obinutuzumab vs chemoimmunotherapy
CRISTALLO (NCT04285567)	Fit patients	165	Recruiting patients [†]	Venetoclax + obinutuzumab vs chemoimmunotherapy
EA9161 (NCT03701282)	Fit patients, 18-69 yrs of age	720	Recruiting patients [†]	Ibrutinib + obinutuzumab vs ibrutinib + obinutuzumab + venetoclax
A041702 (NCT03737981)	Older patients, ≥ 70 yrs of age	454	Recruiting patients [†]	Ibrutinib + obinutuzumab vs ibrutinib + obinutuzumab + venetoclax
CLL17 (NCT04608318)	All patients	897	Not yet recruiting	Ibrutinib vs obinutuzumab + venetoclax vs ibrutinib + venetoclax

*Met primary endpoint of improved PFS at interim analysis according to a press release in May 2020; data to be presented at ASH 2020.

[†]Enrolling patients as of December 2020.

Table 3. Select Ongoing Phase III Clinical Trials in Previously Treated CLL^[4]

Trial	Population	Actual/ Planned N	Status	Treatment Arms
UNITY-CLL* (NCT02612311)	All patients	600	Fully accrued	Ublituximab + umbralisib vs ublituximab vs umbralisib vs obinutuzumab + chlorambucil
ELEVATE-RR (NCT02477696)	High-risk patients	533	Fully accrued	Acalabrutinib vs ibrutinib
UTX-IB-301 (NCT02301156)	High-risk patients	120	Fully accrued	Ublituximab + ibrutinib vs ibrutinib
ALPINE (NCT03734016)	All patients	400	Recruiting patients [†]	Zanubrutinib vs ibrutinib

*Met primary endpoint of improved PFS at interim analysis according to a press release in May 2020; data to be presented at ASH 2020.

[†]Enrolling patients as of December 2020.

References

1. American Cancer Society. Chronic lymphocytic leukemia. 2. Hallek. Blood. 2018;131:2745. 3. NCCN Clinical Practice Guidelines in Oncology for CLL/SLL. V2.2021. 4. ClinicalTrials.gov.