PRACTICE AID

Assessing CLL Progression: iwCLL Criteria and NCCN Guidelines[1,2]

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CLL SOCIETY

iwCLL: Any of These Criteria Should Be Met to Initiate CLL Therapy[1]

- ❑ Progressive marrow failure, Hb <10 g/dL, or PLT <100 × 10^9/L
- ❑ Massive (≥6 cm below left costal margin) or progressive or symptomatic splenomegaly
- ❑ Massive (≥10 cm in longest diameter) or progressive or symptomatic lymphadenopathy
- ❑ Progressive lymphocytosis + increase of ≥50% over a 2-month period or lymphocyte doubling time of <6 months
- ❑ Autoimmune complications of CLL that are poorly responsive to corticosteroids
- ❑ Symptomatic extranodal involvement (eg, skin, kidney, lung, and spine)
- ❑ Disease-related symptoms (classic B symptoms: fever, night sweats, and weight loss)

NCCN Resistance Testing Guidelines[2]

- **Testing for *BTK* mutations may be helpful to confirm resistance to BTKi**
  - Low VAF is often associated with disease progression on ibrutinib, leading to speculation that these mutations do not fully explain clinical resistance
- **Testing for *BTK* or *BCL2* mutations as screening for resistance to BTKi or venetoclax is not currently recommended**
- **Testing for *BTK* and *PLCG2* mutations may be useful for patients with disease progression or who do not respond to BTKi therapy**
  - *BTK* and *PLCG2* mutation status alone is not an indication to change treatment

1. Hallek M et al. *Blood*. 2018;131:2745-2760. 2. NCCN Clinical Practice Guidelines in Oncology. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 3.2024. https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf.

PRACTICE AID

BTKi Dosing and Drug Interactions

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Coadministration With[1]

BTKi Dosing in CLL	Strong CYP3A4 Inhibitors	Moderate CYP3A4 Inhibitors	Moderate or Strong CYP3A4 Inducers	Gastric Acid–Reducing Agents
Ibrutinib 420 mg once daily	• Reduce to 140 mg once daily • For short-term use (≤7 d), interrupt ibrutinib	280 mg once daily	Avoid use	No dosage adjustment recommended
Acalabrutinib[2] 100 mg every 12 hours	Avoid use	100 mg once daily	Avoid use; if unavoidable, increase to 200 mg twice daily	No dosage adjustment recommended
Zanubrutinib 160 mg orally twice daily or 320 mg orally once daily	80 mg once daily	80 mg twice daily	Avoid use	No dosage adjustment recommended
Pirtobrutinib[3] 200 mg orally once daily	Avoid use; if unavoidable, reduce dose by 50 mg	–	Avoid use; if unavoidable, increase the dose to 300 mg if starting dose is 200 mg[a]	No dosage adjustment recommended

[a] If the current dosage is 50 mg or 100 mg once daily, increase the dose by 50 mg.

1. Weis TM et al. *J Oncol Pharm Pract*. 2022;28:1411-1433. 2. Sharma S et al. ASH 2021. Abstract 4365. 3. Jaypirca (pirtobrutinib) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216059Orig1s000Corrected_lbl.pdf.