



Oncology Clinical Pathways

Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)

December 2022 – V1.2022



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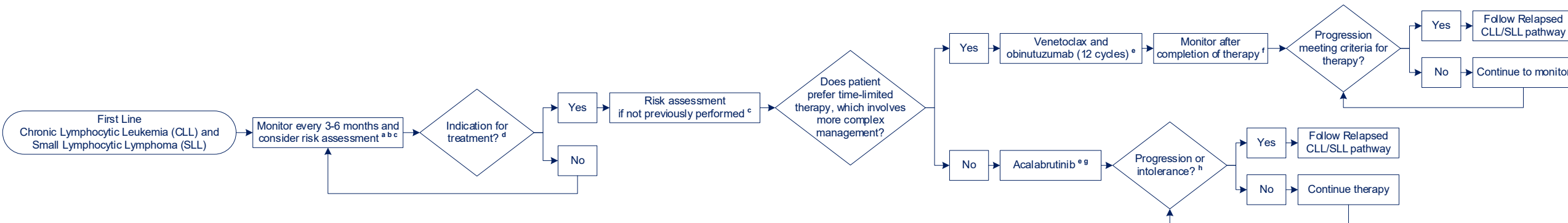
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CLL and SLL – First Line



Clinical trial(s) always considered on pathway.

^a **General Supportive Care for CLL/SLL** includes IVIG for hypogammaglobulinemia and frequent infections, vaccinations (e.g. COVID, influenza, pneumococcus, and varicella-zoster virus); do not administer live attenuated vaccines; screen for secondary malignancies, particularly non-melanoma skin cancers

^b **Monitor** consider hepatitis B and C and HIV testing at baseline; monitoring frequency dependent on current symptoms, patient preference, rise of lymphocytes

^c **Risk Assessment** using CLL/SLL IPI score which includes CLL/SLL FISH panel, TP53 mutation status, serum beta-2-microglobulin, IGHV mutation status, Rai or Binet staging, and age; also consider checking FISH t(11;14) to rule out mantle cell lymphoma, and CpG-stimulated karyotype; CLL FISH panel should include probes for: 13q, 17p, 11q, and 12

^d **Indications for Treatment** include anemia (Hgb <10 g/dL) hemoglobin < 10 g/dL, platelets < 100,000/mm³, thrombocytopenia/anemia must be non-immune and not related to alternate causes, B-symptoms, and symptomatic adenopathy; consider cross-sectional imaging prior to initiation of therapy

^e **Supportive Care and Pre-Treatment Evaluation During Therapy Includes:** 1) Hepatitis B serologies if not already checked, particularly with anti-CD20 antibodies (rituximab, obinutuzumab, ofatumumab), 2) TLS risk stratification prior to Venetoclax initiation, with prevention strategies as recommended by manufacturer, 3) provide COVID prophylaxis dependent on availability, and 4) consider HSV/VZV prophylaxis

^f **Monitor** after completion of therapy for indication for therapy (footnote d); undetectable MRD by flow cytometry or targeted sequencing assay following venetoclax + obinutuzumab is associated with favorable prognosis

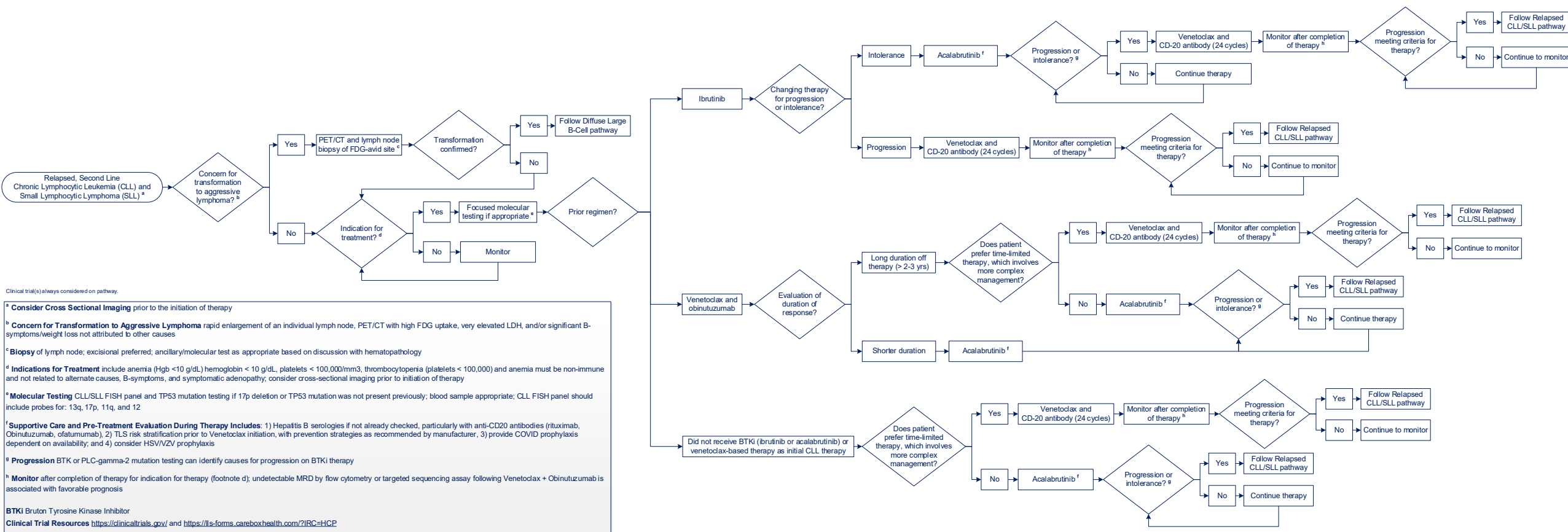
^g **BTK Inhibitor** avoid BTKi in severe hepatic impairment

^h **Progression** BTK or PLC-gamma-2 mutation testing can identify causes for progression on BTKi therapy but is not recommended

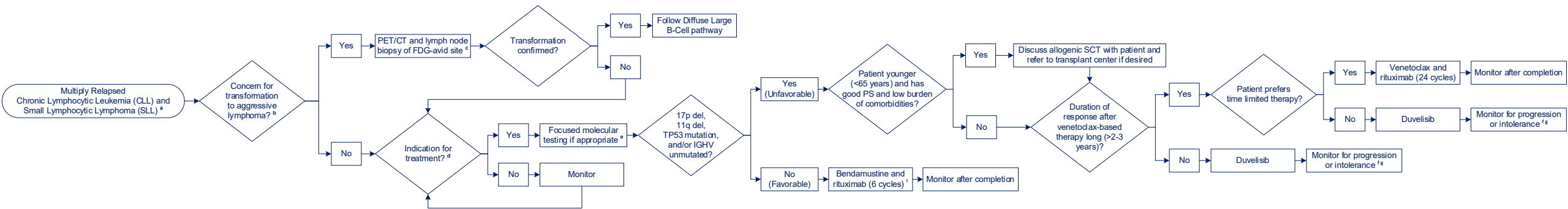
BTKi Bruton Tyrosine Kinase Inhibitor

Clinical Trial Resources <https://clinicaltrials.gov/> and <https://lts-forms.careboxhealth.com/?IRC=HCP>

CLL and SLL – Relapsed Second Line



CLL and SLL – Multiply Relapsed



Clinical trial(s) always considered on pathway.

^a **Relapsed** defined as previously treated with both BTKi and venetoclax-based therapy

^b **Concern for Transformation to Aggressive Lymphoma** rapid enlargement of an individual lymph node, PET/CT with high FDG uptake, very elevated LDH, and/or significant B- symptoms/weight loss not attributed to other causes

^c **Biopsy of Lymph Node** excisional preferred; ancillary/molecular test as appropriate based on discussion with hematopathology

^d **Indications** include anemia (Hgb <10 g/dL hemoglobin < 10 g/dL, platelets < 100,000/mm³, thrombocytopenia (platelets < 100,000) and anemia must be non-immune and not related to alternate causes, B-symptoms, and and painful-symptomatic adenopathy; consider cross-sectional imaging prior to initiation of therapy

^e **Molecular Testing** IGHV mutation status and CLL/SLL FISH panel and TP53 mutation testing if 17p deletion or TP53 mutation was not present previously; blood sample appropriate; CLL FISH panel should include probes for: 13q, 17p, 11q, and 12

^f **Supportive Care and Pre-Treatment Evaluation During Therapy Includes:** 1) Hepatitis B serologies if not already checked, particularly with CD20 antibodies (rituximab, Obinutuzumab, ofatumumab), 2) TLS risk stratification prior to Venetoclax initiation, with prevention strategies as recommended by manufacturer, 3) provide COVID prophylaxis dependent on availability, and 4) consider HSV/VZV prophylaxis

^g **PI3K Inhibitor Therapy** monitor for inflammatory adverse events (pneumonitis, hepatitis, colitis, rash); use anti-infective prophylaxis (i.e., VZV and PJP); the absolute benefit of PI3K inhibitors are conflicted

BTKi Bruton Tyrosine Kinase Inhibitor

Clinical Trial Resources <https://clinicaltrials.gov/> and <https://ils-forms.careboxhealth.com/?IRC=HCP>

Questions?

Contact VHAOncologyPathways@va.gov



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