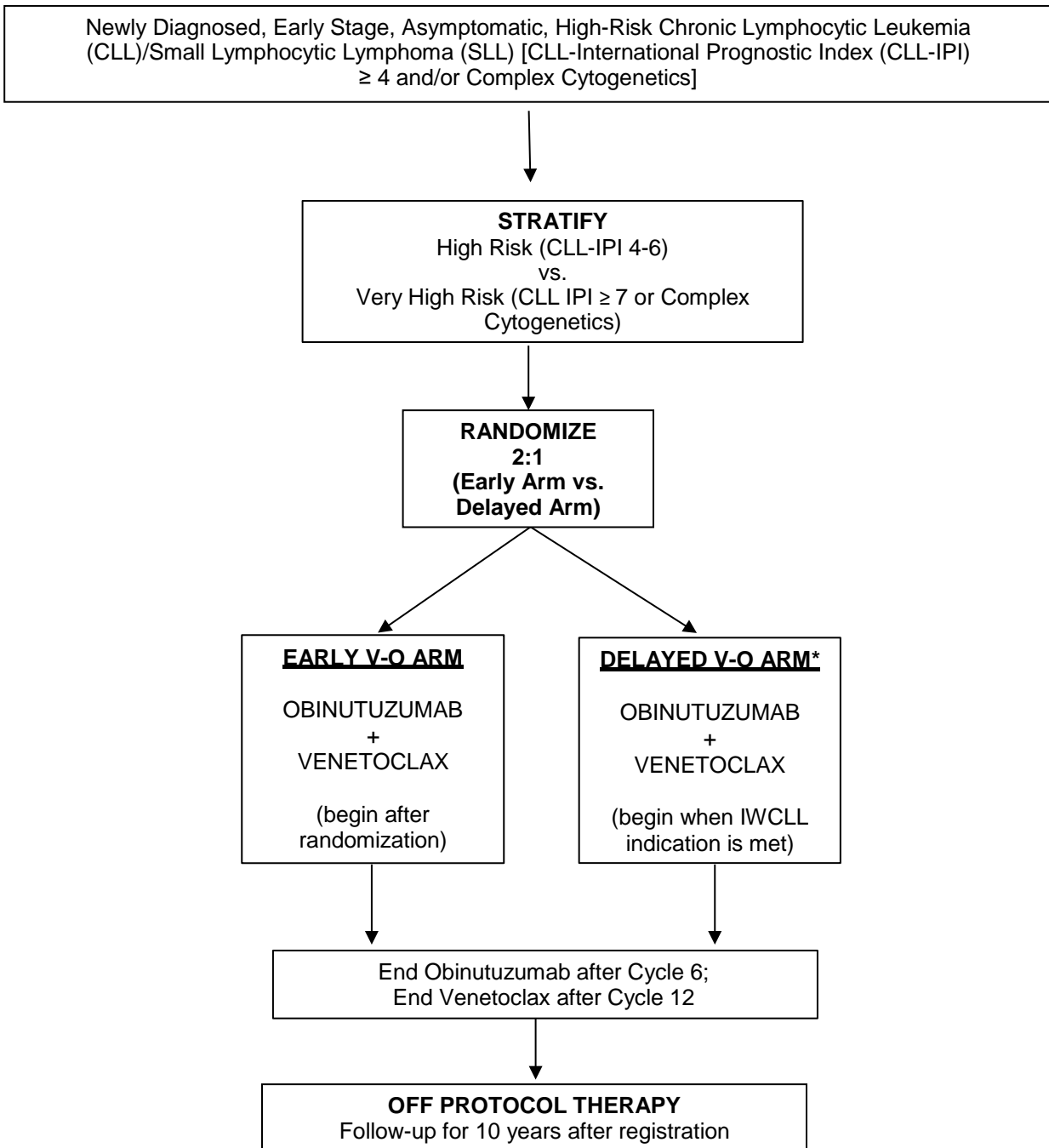


**SCHEMA**



\* Treatment will be initiated once 2018 International Workshop on Chronic Lymphocytic Leukemia (IWCLL, See [Section 4.4](#)) indication is met.

## 5.0 ELIGIBILITY CRITERIA

Each of the criteria in the following section must be met in order for a patient to be considered eligible for registration in OPEN. [Section 5](#) may be printed and used by the site, but is not to be uploaded in RAVE (unless specially stated). For each criterion requiring test results and dates, please record this information on the Onstudy Form and submit via Medidata Rave® (see [Section 14.0](#)). Any potential eligibility issues should be addressed to the SWOG SDMC in Seattle at 206/652-2267 or [leukemiaquestion@crab.org](mailto:leukemiaquestion@crab.org) prior to registration.

**NCI policy does not allow for waiver of any eligibility criterion ([http://ctep.cancer.gov/protocolDevelopment/policies\\_deviations.htm](http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm)).**

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday 4 weeks later would be considered Day 28. This allows for efficient patient scheduling without exceeding the guidelines. **If Day 7 or 28 falls on a weekend or holiday, the limit may be extended to the next working day.**

### 5.1 Disease Related Criteria

- a. Participants must have a confirmed diagnosis of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) (collectively referred to as CLL throughout) according to the 2018 International Workshop on CLL (see [Section 4.0](#)). Participants must have been diagnosed within 12 months prior to registration.
- b. Participants must have CLL-International Prognostic Index (CLL-IPI) Score  $\geq 4$  (See Section 4.3) and/or complex cytogenetics (defined as 3+ chromosomal abnormalities).
- c. Cytogenetic and FISH analyses must be completed at the site's CLIA-approved laboratory within 12 months prior to registration. FISH panel should use probes to detect for abnormalities in chromosomes 13q, 12, 11q, and 17p.
- d. TP53 mutation status (if completed) must be obtained within 12 months prior to registration.
- e. IgVH mutational status must be obtained prior to registration (at any time prior to registration).
- f. Serum beta-2 microglobulin level must be obtained within 28 days prior to registration.
- g. Participants must not meet any of the IWCLL specified criteria for active CLL therapy (see [Section 4.4](#)).



## 5.2 Prior/Concurrent Therapy Criteria

- a. Treatment with high dose corticosteroids and/or intravenous immunoglobulin for autoimmune complications of CLL must be complete at least 4 weeks prior to enrollment.
- b. Palliative steroids must be at a dose of at most 20 mg/day of prednisone or equivalent corticosteroid at the time of registration.
- c. Prior therapy with anti CD20 monoclonal antibodies is not allowed.
- d. Participants must not have received or be currently receiving any prior CLL-directed therapy, including non-protocol-related therapy, anti-cancer immunotherapy, experimental therapy, or radiotherapy.
- e. Participants must not be receiving or planning to receive any other investigational agents before completing protocol therapy.

## 5.3 Clinical/Laboratory Criteria

- a. Participants must be  $\geq 18$  years of age.
- b. Participants must have ECOG Performance Status  $\leq 2$ .
- c. Participants must have adequate marrow function as evidenced by platelet count  $\geq 100,000/\text{mm}^3$  and absolute neutrophil count (ANC)  $\geq 1,000/\text{mm}^3$  within 28 days prior to registration.
- d. Participants must have adequate kidney function as evidenced by creatinine clearance  $\geq 30\text{mL}/\text{min}$  (by Cockcroft Gault) within 28 days prior to registration.  
  
Creatinine clearance =  $\frac{(140 - \text{age}) \times \text{wt (kg)} \times 0.85 \text{ (if female)}}{72 \times \text{creatinine (mg/dl)}}$
- e. Participants must have adequate liver function as evidenced by AST and ALT  $< 3.0 \times$  Upper Limit of Normal (ULN), and total bilirubin  $\leq 2.0 \times$  ULN (or  $5.0 \times$  ULN if the Participant has a history of Gilbert's disease), within 28 days prior to registration.
- f. Participants must be able to take oral medications.
- g. Human immunodeficiency virus (HIV)-infected participants on effective anti-retroviral therapy with undetectable viral load within 6 months prior to registration are eligible for this trial.
- h. Participants with history of malignancy are allowed providing the cancer has not required active treatment within 2 years prior to registration (hormonal therapy is permissible). The following exceptions are permissible: basal cell, squamous cell skin, or non-melanomatous skin cancer, in situ cervical cancer, superficial bladder cancer not treated with intravesical chemotherapy or BCG within 6 months, localized prostate cancer requiring no more than chronic hormonal therapy, or localized breast cancer requiring no more than chronic hormonal therapy.
- i. Participants must not have current, clinically significant gastrointestinal malabsorption, in the opinion of treating doctor.
- j. Participants must not have cirrhosis.



- k. Obinutuzumab has been associated with hepatitis reactivation. Participants must not have uncontrolled active infection with hepatitis B or C. Participants with latent hepatitis B infection must agree to take prophylaxis during and for 6 months following active protocol therapy with V-O.

Active infection with hepatitis B or C:

- Active infection is defined as detectable hepatitis B DNA or hepatitis C RNA by quantitative PCR.

Latent infection with hepatitis B:

- Latent infection is defined as meeting all of the following criteria:
  - Hepatitis B surface antigen positive
  - Anti-hepatitis B total core antibody positive
  - Anti-hepatitis IgM core antibody undetectable
  - Hepatitis B PCR undetectable
- Participants with latent hepatitis B infection must agree to take prophylaxis with anti-hepatitis agents during and for 6 months following active protocol therapy with V-O.
- Participants who have received IVIG therapy within 6 months who are hepatitis B core total antibody positive but PCR undetectable are not mandated to take prophylaxis.

- l. Participants must not have had major surgery within 30 days prior registration or minor surgery within 7 days prior to registration. Examples of major surgery include neurosurgical procedures, joint replacements, and surgeries that occur inside the thoracic or abdomino-pelvic cavities. Examples of minor surgery include dental surgery, insertion of a venous access device, skin biopsy, or aspiration of a joint. If there is a question about whether a surgery is major or minor, this should be discussed with the Study Chair.
- m. Participants must not have known bleeding disorders (e.g., von Willebrand's disease or hemophilia).
- n. Participants must not have a history of stroke or intracranial hemorrhage within 6 months prior to enrollment.
- o. Participants must not require continued therapy with a strong inhibitor or inducer of CYP3A4/5, as venetoclax is extensively metabolized by CYP3A4/5 (see [Section 18.1](#)).
- p. Participants must not have uncontrolled autoimmune hemolytic anemia or idiopathic thrombocytopenia purpura.
- q. Participants must not have any currently active, clinically significant cardiovascular disease, such as uncontrolled arrhythmia or Class 3 or 4 congestive heart failure as defined by the New York Heart Association Functional Classification
- r. Participants must not have a history of myocardial infarction, unstable angina, or acute coronary syndrome within 6 months prior to enrollment (see [Section 18.2](#)).
- s. Participants must not be pregnant or nursing, as there are no safety data available for these drug regimens during pregnancy. Women/men of reproductive potential must have agreed to use an effective contraceptive method. A woman is considered to be of "reproductive potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy

prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation. However, if at any point a previously celibate Participant chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures.

#### 5.4 Specimen Submission Criteria

- a. Participants must agree to have specimens submitted for translational medicine (MRD) and specimens must be submitted as outlined in [Section 15.1](#).
- b. Participants must be offered participation in banking for future research. With participant's consent, specimens must be submitted as outlined in [Section 15.3](#).

#### 5.5 Quality of Life Criteria

- a. Participants who are able to complete patient reported outcome (PRO) forms in English, Spanish, French, German, Russian or Mandarin must agree to participate in the quality of life assessments as outlined in Section 15.4. (Those participants who are unable to read and write in English, Spanish, French, German, Russian or Mandarin may be registered to **S1925** without contributing to the quality of life portion of the study.)

#### 5.6 Regulatory Criteria

- a. Participants **must** be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.

NOTE: As a part of the OPEN registration process (see [Section 13.3](#) for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

