

Brief Report

Cytoreduction-Adapted Outpatient Venetoclax Ramp-Up in CLL/SLL: A Real-World Pilot Study

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Abstract

Venetoclax-based therapy is effective in chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), but tumor lysis syndrome (TLS) risk necessitates a resource-intensive five-week dose ramp-up with intravenous hydration, frequent laboratory monitoring, and clinic-based observation, creating logistical barriers particularly in community settings. We conducted a single-center, IRB-approved retrospective pilot study of 30 patients with CLL/SLL who underwent a cytoreduction-adapted, IV-free outpatient venetoclax ramp-up with reduced laboratory monitoring between 2023 and 2026. All patients received cytoreductive therapy—predominantly single-agent BTKi—and met protocol-defined low-tumor-burden criteria (ALC < 20×10^9 /L, lymph nodes < 5 cm, no splenomegaly, CrCl > 45 mL/min) before venetoclax initiation. Venetoclax was self-administered at home with laboratory monitoring reduced to a single approximately 12-h post-dose assessment per dose-escalation week. Median age was 71 years; 80% had received ≥ 2 prior therapy lines, and 37% had high-risk cytogenetics. Monitoring compliance was 100%. No laboratory or clinical TLS, IV hydration, hospitalizations, dose interruptions, treatment discontinuations, or deaths occurred during ramp-up. These pilot data support the feasibility and early safety of simplified outpatient venetoclax initiation in adequately cytoreduced patients and warrant prospective multicenter validation.

Keywords: venetoclax; chronic lymphocytic leukemia; tumor lysis syndrome

1. Introduction

Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) remain among the most common hematologic malignancies in the Western world, predominantly affecting an older patient population with a median age of diagnosis in the early seventies. The treatment landscape for CLL/SLL has been transformed over the past decade by the advent of targeted therapies, which have supplanted chemoimmunotherapy [1]. Targeted therapy is recommended for frontline and relapsed CLL/SLL treatment [1–4].

Fixed-duration therapy with venetoclax (ven) offers several potential advantages over continuous Bruton tyrosine kinase inhibitor (BTKi) therapy. A defined treatment course and the possibility of a treatment-free interval may be attractive to patients and clinicians from quality of life, long-term toxicity, and healthcare resource utilization perspectives, although continuous BTKi therapy remains a well-supported standard approach [3]. Key trials,



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including M13-982, MURANO, CLL14, GAIA-CLL13, CLL17, and AMPLIFY [3–8], have demonstrated the efficacy and tolerability of fixed-duration venetoclax-based regimens and their ability to achieve undetectable minimal residual disease (uMRD), including in patients with historically adverse genetic features such as del(17p), *TP53* mutations, and unmutated *IGHV* [9].

Despite these advantages, venetoclax-associated tumor lysis syndrome (TLS) was identified as a major safety concern during early-phase dose-escalation trials [10]. TLS results from the rapid destruction of malignant cells with the release of intracellular contents into the bloodstream and may cause renal failure, cardiac arrhythmias, seizures, and death. These early observations led to the development of TLS risk stratification, hydration protocols, anti-hyperuricemia prophylaxis, and a five-week ramp-up strategy to mitigate risk.

Many patients requiring CLL/SLL therapy have bulky adenopathy, splenomegaly, elevated absolute lymphocyte counts (ALCs), or impaired renal function, all of which may increase TLS risk. In approved venetoclax-based combination regimens, anti-CD20 monoclonal antibody therapy and/or BTKi therapy can reduce disease burden before or during venetoclax initiation, thereby mitigating TLS risk [11]. Anti-CD20 monoclonal antibody treatments require multiple infusion visits and carry a risk of infusion-related reactions, though this risk may be lower in patients previously treated with BTKi [4,11], and standard pre-medications are used to mitigate reactions.

Real-world data have been reassuring, with reported rates of laboratory TLS of approximately 1–2% and clinical TLS of less than 1% [12–14], when appropriate precautions are used. However, the logistical requirements of venetoclax initiation, per guidance from the drug label due to early-phase trials, remain a practical barrier, particularly in community settings where many patients with CLL/SLL receive care [15]. Simplified monitoring strategies for carefully selected, cytoreduced patients may reduce operational burden while maintaining safety, but such approaches require careful description and validation.

The objective of this study was to evaluate the feasibility and early safety of a cytoreduction-adapted, IV-free outpatient venetoclax ramp-up strategy using reduced laboratory monitoring in patients with CLL/SLL who met protocol-defined low-tumor-burden criteria before initiation.

2. Results

2.1. Patient Characteristics

As of Jan 2026, thirty patients were transitioned to venetoclax in the outpatient setting. The median age was 71 years (range: 53–86). *IGHV* was mutated in nine patients (30%), unmutated in 18 (60%), indeterminate in one (4%), and unknown in two (8%). Cytogenetic risk stratification classified 16 patients (53%) as low risk, 11 (37%) as high risk, and three (10%) as having unknown cytogenetic risk status. Twenty-four patients (80%) had received at least two prior lines of therapy, and six patients (20%) had received one prior line of therapy, reflecting a predominantly previously real-world population.

2.2. Cytoreductive Therapy Before Venetoclax Initiation

Most patients (24/30 or 80%) received single-agent BTKi as cytoreductive therapy. Of the six patients who did not receive BTKi as cytoreduction, three received combination chemoimmunotherapy for CLL/SLL or transformed disease: two received rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) for transformed disease, and one received reduced-dose R-mini-CHOP for high-grade disease with end-organ compromise before transition to venetoclax monotherapy. The remaining three patients received weekly anti-CD20 therapy with or without daily corticosteroids

for four weeks for CLL complicated by autoimmune hemolytic anemia, followed by venetoclax initiation.

The duration of cytoreductive therapy before venetoclax initiation was heterogeneous because some patients were already receiving BTKi therapy before transfer to our practice ($n = 12$), whereas others were started on cytoreduction specifically to meet venetoclax initiation criteria ($n = 12$). Median time on BTKi when initiated specifically for transition to monotherapy was 3 months and 26 days. Once the clinical decision was made to transition to venetoclax, cytoreductive therapy was continued during the early ramp-up period through W2D7, before continuation of venetoclax monotherapy. Three patients experienced BTKi-associated redistribution lymphocytosis; this did not prolong the cytoreductive phase or delay venetoclax escalation.

2.3. Ramp-Up Feasibility and Safety

Compliance with the outpatient monitoring schedule was 100%. No patient developed laboratory TLS or clinical TLS during the ramp-up period. No patient required scheduled or unscheduled IV hydration, hospitalization, venetoclax dose interruption, treatment discontinuation or intervention for TLS. No clinically relevant isolated electrolyte abnormalities were observed. No patient experienced toxicity greater than grade 1 during ramp-up, and there were no deaths during the dose-escalation period.

All patients experienced a clinical improvement in the disease manifestation that prompted therapy, including normalization or improvement in blood counts, resolution of constitutional symptoms, and/or improvement in disease-related cytopenias. Formal iwCLL response assessment was not uniformly protocol-mandated.

2.4. Exploratory MRD Outcomes

Peripheral blood (PB) NGS-based MRD data were available for 17 of 30 patients (57%). Among patients with reportable MRD data, four of 17 (24%) patients achieved uMRD. Median time from venetoclax initiation to uMRD was 7.5 months (range 6.9–28.7 months), with three of the four patients achieving uMRD within 11 months of initiating single-agent venetoclax. All four patients who achieved uMRD were *IGHV* unmutated. Furthermore, 52% of patients (9/17) had a partial MRD response, defined as at least a logarithmic decrease in residual sequence from baseline, after starting venetoclax monotherapy within 3–11 months. Detailed MRD results are presented in Supplementary Figure S1. These MRD findings are descriptive and should be interpreted cautiously because testing was incomplete, non-random and performed at variable timepoints.

3. Discussion

In this single-center retrospective pilot cohort, a cytoreduction-adapted, IV-free outpatient venetoclax ramp-up strategy using reduced laboratory monitoring was feasible among 30 patients with CLL/SLL who met protocol-defined low-tumor-burden criteria before initiation. No laboratory or clinical TLS events, scheduled or unscheduled IV hydration, hospitalizations, dose interruptions, treatment discontinuations, or deaths occurred during the ramp-up period. These findings support the feasibility of this approach while underscoring that our approach should not be extrapolated to patients who have not undergone adequate cytoreduction or who remain at medium or high risk for TLS. Given the low expected TLS incidence in cytoreduced patients and the modest size of this cohort, these results should be interpreted as pilot feasibility data rather than evidence of non-inferiority to prescribing-information-based monitoring.

The safety of our outpatient, low-frequency monitoring approach was predicated on adequate cytoreductive therapy administered prior to venetoclax initiation. TLS risk is

primarily determined by the volume of venetoclax-sensitive tumor present at the time of drug exposure. Venetoclax is a potent selective inhibitor of BCL2 that induces rapid apoptosis of malignant cells, releasing intracellular potassium, phosphorus, and nucleic acids. In early-phase trials that included patients with high tumor burden, TLS occurred in up to 18% of participants during dose escalation [16,17]. This observation established tumor burden as a central determinant of venetoclax-associated TLS risk and led to the development of stepwise dose escalation, hydration, anti-hyperuricemia prophylaxis, and risk-adapted monitoring strategies. More contemporary CLL regimens increasingly incorporate cytoreductive lead-in approaches, including BTK inhibitor-based debulking, to reduce tumor burden before or during venetoclax exposure [17]. By lowering the volume of venetoclax-sensitive disease present at initiation, these strategies reduce the biological substrate for clinically significant metabolic derangement. Our results are consistent with the low TLS rates observed in real-world analyses [13,14] where such cytoreduction is used prior to venetoclax initiation and provide the biological rationale for evaluating a lower-intensity monitoring protocol in appropriately cytoreduced patients.

Our protocol required patients to meet predefined cytoreduction criteria before venetoclax initiation, including ALC $< 20 \times 10^9/\text{L}$, all clinically assessable lymph nodes < 5 cm, resolution of clinically apparent splenomegaly, and CrCl > 45 mL/min. These criteria were more conservative than the prescribing information's low-risk classification in terms of ALC threshold (<20 vs. $<25 \times 10^9/\text{L}$) but more permissive with respect to renal function (CrCl > 45 vs. > 80 mL/min) [16]. The rationale for accepting a lower CrCl threshold was that, in the setting of confirmed low tumor burden, the absolute burden of cell lysis would be expected to be lower. However, this assumption requires prospective validation, particularly in patients with moderate renal impairment, as 14 patients had CrCl between 45 and 80 mL/min. These criteria should therefore be considered protocol-defined low-tumor-burden criteria rather than equivalent to prescribing information low-risk classification.

After patients met these initiation criteria, three specific de-escalations from prescribing information recommendations were evaluated: omission of routine IV hydration, reduction in laboratory monitoring to a single approximately 12 h post-dose assessment, and patient self-administration of venetoclax at home. The omission of IV hydration was predicated on the expectation that adequately cytoreduced patients with preserved renal function above the protocol threshold and adequate oral intake would not require parenteral volume support. All patients were instructed to maintain oral hydration of at least 1.5–2 L daily beginning 48 h before and continuing through 24 h after each dose escalation, consistent with prescribing information oral hydration recommendations [16]. No patient required scheduled or unscheduled IV hydration during ramp-up.

The reduction in laboratory monitoring to a single approximately 12 h post-dose draw represented the most significant change. The prescribing information recommends pre-dose, 6–8 h, and 24 h laboratory assessments during the initial dose levels, a schedule established during early-phase trials that included patients with high tumor burden who had not undergone systematic cytoreduction [14,16]. In this protocol, the 12 h timepoint was selected to align evening home administration with next-morning outpatient laboratory testing while capturing a clinically relevant interval within the 6–24 h window during which TLS-related metabolic abnormalities may emerge [18,19]. This workflow avoids same-day clinic visits, prolonged observation, and after-hours laboratory access. Furthermore, our monitoring schedule potentially requires as few as five laboratory assessments, which have meaningful implications for patient convenience, particularly for elderly patients or those who travel long distances to their respective treatment centers. Our results

also support the future evaluation of Week 1 laboratory monitoring omission in selected cytoreduced patients.

Cytoreductive therapy before venetoclax initiation was central to our strategy, and the predominant use of time-limited BTKi therapy for this purpose represents a distinguishing feature of this protocol. BTKi lead-in strategies as a means to rapidly reduce lymphocyte counts and lymphadenopathy in CLL have been employed in fixed-duration venetoclax combination trials. In the CAPTIVATE trial, three cycles of ibrutinib lead-in before venetoclax initiation reduced the proportion of patients with high TLS risk from 23% to 2% and decreased the percentage with lymph node diameter ≥ 5 cm from 31% to 4% [20,21]. Similar BTKi lead-in approaches were used in the GLOW trial, the FLAIR trial, and the AMPLIFY trial [4,22,23]. Our approach differs from these regimens in an important respect: BTKi was used as a time-limited short-term cytoreductive bridge to venetoclax monotherapy rather than as part of an approved concurrent combination regimen.

The duration of cytoreductive therapy before venetoclax initiation was response-adapted rather than time-defined. There was no protocol-mandated minimum or maximum duration of cytoreduction before venetoclax initiation. Instead, cytoreductive therapy was continued until patients met the predefined initiation criteria. Once venetoclax was initiated, cytoreductive therapy was generally continued through W2D7 to maintain disease control during the earliest venetoclax dose levels before transition to venetoclax monotherapy. This overlap strategy was consistent with the NCCN CLL guidelines, noting that when transitioning from a BTKi to a BCL2 inhibitor, overlapping BTKi and BCL2i during ramp-up should be considered until disease control is achieved [18]. In our cohort, no patients experienced BTKi withdrawal flare or required BTKi reinitiation after discontinuation. Three patients experienced BTKi-associated redistribution lymphocytosis during cytoreduction, although this did not delay venetoclax escalation or affect safety outcomes.

This all-oral cytoreductive strategy may have practical advantages in selected patients. Infusion-based debulking with anti-CD20 monoclonal antibodies remains an established and effective approach, but it requires infusion center access and may be associated with infusion-related reactions. For selected patients, an all-oral cytoreductive pathway followed by home-based venetoclax initiation and reduced laboratory monitoring may reduce logistical barriers, particularly for patients with limited infusion center access, transportation barriers, or caregiver constraints. However, no formal cost-effectiveness analysis was performed, and patient-level costs, visit burden, caregiver time, transportation, and health system utilization data were not collected. These implications should be evaluated prospectively using standardized resource utilization and patient-reported burden metrics.

All patients completed venetoclax ramp-up without dose interruption or treatment discontinuation, and all experienced clinical improvement, supporting the feasibility of treatment delivery with this approach. Although our MRD results were exploratory, they were broadly consistent with reported rates in single-agent venetoclax [24]. Notably, all four patients who achieved uMRD in this cohort had unmutated IGHV, which is typically associated with inferior prognosis in CLL/SLL. Because MRD testing was incomplete, non-random, and performed at variable intervals, these findings should be interpreted descriptively and not as evidence that the monitoring strategy preserves or compromises efficacy.

Limitations

Several limitations warrant emphasis. This is a single-center retrospective cohort of 30 patients and is underpowered to establish non-inferiority to prescribing information-based monitoring; given the low expected TLS incidence in cytoreduced patients, substantially larger prospective cohorts are needed. The protocol was applied only to patients

meeting protocol-defined low-tumor-burden criteria, and findings should not be generalized to patients with persistent bulky adenopathy, elevated ALC, splenomegaly, renal impairment below the protocol threshold, or other medium- or high-risk TLS features. The protocol also inherently selects for patients who respond to cytoreductive therapy, which may itself identify a population with more favorable disease biology or treatment sensitivity; patients who fail to achieve adequate cytoreduction would not meet initiation criteria and would require standard or intensified TLS monitoring. The single 12 h post-dose monitoring timepoint may have missed transient metabolic abnormalities that would have been detected with more frequent assessments. MRD testing was incomplete and performed at variable timepoints, limiting efficacy interpretation. Most patients continued venetoclax as single-agent monotherapy after cytoreductive bridging. Although continuous single-agent venetoclax is an approved approach in relapsed/refractory CLL/SLL, it is not a preferred contemporary frontline strategy, and time-limited single-agent use remains off-label. The cohort was predominantly relapsed/refractory (80% had received ≥ 2 prior lines of therapy), and the applicability of this approach in the frontline setting has not been evaluated. Finally, all patients in this cohort obtained insurance approval for oral BTKi therapy, which may limit generalizability to settings where payer coverage for BTKi bridging is not assured.

4. Methods

4.1. Study Design and Population

Between 2023 and 2026, we conducted an Institutional Review Board (IRB) approved, single-center, retrospective cohort study evaluating the implementation of an outpatient venetoclax initiation and dose ramp-up program (Figure 1). All patients had a confirmed diagnosis of CLL/SLL and met standard treatment indications per International Workshop on CLL (iwCLL) criteria.

All patients were receiving prior therapy or were initiated on cytoreductive therapy before venetoclax initiation. Cytoreductive therapy was selected by the treating physician based on clinical context, prior treatment history, disease-specific indication, comorbidities and feasibility of infusion-based versus oral therapy.

4.2. Cytoreduction and Venetoclax Initiation Criteria

Cytoreductive therapy was response-adapted, not time-defined. There was no required minimum or maximum duration of cytoreduction. Patients continued cytoreductive therapy to reach the initiation criteria if they were responding well and tolerating treatment. Venetoclax was initiated only after patients met all protocol-defined initiation criteria: (1) absolute lymphocyte count $< 20 \times 10^9/L$, (2) adenopathy < 5 cm by physical examination and available clinical imaging when performed, (3) resolution of splenomegaly if present, per physical exam and available clinical imaging when performed and (4) CrCl ≥ 45 mL/min.

After venetoclax initiation, the cytoreductive agent was continued through Week 2 Day 7 (W2D7) and then discontinued, provided there was no clinical concern for disease rebound. This overlap was intended to maintain disease control during the earliest venetoclax dose levels, where venetoclax may not have reached therapeutic levels.

4.3. Venetoclax Ramp-Up and TLS Monitoring

Once the initiation criteria were met, venetoclax dosing followed a standardized five-week (W) dose-escalation protocol: W1, 20 mg daily; W2, 50 mg daily; W3, 100 mg daily; W4, 200 mg daily; and W5, 400 mg daily. Prophylactic allopurinol was initiated one day before the first venetoclax dose and continued during the ramp-up period. Patients were

instructed to maintain oral hydration of at least 1.5–2 L of water daily beginning 48 h before and continuing through the first 24 h after each dose escalation.

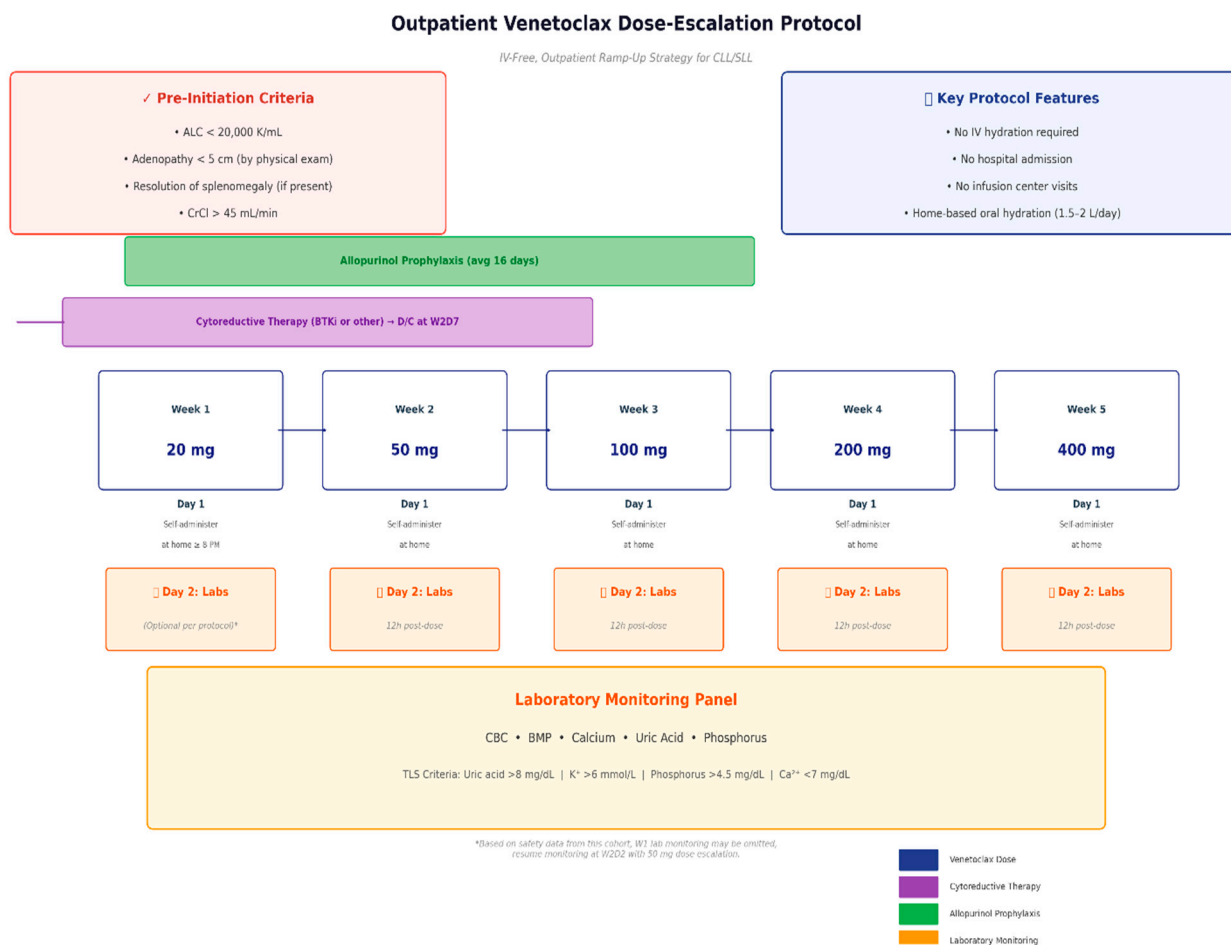


Figure 1. Outpatient venetoclax dose-escalation ramp-up protocol. Schematic representation of the five-week outpatient venetoclax initiation strategy. Venetoclax was initiated only after predefined cytoreduction criteria were met (upper left box). Allopurinol prophylaxis (green bar) was started one day prior to Week 1 and maintained for an average of 16 days. Cytreductive therapy (purple bar) continued through Week 2, Day 7 of venetoclax ramp-up before discontinuation. Venetoclax doses (blue font boxes) were self-administered at home on Day 1 of each week, with the initial dose (Week 1) taken no earlier than 8:00 PM. Laboratory monitoring (orange boxes) was performed approximately 12 h post-dose on Day 2 of each week. Based on the safety observed in this cohort, Week 1 laboratory monitoring may be considered optional (dashed border), with monitoring resuming at Week 2. Key protocol features (upper right box) highlight the elimination of IV hydration, hospital admission, and infusion center visits. The laboratory monitoring panel (bottom box) details the assessments performed and the TLS-defining thresholds. Abbreviations: ALC, absolute lymphocyte count; BMP, basic metabolic panel; BTKi, Bruton's tyrosine kinase inhibitor; CBC, complete blood count; CrCl, creatinine clearance; D/C, discontinue; TLS, tumor lysis syndrome.

Patients self-administered the initial venetoclax dose of each weekly venetoclax dose level at home no earlier than 8:00 PM. Patients were instructed to take venetoclax with a meal or a substantial snack at the time of dosing to ensure adequate absorption. Subsequent daily doses were also recommended to be taken approximately 24 h apart and always with food.

Laboratory monitoring was performed approximately 12 h after the first dose of each weekly dose level escalation. The monitoring panel included complete blood counts, basic metabolic panel, calcium, uric acid, and phosphorus levels. This protocol differed

from venetoclax prescribing information recommendations, which include pre-dose and serial post-dose laboratory assessments during the initial dose levels. No scheduled IV hydration visits were included in the protocol. Scheduled or unscheduled IV hydration visits for any reason during ramp-up, including electrolyte abnormalities, inadequate oral intake, or other clinical indications, were recorded. A comparison of venetoclax prescribing information monitoring recommendations to our protocol is presented in Table 1 [16].

Table 1. Specific interventions recommended by the venetoclax prescribing label [16]. The key de-escalations include: (1) elimination of IV hydration, (2) patient self-administration of venetoclax at home, (3) reduction in post-dose laboratory monitoring from two timepoints (6–8 h and 24 h) to a single assessment at approximately 12 h post-dose.

Intervention	Prescribing Label Low TLS Risk	Prescribing Label Medium TLS Risk	Outpatient Protocol Outlined in This Study
Pre-dose hydration	Oral hydration (1.5–2 L/day starting 2 days pre-dose).	Oral hydration (1.5–2 L/day starting 2 days pre-dose) and consider additional intravenous hydration.	Oral hydration only (1.5–2 L/day); IV hydration omitted.
Timing of post-dose TLS labs	For 20 mg and 50 mg doses, 6–8 h and 24 h post-first dose; all other escalations only require pre-dose labs.	For 20 mg and 50 mg, 6–8 h and 24 h post-dose; all other escalations only require pre-dose labs.	Single lab draw at ~12 h post-dose on Day 2 only.
Post-dose TLS labs: Week 1 (20 mg)	Recommended 6–8 h and 24 h.	Recommended 6–8 h and 24 h.	Optional (may be omitted based on safety data in this cohort); monitoring can be resumed at Week 2.
Post-dose TLS labs: Weeks 2–5	For 50 mg dose, labs at 6 to 8 h and 24 h. For subsequent ramp-up doses, only labs recommend pre-dose.	At each dose escalation.	At ~12 h post-dose, Day 2 of each escalation week.
Anti-hyperuricemia prophylaxis	Allopurinol starting 2–3 days pre-venetoclax. Typically continued for entire ramp up period.	Allopurinol starting 2–3 days pre-venetoclax. Continued for entire ramp up period. One can add rasburicase if baseline uric acid is elevated.	Allopurinol starting 1 day prior to venetoclax initiation. Can be discontinued in the middle of the ramp-up per clinician discretion.
Criteria required for outpatient initiation of venetoclax	Low risk defined as meeting all three criteria: (1) all lymph nodes < 5 cm, (2) absolute lymphocyte count < 25×10^9 , and (3) creatinine clearance > 80 mL/min.	Medium risk defined as: (1) all lymph nodes 5 cm to <10 cm, (2) absolute lymphocyte count $\geq 25 \times 10^9$ /L, and (3) creatinine clearance > 80 mL/min (if below the first dose of 20 mg and 50 mg are recommended to be administered in hospital).	Protocol-defined initiation criteria: ALC < 20×10^9 /L, nodes < 5 cm, no splenomegaly, and CrCl > 45 mL/min.

Tumor lysis syndrome was classified according to the Cairo–Bishop criteria [25]. Laboratory TLS was defined as the occurrence of ≥ 2 of the following metabolic abnormalities within 24 h of venetoclax dosing: uric acid > 8 mg/dL, potassium > 6 mmol/L, phosphorus > 4.5 mg/dL, or corrected calcium < 7 mg/dL. Clinical TLS was defined as laboratory TLS accompanied by one or more of the following clinical manifestations:

acute kidney injury (creatinine $\geq 1.5 \times$ upper limit of normal), cardiac arrhythmia, seizure, or death.

4.4. Disease Risk Classification and MRD Assessment

Cytogenetic risk stratification was classified based on fluorescence in situ hybridization (FISH) results and *TP53* mutational status. High-risk cytogenetics were defined as the presence of del(17p), *TP53* mutation, del(11q) [26], or complex karyotype. Low-risk cytogenetics were defined as the absence of these features, including patients with del(13q), trisomy 12, or normal FISH. Patients with unavailable data were classified as unknown. Minimal residual disease (MRD) was assessed using next-generation sequencing (NGS)-based assays on peripheral blood samples, most commonly between 3 and 11 months after venetoclax initiation and annually thereafter or as clinically indicated. Because MRD testing was not protocol-mandated and was performed at variable timepoints as decided by the clinician, MRD outcomes were considered exploratory.

4.5. Treatment Duration and Study Outcomes

After completion of ramp-up, venetoclax was generally continued as single-agent therapy until disease progression or unacceptable toxicity, consistent with the approved single-agent dosing approach in CLL/SLL. In selected patients with favorable disease features, limited performance status, and deep response, an individualized off-label time-limited strategy was considered at the clinician's discretion.

The primary outcome was feasibility and early safety of the outpatient ramp-up strategy, defined by completion of venetoclax dose escalation without laboratory TLS, clinical TLS, scheduled or unscheduled IV hydration, hospitalization, dose interruption, treatment discontinuation, or death during the ramp-up period. Secondary outcomes included monitoring compliance, clinically relevant isolated electrolyte abnormalities, clinical improvement in disease manifestation prompting treatment, and MRD response among patients with available testing.

5. Conclusions

In this single-center pilot cohort, a cytoreduction-adapted, IV-free outpatient venetoclax ramp-up strategy using reduced laboratory monitoring was feasible and safe in patients with CLL/SLL who met protocol-defined low tumor burden before venetoclax initiation. No laboratory or clinical TLS events, IV hydration, hospitalizations, dose interruptions, treatment discontinuations or deaths occurred in this real-world, predominantly heavily pre-treated patient population. By reducing the monitoring schedule and enabling home-based venetoclax initiation without infusion center utilization, this approach has the potential to reduce the logistical and resource burden that currently limits broader adoption of venetoclax-based therapy, particularly in community practice settings. These pilot data support the design of prospective, multicenter quality improvement projects or observational studies to formally evaluate the safety and operational advantages of reduced-intensity outpatient monitoring during venetoclax dose escalation in cytoreduced patients with CLL/SLL. We encourage the reporting of more experiences like ours to help reinforce the ease and safety of an outpatient venetoclax ramp-up within the community, ultimately ensuring that more patients have access to the benefits of fixed-duration CLL therapy.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/lymphatics4030040/s1>.

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Institutional Review Board Statement: This study meets the regulatory definition of human subjects research as defined by (45 CFR 46.101 IRB #: 25-0576), Date: 9 July 2025, research was conducted in accordance with all applicable Department of Health and Human Services regulations, Food and Drug Administration regulations and the Health Insurance Portability and Accountability Act (HIPAA).

Informed Consent Statement: The requirement for informed consent was waived due to the retrospective nature of the study.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest.

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