




## SHORT REPORT

# Venetoclax ramp-up strategies for chronic lymphocytic leukaemia in the United Kingdom: a real world multicentre retrospective study

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## Summary

This retrospective, observational study evaluated patterns of inpatient versus outpatient tumour lysis syndrome (TLS) monitoring during venetoclax ramp-up in 170 patients with chronic lymphocytic leukaemia. The primary outcome was clinical/biochemical TLS. Two clinical and four biochemical TLS occurred (4.1%). Five of the six events occurred in high-risk patients, four occurred at 20 mg dose and three at the 6-h time-point. Inpatient versus outpatient TLS rates within the high-risk subgroup were 15% and 8%. Risk category was the only predictor of TLS events in multivariate analysis. Outpatient escalation did not associate with clinically meaningful TLS events, suggesting outpatient escalation has manageable associated TLS risks, including in high-risk cohorts. These observations require confirmation in larger studies.

## KEY WORDS

chronic lymphocytic leukaemia, dose ramp-up, tumour lysis syndrome, Venetoclax

**Abbreviations:** ALC, absolute lymphocyte count; Allo-BMT, allogeneic bone marrow transplantation; BTKi, Bruton tyrosine kinase inhibitor; CLL, chronic lymphocytic leukaemia; COPD, chronic obstructive pulmonary disease; CR, complete response; CRF, case report form; GDPR, General Data Protection Requirements; IGHV, immunoglobulin heavy-chain variable-region; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; LN, Lymph Node; MRD, minimal residual disease; NHS, National Health Service; PI3Ki, phosphatidylinositol 3-kinase inhibitor; PR, partial response; R/R, relapsed/refractory; SLL, Small Lymphocytic Lymphoma; SPSS, Statistical Package for the Social Sciences; TLS, tumour lysis syndrome; uCR, unconfirmed complete response; UK, United Kingdom; ULN, Upper Limit of Normal.

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## INTRODUCTION

Venetoclax is currently available for treatment of chronic lymphocytic leukaemia (CLL) both at first (venetoclax/obinutuzumab) and subsequent lines of therapy (venetoclax/rituximab or venetoclax monotherapy), irrespective of *TP53* aberration status.<sup>1–5</sup>

The early results of the Phase Ib trial of venetoclax in 49 patients with relapsed/refractory (R/R) CLL, observed five tumour lysis syndrome (TLS) cases during dose escalation including two clinical-TLS events, one of which was fatal.<sup>6,7</sup> Subsequently, a dose escalation ramp-up schedule was designed, with a starting dose of 20 mg and weekly escalation until reaching the therapeutic dose of 400 mg. This modification led to only five biochemical TLS events and no clinical TLS in a Phase II study of venetoclax in 107 patients with R/R CLL.<sup>8</sup> Current recommendations require dynamic risk assessment of TLS risk before each dose increase and risk-adapted TLS monitoring schedules. In particular, for patients with a high risk of TLS, hospitalisation and more frequent blood monitoring is recommended.<sup>1</sup>

Despite recommendations, local practice is variable regarding the frequency of blood monitoring and the hospitalisation of patients mainly due to local availability of beds and outpatient monitoring facilities. Outpatient-based monitoring for patients with all levels of TLS risk has been developed in some centres to reduce hospital inpatient utilisation. We have designed this present study to evaluate patterns of TLS monitoring and the safety of this outpatient monitoring practice in the real world setting within the UK.

## STUDY DESIGN AND RESULTS

Our multicentre retrospective observational study, included consecutive patients with CLL treated with venetoclax monotherapy or in combination with an anti-CD20 monoclonal antibody between 1 March 2016 and 31 December 2020. Patients were identified at participating hospitals from existing registries and/or pharmacy/pathology databases.

Data collection was based on the electronic case report form (CRF) completed at participating sites; patient data was anonymised at source. All CRF database files (local and central) were compliant with General Data Protection Requirements (GDPR) guidelines and the declaration of Helsinki. This study was considered a service evaluation NHS audit, ethics committee approval was not required. Inclusion criteria are summarised in the supplementary file.

The primary outcome measure was development of clinical or biochemical TLS defined by Cairo–Bishop criteria.<sup>9</sup> TLS risk stratification followed the Seymour classification.<sup>10</sup> Secondary outcome measures were delay/discontinuation of venetoclax, haemodialysis requirement and TLS mortality rate. Biochemical TLS parameters after each venetoclax step-up dose were analysed separately. Response rates to venetoclax using International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria<sup>11</sup> and

minimal residual disease (MRD) status was recorded where available.

Differences in baseline characteristics were explored using chi-squared (or Fisher's exact) tests or *t*/Wilcoxon–Mann–Whitney tests. Uni- and multivariable Cox proportional hazards regression for TLS occurrence were performed. Statistical analyses were performed using the IBM Statistical Package for the Social Sciences (SPSS), version 22.0.

A total of 170 venetoclax-treated patients from 11 UK centres were included. Patient characteristics are shown in [Table 1](#). The median age was 69 years and 26.5% had baseline renal impairment. Prior therapy included Bruton tyrosine kinase inhibitor (BTKi) in almost two thirds of the patients (66.5%). TLS risk assessment and TLS prophylactic measures are shown in [Table 1](#).

All patients completed the venetoclax ramp-up dosing schedule. The percentages of patients receiving TLS prophylaxis, the distribution of TLS risk groups in each step of the ramp-up phase and the proportion of inpatient and outpatient escalations are summarised in [Figure 1](#). The proportion of patients escalated as outpatients tended to increase in later doses of the ramp-up schedule alongside a reduction of the percentage of patients in the high-risk TLS group. The percentage of high-risk TLS monitored as outpatients increased from 33% to 60% between the first and last dose ramp-up.

Overall, TLS events occurred in six patients (3.5%). Two were clinical TLS and four biochemical TLS, resulting in an incidence of clinical TLS of 1.1%. Five of the six (83%) TLS events occurred in high TLS risk patients, four events (57%) occurred in the first step of ramp-up, one at 50 mg, and one at 100 mg. Regarding timing of TLS onset, three events occurred at the 6-h post-dose time-point and three events occurred at 24-h. Within the high TLS risk subgroup, the incidence of biochemical TLS and clinical TLS were 7.5% and 5% respectively. When risk was analysed according to the inpatient versus outpatient monitoring, TLS in high-risk subgroup was observed in 15% (four of 26) and 8% (one of 13) respectively.

Two patients were outpatients at TLS event onset: both meeting biochemical TLS criteria and were detected at 6 h. Both had high TLS-risk pre-dose, one occurred at 20 mg dose and the other one at 100 mg dose. One patient required hospital admission and the other was managed as outpatient with additional monitoring and intravenous hydration. Clinical TLS were treated with additional rasburicase in both patients, with only one patient requiring haemodialysis. There were no deaths or treatment discontinuations related to TLS; however, the majority of patients (four of six) had subsequent venetoclax dose delayed  $\geq 1$  day.

In our series, retrospective analysis of response showed a complete response rate (CR and CR-unconfirmed) of 45.9% and a partial response (PR) rate of 39.1%. In all, 19/40 patients (47.5%), achieved a negative MRD during follow-up in either the peripheral blood or bone marrow. Progressive disease was observed in 24/126 patients (19.1%), 27.1% of

**TABLE 1** Patient demographics and baseline characteristics ( $n = 170$ ).

Characteristic	Value
Male, $n$ (%)	117 (68.8)
Age at start of venetoclax, years, mean (range)	69 (38–88)
Baseline comorbidities, $n/N$ (%)	
Cardiac	50 (29.4)
COPD*	22 (12.9)
Renal	45 (26.5)
Diabetes	21 (12.3)
Hypogammaglobulinaemia	91 (53.5)
TP53 disruption*	53/153 (34.6)
IGHV mutation	14/77 (18.2)
Other cytogenetic aberrations	76/166 (45.8)
Bulky disease (>7 cm / spleen >16 cm)	88/170 (51.7)
Prior treatments	
Prior lines, $n$ , median (range)	2 (1–16)
Chemo-immunotherapy, $n/N$ (%)	135/170 (79.4)
BTKi, $n/N$ (%)	113/170 (66.5)
PI3Ki, $n/N$ (%)	33/170 (19.4)
Alemtuzumab, $n/N$ (%)	17/170 (10)
Allo-BMT, $n/N$ (%)	11/170 (6.5)
Treatment disposition, $n$ (%)	
Venetoclax monotherapy	99 (58.2)
Venetoclax–rituximab	68 (40)
Venetoclax–obinutuzumab	3 (1.8)
TLS prophylaxis, $n/N$ (%)	
Rasburicase	80/126 (63.5)
Allopurinol	97/169 (57.4)
Both	29/127 (22.8)
Baseline TLS risk, $n$ (%)	
High	40 (23.5)
Medium	91 (53.5)
Low	39 (22.9)

Note: Base line comorbidities according to CIRS definitions: Cardiac: myocardial infarction, past percutaneous transluminal coronary angioplasty or coronary artery bypass, congestive heart failure, left ventricular hypertrophy, atrial fibrillation, bundle branch block, daily antiarrhythmic drugs, marked activity restriction secondary to cardiac status; Renal: serum creatinine  $\geq 1.5$  mg/dL; Diabetes: Type 2 diabetes mellitus; Hypogammaglobulinaemia: immunoglobulin G (Ig G)  $< 4$  mg/L.\*TP53 disruption: TP53 mutation or deletion. Abbreviations: Allo-BMT, allogeneic bone marrow transplantation; BTKi, Bruton tyrosine kinase inhibitor; COPD, chronic obstructive pulmonary disease; IGHV, immunoglobulin heavy-chain variable-region; PI3Ki, phosphatidylinositol 3-kinase inhibitor; TLS, tumour lysis syndrome.

patients died during study follow-up. The mortality causes were not collected for this study, but no deaths occurred during the ramp-up phase.

Uni- and multivariable analysis of risk factors for TLS events, showed high risk as the only variable associated independently with TLS events in our cohort (High risk vs. intermediate/low risk; hazard ratio 12.6, 95% confidence interval

1.1–144.4,  $p = 0.004$ ). Complete results of the analysis are shown in supplementary table.

## Single TLS parameter abnormalities

A total of 46 single laboratory abnormalities were recorded during venetoclax dose escalation across all levels of the ramp-up schedule. Elevated serum phosphate the most frequent finding (67.4%) followed by increased urate (19.6%), increased potassium (8.7%) and low calcium (4.3%). Isolated hyperphosphataemia was enriched in patients who subsequently obtained a confirmed/unconfirmed CR (CR/uCR rate 72% vs. 45% in patients without this abnormality;  $p = 0.01$  Mann-Whitney).

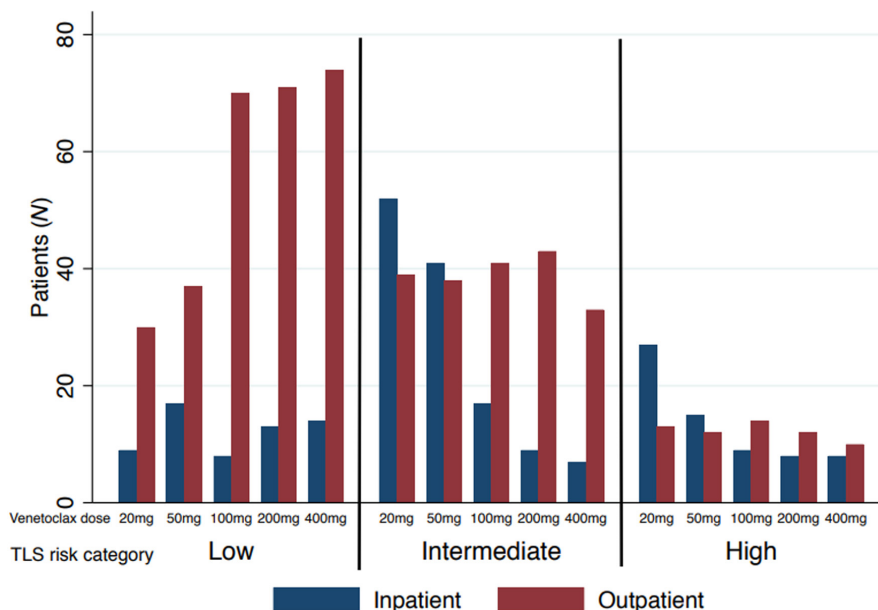
Most laboratory abnormalities occurred in the early stages of the ramp-up schedule; 56% occurred in the first two steps of ramp-up. In all, 47.8% of these events happened at 6 h post-dose. There was no correlation between these events and baseline TLS risk, only 22% of the patients with single biochemical abnormality had high TLS-risk.

## DISCUSSION

Risk of clinical TLS for venetoclax-containing regimes is relatively low, large randomised trials of venetoclax-containing regimens range from 0% to 3.1%.<sup>3,4,12–15</sup> The frequency of clinical TLS in our study is in keeping with prior publications, which demonstrates adequate compliance with the monitoring schedules in routine practice. Risk of TLS in the most recent studies is lower, by virtue of the timing of venetoclax introduction following anti-CD20 antibody or ibrutinib tumour debulking. In our study population, only three patients received venetoclax-obinutuzumab, hence we cannot draw conclusions on the real-world TLS risk of these regimens.

In our study, high TSL risk was the only variable associated independently with TLS events. This correlates with a previous multicentre retrospective study.<sup>15</sup> The risk of TLS observed in our cohort must be analysed in the context of the baseline characteristics and the period of data collection, where venetoclax was most frequently following BTKi exposure and mostly in the third line or later setting. A quarter of patients had some degree of renal impairment (and de facto excluded from most trials). Our data suggests that the ramp-up schedule can adequately mitigate TLS risk in patients with renal impairment. In the above-mentioned study, creatinine clearance predicted TLS development in multivariable analysis.<sup>15</sup>

We provide evidence for a manageable TLS risk with exclusive outpatient ramp-up schedule across all risk groups. This is of particular relevance for patients with a high risk of TLS and suggests that this subgroup can safely be escalated without the need of hospital inpatient bed utilisation. To our knowledge, there is no published evidence of exclusive outpatient escalation of venetoclax in high-risk patients. Biochemical monitoring at 6 and 24 h permitted



**FIGURE 1** Distribution of patients during ramp-up period according to inpatient/outpatient escalation and tumour lysis syndrome (TLS) risk. Both high- and intermediate-risk groups depict predominant inpatient escalation for initial doses and progressive increase of outpatient escalation in later doses of ramp-up. For low TLS risk patient, outpatient escalation is predominant.

identification of all cases of biochemical TLS, allowing for timely management and prevention on clinical TLS in most cases, including the two cases that were identified during the outpatient ramp-up schedule.

The common denominators of centres where outpatient ramp-up was feasible were: (i) dedicated CLL/haematology nurse specialists, (ii) immediate availability of acute hospital admission beds and (iii) relatively rapid laboratory turn-around time to manage 6h blood results during working hours. The authors appreciate these conditions might not be met in all CLL-treating centres, as suggested by the unexpectedly high proportion of low-risk patients escalated as inpatients, which was maintained up to 15% even in the final steps of the ramp-up phase. We propose these as minimal standards to conduct outpatient venetoclax dose escalation.

No patients had TLS blood monitoring at the 4-h time-point, and we are unable to conclude whether earlier TLS monitoring reduces clinical TLS risk further, as suggested by the most recent modification of the ramp-up recommendations (Summary of Product Characteristics).

The analysis of single parameter abnormalities was hypothesis generating. Our results suggest serum phosphate could be a surrogate marker of venetoclax activity; however, this requires independent validation in large, prospective patient cohorts.

The main limitations of our study were the low number of TLS events and the potential for selection bias in the inpatient/outpatient groups. Nonetheless, provided appropriate infrastructure and staffing levels permitting it, we provide evidence of relative safety of the outpatient escalation for venetoclax and validate the effectiveness of the venetoclax ramp-up scheme mitigating TLS risk in this context.

#### AUTHOR CONTRIBUTIONS

Rocio Figueroa-Mora, Nicolas Martinez-Calle, Tahla Munir and Christopher P. Fox designed the study. Rocio Figueroa-Mora analysed data and wrote the manuscript, Alexandros Rampotas, Daniel Halperin, Tina Worth, Jennifer Vidler, Dario Melotti, Paul Ferguson, Nagah Elmusharaf, Gavin Preston, Michelle Furtado, Moez Dungarwalla, Satyen Gohill, Piers Patten, Ben Kennedy, Toby A. Eyre, Anna Schuh treated patients, contributed to data collection and reviewed the manuscript.

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Alexandros Rampotas contributed to collect the study data, wrote the paper and approved the final version. Daniel Hapelrin contributed to collect the study data, wrote the paper and approved the final version. Tina Worth contributed to collect the study data, wrote the paper and approved the final version. Jennifer Vidler contributed to collect the study data, wrote the paper and approved the final version. Dario Mellotti contributed to collect the study data, wrote the paper and approved the final version. Paul Ferguson contributed to collect the study data, wrote the paper and approved the final version. Nagah Elmusharaf contributed to collect the study data, wrote the paper and approved the final version. Gavin Preston contributed to collect the study data, wrote the paper and approved the final version. Michelle Furtado contributed to collect the study data, wrote the paper and approved the final version. Moez Dungarwalla contributed to collect the study data, wrote the paper and approved the final version. Satyen Gohill contributed to collect the study data, wrote the paper and approved the final version. Piers Patten contributed to collect the study data, wrote the paper and approved the final

version. Ben Kennedy contributed to collect the study data, wrote the paper and approved the final version. Toby A. Eyre contributed to collect the study data, wrote the paper and approved the final version. Anna Schuh contributed to collect the study data, wrote the paper and approved the final version. Christopher P. Fox contributed to collect the study data, wrote the paper and approved the final version. Tahla Munir contributed to collect the study data, wrote the paper and approved the final version. Nicolas Martínez-Calle performed study design, contributed to collect the study data, analysed the data, wrote the paper and approved the final version. Rocio Figueroa-Mora performed study design, contributed to collect the study data, analysed the data, wrote the paper and approved the final version. Christopher P. Fox, Tahla Munir and Nicolas Martínez also performed study design, contributed collecting the study data, analysed the data, wrote the paper and approved the final version.

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This study was undertaken as a NHS service evaluation project.

### CONFLICT OF INTEREST STATEMENT

All authors declare no conflicts of interest.

### DATA AVAILABILITY STATEMENT

Not applicable.

### DISCLOSURES

Nicolas Martinez-Calle: conference travel and accommodation support from Takeda, Abbvie, Astra Zeneca. Speaker honoraria from Roche, Astra Zeneca and Jansen. Toby A. Eyre: Roche: Education Honorarium, Advisory Board Honorarium, Travel to scientific conferences. Gilead: Honorarium; Research support; Travel to scientific conferences. KITE: Education Honorarium, Advisory Board Honorarium, Janssen: Honorarium. Abbvie: Honorarium; Travel to scientific conferences. AstraZeneca: Honorarium, Research funding, Travel to scientific conferences. Loxo Oncology: Advisory Board Honorarium, Trial steering committee. Beigene: Advisory Board Honorarium, Research funding. Incyte: Advisory Board Honorarium. Secura Bio: Advisory Board Honorarium.

### PATIENT CONSENT STATEMENT

Clinical audits do not require subject consent as not considered research.

### PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Not applicable.

### CLINICAL TRIAL REGISTRATION (INCLUDING TRIAL NUMBER)

Not applicable.

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### REFERENCES

- Venclyxto (venetoclax) summary of product characteristics (SpC). [Internet] [cited 20th October 2022]. Available from: <https://www.medicines.org.uk/emc/product/2267/smpc—gref> [October, 2022].
- Eichhorst B, Robak T, Montserrat E, Ghia P, Niemann CU, Kater AP, et al. Chronic lymphocytic leukaemia: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2021;1(32):23–33.
- Fischer K, Al-Sawaf O, Bahlo J, Fink AM, Tandon M, Dixon M, et al. Venetoclax and obinutuzumab in patients with CLL and coexisting conditions. *N Engl J Med.* 2019;23(380):2225–36.
- Seymour JF, Kipps TJ, Eichhorst B, Hillmen P, D’Rozario J, Assouline S, et al. Venetoclax-rituximab in relapsed or refractory chronic lymphocytic leukemia. *N Engl J Med.* 2018;12(378):1107–20.
- Walewska R, Parry-Jones N, Eyre TA, Follows G, Martinez-Calle N, McCarthy H, et al. Guideline for the treatment of chronic lymphocytic leukaemia. *Br J Haematol.* 2022;5(197):544–57.
- Roberts AW, Davids MS, Pagel JM, Kahl BS, Puvvada Sd, Gerecitano JF, et al. Targeting BCL2 with Venetoclax in relapsed chronic lymphocytic leukemia. *N Engl J Med.* 2015;4(374):311–22.
- Seymour JF. Effective mitigation of tumor lysis syndrome with gradual venetoclax dose ramp, prophylaxis, and monitoring in patients with chronic lymphocytic leukemia. *Ann Hematol.* 2016;8(95):1361–2.
- Stilgenbauer S, Eichhorst B, Schetelig J, Coutre S, Seymour JF, Munir T, et al. Venetoclax in relapsed or refractory chronic lymphocytic leukaemia with 17p deletion: a multicentre, open-label, phase 2 study. *Lancet Oncol.* 2016;6(17):768–78.
- Cairo MS, Bishop M. Tumour lysis syndrome: new therapeutic strategies and classification. *Br J Haematol.* 2004;1(127):3–11.
- Seymour J, Roberts A, Stilgenbauer S, Gressick LA, Rudersdorf NK, Busman T, et al. P868. Reduction of tumor lysis syndrome (TLS) risk IN chronic lymphocytic leukemia (CLL) patients treated with ABT-199 (GDC-0199): results of modifications to dosing schedule and TLS prophylaxis. 19th congress of the European Hematology Association 2014 Haematologica. 2014, suppl\_1 (99):321.Milan, Italy, June 12–15
- Hallek M, Cheson BD, Catovsky D, Caligaris-Cappio F, Dighiero G, Döhner H, et al. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. *Blood.* 2018;25(131):2745–60.
- Eichhorst B, Niemann C, Kater AP, Fürstenau M, Von Tresckow J, Zhang C, et al. A randomized phase III study of Venetoclax-based time-limited combination treatments (RvE, GvE, GIVe) vs standard chemoimmunotherapy (CIT: FCR/BR) in frontline chronic lymphocytic leukemia (CLL) of fit patients: first Co-primary endpoint analysis of the international intergroup GAIA (CLL13) trial. *Blood.* 2021;1(138):71.
- Kater A, Owen C, Moreno C, Follows G, Munir T, Levin MD, et al. Fixed duration ibrutinib and venetoclax versus chlorambucil plus obinutuzumab for first-line chronic lymphocytic leukemia: primary analysis of the phase 3 GLOW study. *European Hematology Association.* 2021; Virtual Congress Abstract LB1902 Presented June 12, 2021. EHA Library; 3320172; LB1902.
- Wierda WG, Allan JN, Siddiqi T, Kipps TJ, Opat S, Tedeschi A, et al. Ibrutinib plus Venetoclax for first-line treatment of chronic lymphocytic leukemia: primary analysis results from the minimal residual disease cohort of the randomized phase II CAPTIVATE study. *J Clin Oncol.* 2021;34(39):3853–65.

15. Roeker LE, Fox C, Eyre TA, Brander DM, Allan JM, Schuster SJ, et al. Tumor lysis, adverse events, and dose adjustments in 297 venetoclax-treated CLL patients in routine clinical practice. *Clin Cancer Res*. 2019;25(14):4264–70.

### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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