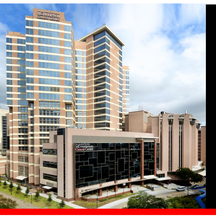

Venetoclax Initiation Monitoring and Interventions after Acalabrutinib Lead-in for Chronic Lymphocytic Leukemia

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BACKGROUND

- Tumor lysis syndrome (TLS) is a known risk with venetoclax (VEN) initiation in chronic lymphocytic leukemia (CLL) and small lymphocytic leukemia (SLL), requiring risk stratification by tumor burden (TB) based on absolute lymphocyte count (ALC), lymph node (LN) size, and renal function prior to VEN initiation.
- Acalabrutinib (acala) is a covalent BTK inhibitor known to reduce disease burden, but the impact of acala lead-in on TLS risk during subsequent VEN initiation remains incompletely characterized.
- We report on the use of acala debulking prior to VEN initiation and its effect on TB reduction, TLS risk stratification, lab monitoring, interventions, and observed TLS events.

METHODS

- This is a retrospective cohort observational analysis of the single center investigator-initiated clinical trial NCT04169737.
- **Inclusion Criteria**: Patients with CLL/SLL ≥ 18 years of age with a 2018 iwCLL indication for treatment
  - Completed 2 cycles of lead-in with acala prior to VEN initiation
  - Had TLS risk assessment prior to the standard 5-week venetoclax initiation
- **Exclusion Criteria**: Patients without 5 weeks of follow up or without lab monitoring after VEN

Figure 1. Tumor Burden Reduction

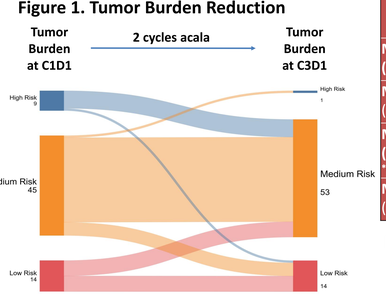
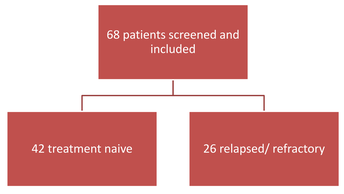


Figure 2. Patient Flow Diagram



OBJECTIVES

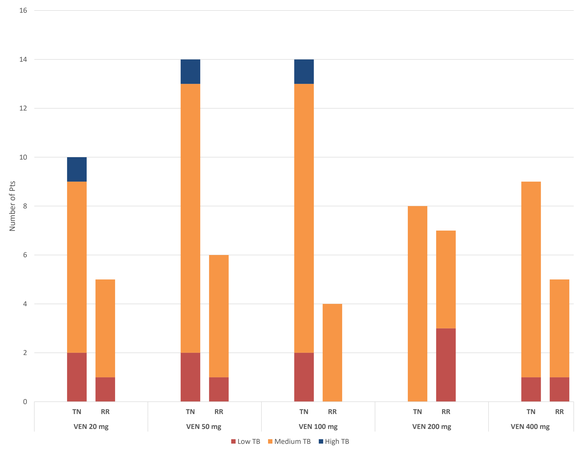
- **Primary Objective**: To evaluate the incidence of the composite of laboratory or clinical TLS per Howard criteria or hyperkalemia (potassium >6.0 mmol/L) during the 5-week venetoclax initiation period in patients with treatment naïve (TN) or relapsed/refractory (R/R) CLL after two cycles of acala.

RESULTS

Table 1. Baseline Characteristics

	Total Population (N=68)	Treatment Naive (N=42)	Relapsed/ Refractory (N=26)
Median Age, years (range)	60 (38-77)	61 (41-77)	62.5 (38-75)
Male, n (%)	37 (54)	22 (52)	15 (58)
Race, n (%)			
White	61 (90)	39 (93)	22 (85)
African American	3 (4)	0 (0)	3 (12)
Other	4 (6)	3 (8)	1 (4)
Median lines of prior therapy, n (range)	--	--	1 (1-3)
TB at C3D1, n (%)			
Low	14 (21)	8 (20)	6 (23)
Medium	53 (78)	33 (79)	20 (77)
High	1 (1)	1 (2)	0 (0)
Median LN Size at C1D1, cm (range)	3.95 (1-16.7)	4 (1.6-16.7)	4 (1-7.4)
Median ALC at C1D1, K/μL (range)	50.89 (1.52-227.8)	53.13 (3.01-227.8)	39.85 (1.52-209.71)
Median LN Size at C3D1, cm (range) *N=18 with imaging prior to C3D1	3.15 (1.6-4.3)	3.1 (1.6-4.3) N=13	3.55 (2.1-4.2) N=5
Median ALC at C3D1, K/μL (range)	60.28 (1.62-209.81)	60 (1.62-209.81)	60.93 (1.63-196.18)

Figure 3. Elevated Potassium (4.6-6 mmol/L)



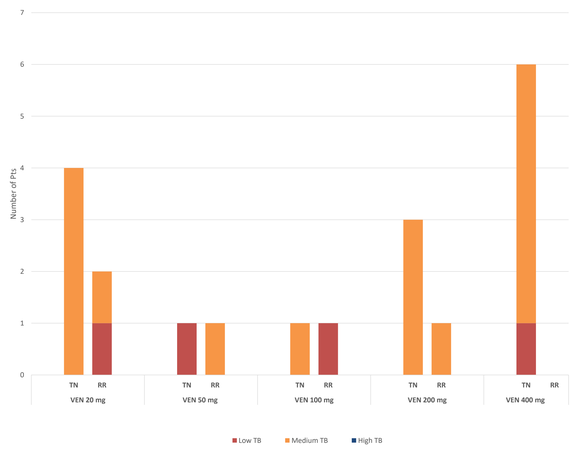
No pts experienced the composite primary outcome of laboratory or clinical TLS or hyperkalemia>6 mmol/L during VEN initiation

- One TN pt with medium TB had elevated creatinine>0.3 mg/dL above baseline during week 1 of VEN initiation
- One TN pt with medium TB had uric acid>8 mg/dL during VEN week 5 at pre-dose labs
- At any point during VEN initiation, 80% of elevated potassium levels occurred in pts with medium TB
- Hyperphosphatemia>4.5 mg/dL was the second most common abnormality observed (6%)
- In 22 patients with CrCl<80 ml/min, there were 39 occurrences of elevated potassium or phosphorus levels at any week

Table 2. Pts Who Received Prophylactic Intravenous Fluid

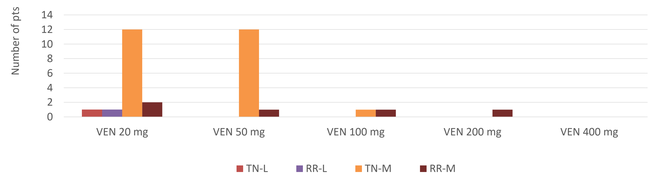
Week/Ven dose	Low TB (N=14)		Medium TB (N=53)		High TB (N=1)	
	TN	RR	TN	RR	TN	
VEN 20 mg, n (%)	5 (36)	4 (28)	23 (60)	13 (34)	1 (100)	
VEN 50 mg, n (%)	3 (21)	3 (21)	21 (55)	11 (28)	1 (100)	
VEN 100 mg, n (%)	1 (7)	0 (0)	8 (21)	2 (5)	1 (100)	
VEN 200 mg, n (%)	0 (0)	0 (0)	2 (5)	2 (5)	0 (0)	
VEN 400 mg, n (%)	0 (0)	0 (0)	3 (8)	1 (3)	0 (0)	

Figure 4. Elevated Phosphorous (>4.5-6 mg/dL)



TREATMENT SETTING

Figure 4. Pts Who Were Admitted



COMMON INTERVENTIONS

- MD interventions for electrolyte and lab abnormalities were based on the provider discretion. Most interventions occurred during the first two weeks of the ramp-up in patients with medium TB, including potassium-lowering agents, phosphorous-lowering agents, intravenous fluids, loop diuretics.

DISCUSSION

- The majority of patients maintained the same TB after acala lead-in, while 25% of pts lowered their TB, and 8% increased TB.
- None of the patients experienced laboratory or clinical TLS during VEN initiation. Elevations in potassium and phosphorous were observed, however these were mild.
- There were no appreciable differences in incidence of lab abnormalities between TN and RR pts, however numbers are small.
- Most patients were treated in the outpatient setting, with most patients with medium tumor burden receiving additional IV fluids for prophylaxis.

CONCLUSION

- In this retrospective analysis, patients did not experience laboratory or clinical TLS during venetoclax initiation after debulking with acala.
- Acala lead-in may debulk CLL TB prior to venetoclax initiation, leading to reduce risk of TLS.

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DISCLOSURES

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