CLINICAL SIGNIFICANCE AND TREATMENT OUTCOMES OF PLEURAL EFFUSION IN CHRONIC LYMPHOCYTIC LEUKEMIA

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Introduction

Pleural effusions, while uncommon, may significantly complicate the care of a patient with chronic lymphocytic leukemia (CLL). Effusions can be directly caused by lymphatic obstruction from bulky lymphadenopathy and pleural space invasion or non-malignant causes like infection and medication side-effects. The clinical, prognostic, and treatment implications for pleural effusion in CLL remains unclear.

Methods

We retrospectively identified patients (n=17) with CLL or SLL with radiographic pleural effusion at our tertiary academic institution. Post-effusion survival was defined as the time from radiographic pleural effusion to death or censorship at end of our study period 4/1/2025. Effusion cause was determined by the primary treating oncologist as documented in the chart. CLL cytogenetic data prior to pleural effusion was used. Closest peripheral and pleural studies within 3 months were associated.

Results

The median post-effusion survival was 43 months (Range: 4 - 142 months). Notably, among two patients with Richter transformation, the one that had pleural involvement with CLL, but not large cell lymphoma experienced pleural effusion resolution after treatment. CLL involvement in pleural flow generally decreased after effective systemic treatment on repeat thoracentesis, especially relative to peripheral flow.

The median duration of pleural effusion was 7 months (SD 7.5 months). Median time from treatment start to effusion resolution for tyrosine kinase inhibitors (not including cases 7, 10) was 3 months (SD 7.9 months). Median time from treatment start to resolution for venetoclax and/or CD20 inhibitor was 7.5 months (SD 4.9 months).

Trisomy 12 was found in 4/6 unresolved effusions (or requiring pleurodesis to resolve). ZAP70 > 20% was found in 7/11 resolved effusions.

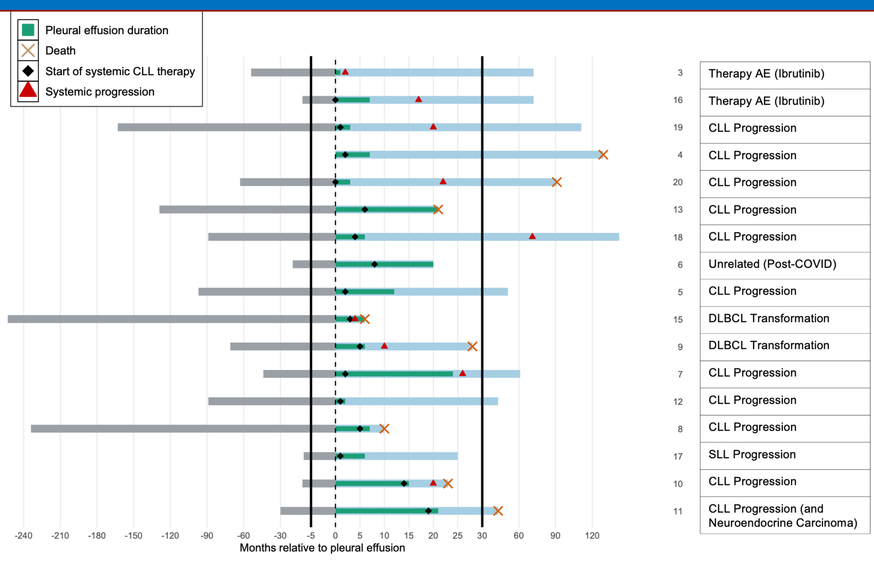


Figure 1. CLL-Related Pleural Effusion Timelines and Survival

Patient	Age at Dx	Rai Stage	Del 11q	Del 13q	Del 17p	Trisomy 12	IGHV-mut	ZAP70 > 20%	Prior Lines	Systemic CLL Treatment	Effusion Outcome
3	67	2							2	x	
16	86	2							1	HDMP	
19	59	2							1	HDMP	
4	75	2							0	HDMP/rituximab	
20	60	0							0	HDMP/rituximab	
13	77	2							8	Venetoclax	
18	62	0							2	Venetoclax/rituximab	
6	75	0							0	Venetoclax/obinutuzumab	
5	56	0							2	Obinutuzumab	
15	46	4							3	Ibrutinib	
9	49	1							7	Ibrutinib/CAR-T	
7	62	1							0	Acalabrutinib	
12	64	4							0	Acalabrutinib	
8	66	2							4	Zanubrutinib	
17	64	(SLL)							0	Zanubrutinib	
10	73	4							6	CAR-T/pirtobrutinib	
11	50	1							0*	N/A (Ipilimumab/nivolumab)	

Resolved
Decreased
No improvement
Not available
Mutated
Wild-Type

Table 2. Prognosticators and Treatment CLL-Related Pleural Effusion

	Initial Thoracentesis							Latest Thoracentesis								
		Pleural				Peripheral			Pleural				Peripheral			
	Light's	WBC	Diff	RBC (1000s)	Flow	Flow	ALC	Light's	WBC	Diff	RBC (1000s)	Flow	Flow	ALC	Total Thoras	Pleuro-desis
3	-				14%*		9.7								1	0
16	-	861*	8/68/24*	5.0*	20%*		1.3								0*	0
19	T	2429	2/64/24	13	0.27%		1.2	E	1383	1/44/55	3.0			1.4	3	0
4	T	800	7/53/40	495	23%	11%	12.4	E	1200	34/43/13	609			7.0	2	0
20	-	46000		1170			62.6								0*	0
13	T	8141	33/62/5	16	72%	83%	47	T	576	32/45/23	4.0	<0.01%	<0.01%	0.5	10	1
18	E	3250	3/54/35	3.35	10%	48%	5.2	E	2887	0/73/3	4.0	4%	48%	4.7	2	0
6	E	2676	2/68/13	119	2.6%	24%	6.4	E	99	2/81/17	0.3	3.2%	24%	6.8	11	1
5	E	1858	4/82/9	2.0	5.6%	2.0%	1.1	E	1207	10/67/20	2.0	0.04%		0.7	7	0
15	E	1033	38/10/13	975			0.2								1	0
9	E	3735	0/84/7	12	43%	0.2%	0.9								5	1
7	E	1919		4.3	43%		21					2.5%		0.9	16	0
12							98								0	0
8															8	0
17	E	2710	5/76/19	150	22%	11%	5.2		924	71/16/13	1513	1.9%		1.0	8	1
10	E	701	5/82/9	1.0	41%	<0.01%	0.1	E	410	8/29/50	5.0		<0.01%	0.1	2	0
11	E	5026	1/93/6	113	<0.01%	16%	2.0	T	845	3/89/8	3.0	14%	14%	2.3	4	1

Table 1. Pleural Effusion Characteristics

Summary and Discussion

We observed that a majority of our patients had improvement in pleural effusion after systemic treatment initiation or modification. Our findings suggest that pleural effusions in CLL may be signs of disease progression and can respond to effective systemic CLL-directed treatment

References

Alexandrakis MG, Passam FH, Kyriakou DS, Bouros D. Pleural Effusions in Hematologic Malignancies. *Chest.* 2004;125(4):1546-1555. doi:10.1378/chest.125.4.1546