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Real-World Implementation of Tumor-Informed ctDNA MRD Testing in Frontline Diffuse Large B-Cell Lymphoma: A Single-Center Experience

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Abstract

Background

Circulating tumor DNA (ctDNA) based measurable residual disease (MRD) assessment is recommended by NCCN to clarify equivocal end-of-treatment PET/CT in frontline diffuse large B-cell lymphoma when biopsy is not feasible. Unlike B-ALL, where bone marrow routinely provides an accessible disease-rich specimen, DLBCL requires retrieval of adequate diagnostic lymph node or soft tissue to identify a tumor-specific clonotype before it can be tracked in blood. This multistep workflow creates opportunities for delay that may limit MRD availability at clinical decision points. We evaluated real-world adoption, operational barriers, and turnaround times following implementation of an institutional clonoSEQ® workflow.

Methods

We retrospectively identified patients with newly diagnosed DLBCL treated at the University of Nebraska Medical Center (UNMC) from January 2024 through December 2025 following implementation of upfront clonality testing. Patients were classified as MRD-attempted (clonality ordered) or MRD-not-attempted. We compared baseline characteristics and quantified intervals from consultation through tissue-based clonotype identification and subsequent blood-based MRD reporting.

Results

Among 112 eligible patients, MRD was attempted in 67 (60%) and succeeded in 60/67 (90%)(Figure 1); MRD-attempted patients lived closer to the institution (median 11.7 vs 72.5 miles; P<0.001), while other clinical and access factors were similar(Table 1). Once ordered, testing proceeded rapidly: median times from order to tissue receipt, tissue receipt to identification of a trackable tumor-specific DNA sequence, and blood collection to MRD reporting were 6 days (IQR, 3–9; range, 1–59), 11 days (IQR, 9–12; range, 7–15), and 9 days (IQR, 7–11; range, 6–26), respectively. The main delay occurred before testing was initiated: the median consultation-to-order interval was 20 days (IQR, 4–112; range, 0–239), with only 10% ordered at consultation and 36% ordered >90 days later. Among 49 patients with paired end-of-treatment PET/CT and MRD, MRD was available a median of 10 days after PET/CT (IQR, 7–20; range, −13 to 155); 8 (16%) experienced delays >60 days, attributable to late ordering and tissue submission rather than laboratory processing. Of 102 patients

undergoing end-of-treatment PET/CT, 29 (28%) had residual metabolic activity. Concurrent MRD was available in 15: all 4 with detectable MRD progressed, whereas none of 11 with undetectable MRD progressed during a median follow-up of 15 months.

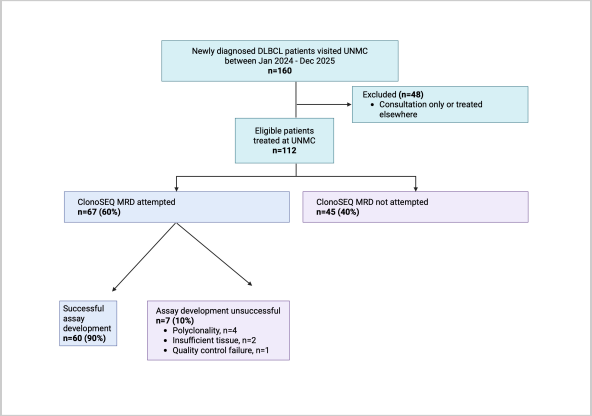


Figure 1.

Conclusion

Timely MRD may help clarify residual end-of-treatment PET activity. Laboratory turnaround was reasonable, with delays primarily driven by late clonality ordering and tissue submission. Standardizing these steps at diagnosis may improve MRD availability and clinical utility.

Table 1:

Characteristic	Attempted (n=67)	Not attempted (n=45)	P value
Age, median, years	67	69	0.682
Distance from UNMC, median, miles	11.77	72.52	<0.001
Diagnosis setting, n (%)			0.661
Inpatient	16 (23.9)	13 (28.9)	
Outpatient	51 (76.1)	32 (71.1)	
Diagnosis-to-treatment interval, median, days	19	16	0.282
Biopsy type, n (%)			0.058
Excisional	14 (20.9)	3 (6.7)	
Core needle/aspiration	53 (79.1)	42 (93.3)	
Biopsy location, n (%)			0.268
UNMC	53 (79.1)	31 (68.9)	
Outside institution	14 (20.9)	14 (31.1)	
Insurance, n (%)			0.837
Medicare/Medicaid	42 (62.7)	26 (57.8)	
Commercial/other	23 (34.3)	17 (37.8)	
Uninsured	2 (3.0)	2 (4.4)	

Table 1.

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