

Circulating tumor DNA (ctDNA) has rapidly moved from being an emerging technology to an integral component of precision oncology. With the publication of its first dedicated Clinical Practice Guideline on ctDNA testing in solid tumors and lymphoma, ASCO has provided much needed clarity on when liquid biopsy should be used and, equally importantly, when it should not.

The central message of this guideline is simple. Do not perform ctDNA testing simply because it is available. Perform it only when the result will influence patient management.

ASCO recommends ctDNA testing when tissue biopsy is unsafe, technically challenging, unavailable within a clinically actionable timeframe, or when regulatory approved companion diagnostics support its use. However, a negative or inconclusive ctDNA result should never be considered sufficient to exclude actionable genomic alterations. Whenever feasible, tissue based confirmation remains the standard of care.

The guideline also cautions against using ctDNA as a replacement for tissue biopsy, radiological surveillance, or disease burden assessment using quantitative ctDNA levels alone. Instead, ctDNA should be viewed as a complementary tool that strengthens clinical decision making alongside pathology, imaging, and multidisciplinary evaluation.

Evidence highlighted within the guideline demonstrates meaningful clinical utility across multiple cancers, including earlier initiation of targeted therapy in non small cell lung cancer, reduced chemotherapy exposure in selected patients with stage II colon cancer, earlier endocrine therapy adaptation in metastatic breast cancer, MRD guided immunotherapy in muscle invasive bladder cancer, and an emerging role for treatment response assessment and molecular residual disease detection in lymphoma.

This guideline marks an important milestone for molecular oncology. The future of precision cancer care is not tissue biopsy versus liquid biopsy. It is choosing the right test, for the right patient, at the right time.

**NEW GUIDELINE ALERT**  
**ASCO 2026 Clinical Practice Guideline**  
**Circulating Tumor DNA (ctDNA) Testing**  
**in Solid Tumors & Lymphoma**  
 Published: June 18, 2026

**WHEN SHOULD YOU USE ctDNA?**  
**Appropriate Uses**  
 Tissue biopsy is difficult, unsafe or insufficient  
 Tissue results will not be available within a clinically actionable time frame  
 Regulatory-approved companion diagnostic permits ctDNA testing (or is required)  
 When a positive result directly changes clinical management

**WHEN SHOULD ctDNA NOT BE USED?**  
 As a replacement for standard imaging  
 As the only surveillance modality  
 As a substitute for tissue biopsy in routine practice  
 To estimate tumour burden using ctDNA concentration alone  
 When results will not alter treatment

**CLINICAL WORKFLOW: INTEGRATING ctDNA TESTING**  
 Patient with cancer  
 Need molecular profiling?  
 Is tissue available?  
 YES: Tissue available → Tissue NGS remains the standard → Consider ctDNA as complementary when clinically useful  
 NO / Unsafe biopsy / Inadequate tissue → Perform ctDNA testing → Positive actionable mutation → Initiate evidence-based targeted therapy  
 Negative or inconclusive result → Perform tissue biopsy whenever feasible  
 Negative ctDNA DOES NOT exclude actionable disease. Tissue confirmation is recommended whenever feasible.

**FIVE MAJOR ASCO TAKE-HOME MESSAGES**  
 1. Test only when results will change management.  
 2. Tissue remains the gold standard for diagnosis and molecular profiling.  
 3. ctDNA complements, not replaces, clinical decision-making.  
 4. Negative or inconclusive ctDNA requires tissue confirmation whenever feasible.  
 5. Quantitative ctDNA levels (fraction, percentage or concentration) alone should not guide treatment decisions.

**LYMPHOMA: CURRENT ROLE OF ctDNA**  
 Baseline molecular profiling  
 Supports genomic characterization when tissue is limited.  
 Treatment response assessment  
 Dynamic ctDNA decline correlates with response in several studies.  
 Minimal residual disease (MRD)  
 Highly promising for early relapse detection. Routine implementation still requires disease-specific evidence.  
 Clinical caution  
 ctDNA should complement, not replace, tissue biopsy and PET-CT in lymphoma.

**PRACTICE-CHANGING EVIDENCE: SELECT EXAMPLES FROM THE LITERATURE**  
 NON-SMALL CELL LUNG CANCER (NSCLC): Earlier molecular results → Earlier initiation of targeted therapy; ctDNA-guided adjuvant chemotherapy → Shorter time to treatment and improved outcomes in multiple studies; Reduced chemotherapy use → Maintained recurrence-free survival.  
 STAGE II COLON CANCER: ctDNA-guided adjuvant chemotherapy → De-escalation of chemotherapy without compromising outcomes in selected patients.  
 METASTATIC BREAST CANCER (ER+/HER2-): Early ESR1 mutation detection → Earlier endocrine therapy adaptation → Improved progression-free survival.  
 Lymphoma: ctDNA decline during treatment → Correlates with response; Early relapse detection with rising ctDNA → Earlier adaptation of therapy improves disease control.  
 MUSCLE-INVASIVE BLADDER CANCER: MRD-positive patients after surgery → Benefit from adjuvant immunotherapy → Improved disease-free survival in ctDNA-guided strategies.

ASCO Clinical Practice Guideline  
 Evidence based. Patient centered. Expert driven.  
 Read the full guideline and accompanying materials at [www.asco.org/molecular-testing-and-biomarkers-guidelines](http://www.asco.org/molecular-testing-and-biomarkers-guidelines)  
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