FORESIGHT DIAGNOSTICS

ASH 2023
Presentation Summaries

Foresight Diagnostic's PhasED-Seq™ ultra-sensitive ctDNA platform has been studied in B-cell malignancies for its **prognostic value** and as a **surrogate endpoint** for earlier and more accurate response assessment vs. radiographic imaging in clinical trials.

Research Highlights:

MRD measurements at most time points before, during, and at end of treatment were **significantly more prognostic** than PET/CT.

Ultra-sensitive ctDNA measurement using PhasED-Seq™ enabled end-of-treatment (EOT) response assessment **12 months earlier** than using PET/CT-based PFS alone.

Improving the limit of detection (LOD) for ctDNA-MRD down to **1 in 1,000,000** improves prediction of clinical outcomes **across multiple timepoints** (pre-treatment through EOT).

Publication 1

Circulating Tumor DNA Dynamics as Early Outcome Predictors for Lisocabtagene Maraleucel as Second-Line Therapy for Large B-Cell Lymphoma from the Phase 3 TRANSFORM Study

Stepan L, Ansari S, Okal A, et al. Blood. 2023;142(Supplement 1):225-225. doi:10.1182/blood-2023-181007

- In this presentation, a retrospective analysis of Celgene's (a Bristol-Myers Squibb company) TRANSFORM study demonstrated MRD as a predictor of response as early as fifteen days following second-line lisocabtagene maraleucel (liso-cel) therapy.
- Achieving undetectable ctDNA status as early as Day 15 and Month 3 was strongly correlated with CR and longer EFS, enabling early prediction of durable clinical benefit. Non-responders did not achieve a sufficient reduction of MRD levels.
- All patients with complete response by imaging at M12 who were MRD positive went on to experience an EFS event, indicating the prognostic value of ctDNA beyond PET/CT.

Figure 1:

Achieving undetectable ctDNA status after liso-cel treatment strongly correlated with longer EFS

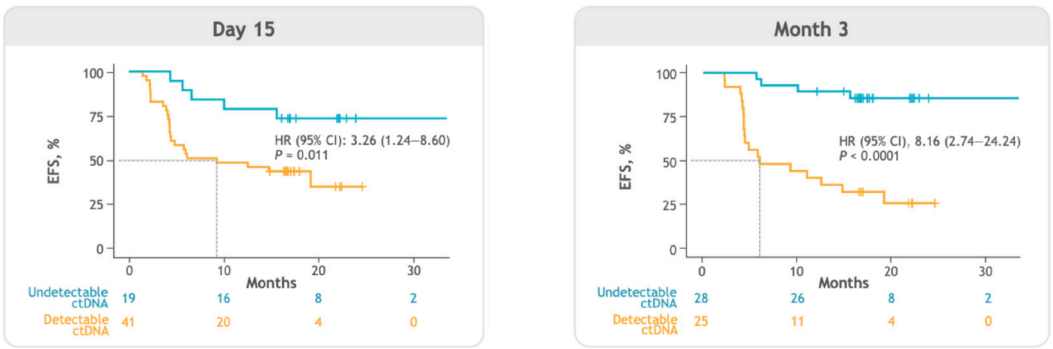


Figure 2:

ctDNA positivity identified patients with CR by PET/CT who were at risk for relapse

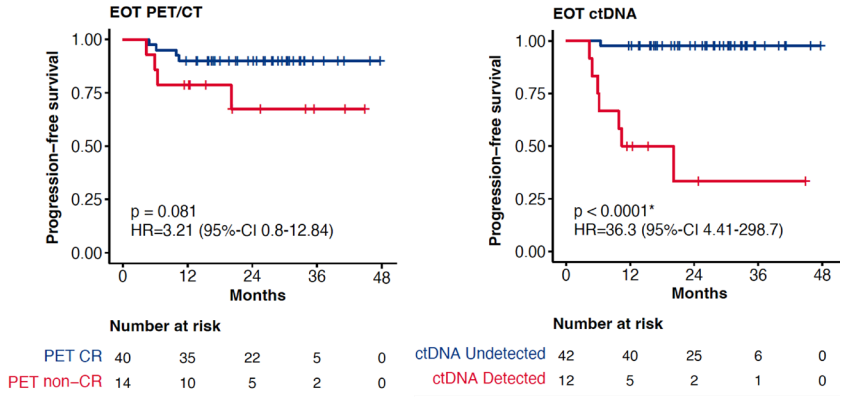
Publication 2

End-of-Treatment Response Assessment after Frontline Therapy for Aggressive B-Cell Lymphoma: Landmark Comparison of a Singular PET/CT Scan Versus Ultrasensitive Circulating Tumor DNA

Roschewski M, Lindenberg L, Mena E, et al. Blood. 2023;142(Supplement 1):192-192. doi:10.1182/blood-2023-180007

- Response assessment to first-line DLBCL therapy relies on PET/CT scans and often requires additional tests and procedures (e.g., tissue biopsy, repeat PET/CT) to adjudicate positive findings prior to initiating additional treatment.
- In a prospective study comparing PET/CT and ctDNA-MRD detection at end of treatment, ctDNA-MRD was a significant predictor of 2-year PFS overall and in PET/CT positive cases. In contrast, PET/CT did not significantly predict 2-year PFS.
- These results suggest that integration of ctDNA-MRD testing in response assessment may both reduce unnecessary additional tests and minimize overtreatment of patients who are PET/CT positive at EOT.

Comparison of end-of-treatment PET/CT complete response vs. detectable ctDNA-MRD



Publication 3

Optimizing Circulating Tumor DNA Limits of Detection for DLBCL during First Line Therapy

Goldstein J, Kim WS, Yoon SE, et al. Blood. 2023;142(Supplement 1):187-187. doi:10.1182/blood-2023-187759

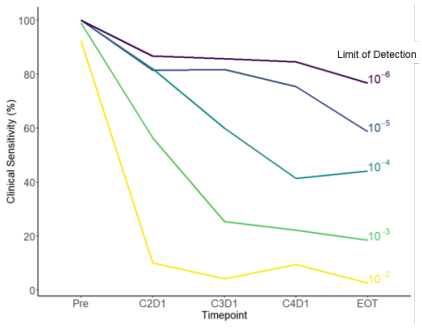
- The relationship between the analytical sensitivity of ctDNA assays (limits of detection ranging from 1 in 100 through 1 in 1,000,000) and clinical sensitivity (prediction of clinical outcomes) was modeled using data from 6 LBCL cohorts (first-line anthracycline-based treatment; pre-treatment, C2D1, C3D1, M4D1, and EOT timepoints).
- ctDNA-MRD assessment predicted outcomes at all time points, with the greatest prognostic value observed at later timepoints; for C3D1-EOT timepoints, clinical sensitivity improved with analytical sensitivity down to 1 in 1,000,000.

- Additional modeling showed that ctDNA-MRD detection with PhasED-seq at EOT could enable response assessment up to 12 months earlier than PET/CT-based PFS; using ctDNA as a modified endpoint for PFS could reduce clinical trial timelines by up to 65%.

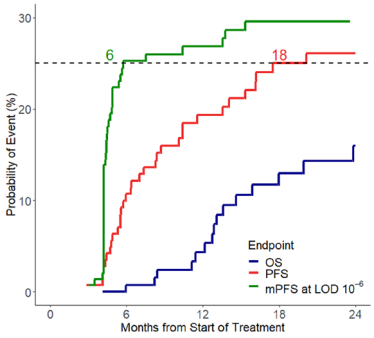
Modified PFS (mPFS)

A proposed surrogate endpoint for PFS in clinical trials that utilizes ctDNA levels at end of treatment to assess response earlier and accelerate clinical trial timelines

Clinical Sensitivity by Assay Limit of Detection and Timepoint



Probability of 25% Event Occurrence: Predicted PFS by ctDNA vs. imaging-based PFS and OS



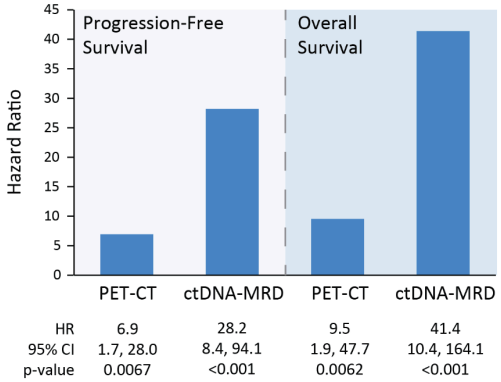
Publication 4

Prognostic Utility of Minimal Residual Disease (MRD) after Curative Intent Induction Therapy for DLBCL: A Prospective Real-World ctDNA Study

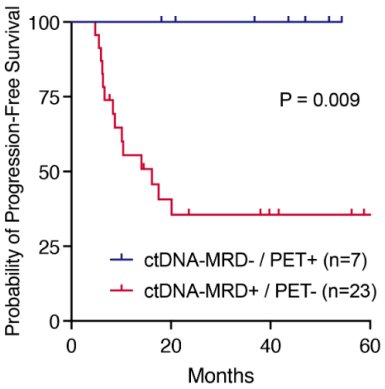
Sworder BJ, Yoon SE, Kim SJ, et al. Blood. 2023;142(Supplement 1):69-69. doi:10.1182/blood-2023-187650

- This prospective real-world study found that ctDNA-MRD levels were prognostic for both progression-free survival and overall survival at interim (during treatment) and EOT timepoints.
- ctDNA-MRD assessment outperformed PET/CT response assessment at interim and EOT timepoints. Only ctDNA-MRD assessment was a significant predictor of overall survival in multivariate analysis.
- When this cohort was combined with a pooled analysis of 5 LBCL studies, ctDNA-MRD status was highly prognostic in cases with discordant ctDNA-MRD and PET/CT at EOT, which suggests opportunities for integration of such assays in lymphoma response criteria.

Hazard ratio comparison: Kaplan Meier survival analysis (prospective study)



Prognostic performance of ctDNA in cases with discordant PET/CT and ctDNA-MRD at EOT



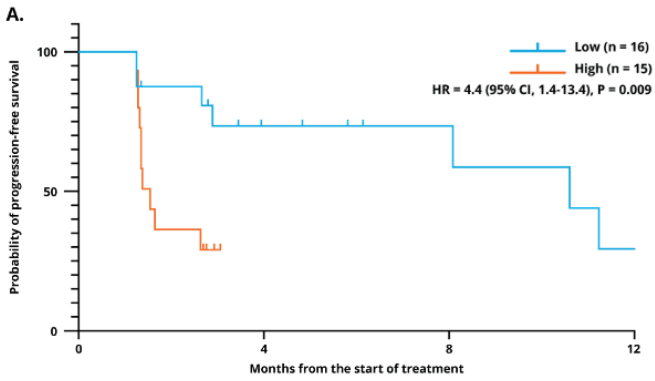
Publication 5

Early and Sustained Circulating Tumor DNA Response Dynamics after Loncastuximab Tesirine for Relapsed/ Refractory Diffuse Large B-Cell Lymphoma

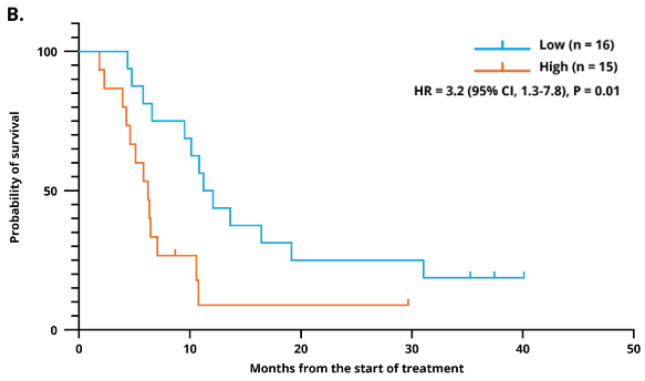
Kurtz DM, Hogan G, Schultz A, et al. Blood. 2023;142(Supplement 1):3133-3133. doi:10.1182/blood-2023-179977

- A retrospective analysis of ADC Therapeutic's loncastuximab tesirine (Lonca) therapy in relapsed/ refractory DLBCL after at least two cycles of prior therapy demonstrated that ctDNA levels can predict progression-free and overall survival as early as Cycle 2 Day 1, and molecular response can deepen with additional treatment cycles.
- These results point to the further consideration of ctDNA-MRD as a universal biomarker in patients with DLBCL treated with Lonca.

C2D1 ctDNA levels vs PFS



C2D1 ctDNA levels vs OS



Publication 6

Phased Variants Allow Robust Profiling of Circulating Tumor DNA in Untreated Follicular Lymphomas

Nagy Á, Bátai B, Hogan G, et al. Blood. 2023;142(Supplement 1):1626-1626. doi:10.1182/blood-2023-189824

- Despite lower baseline ctDNA levels in follicular lymphomas (FL) vs. in DLBCL, ctDNA-MRD testing with PhasED-seq enabled disease monitoring in 75% of patients, suggesting that plasma genotyping may serve as a surrogate when tissue samples are not available.
- ctDNA-MRD status after two cycles of therapy (C3D1) was significantly prognostic for progression-free survival.
- In patients with subsequent clinical relapse, detection of ctDNA-MRD occurred up to two years prior to clinical disease progression.

ctDNA levels at C3D1 Predict PFS