The ctMoniTR Project

ctDNA for Monitoring Treatment Response

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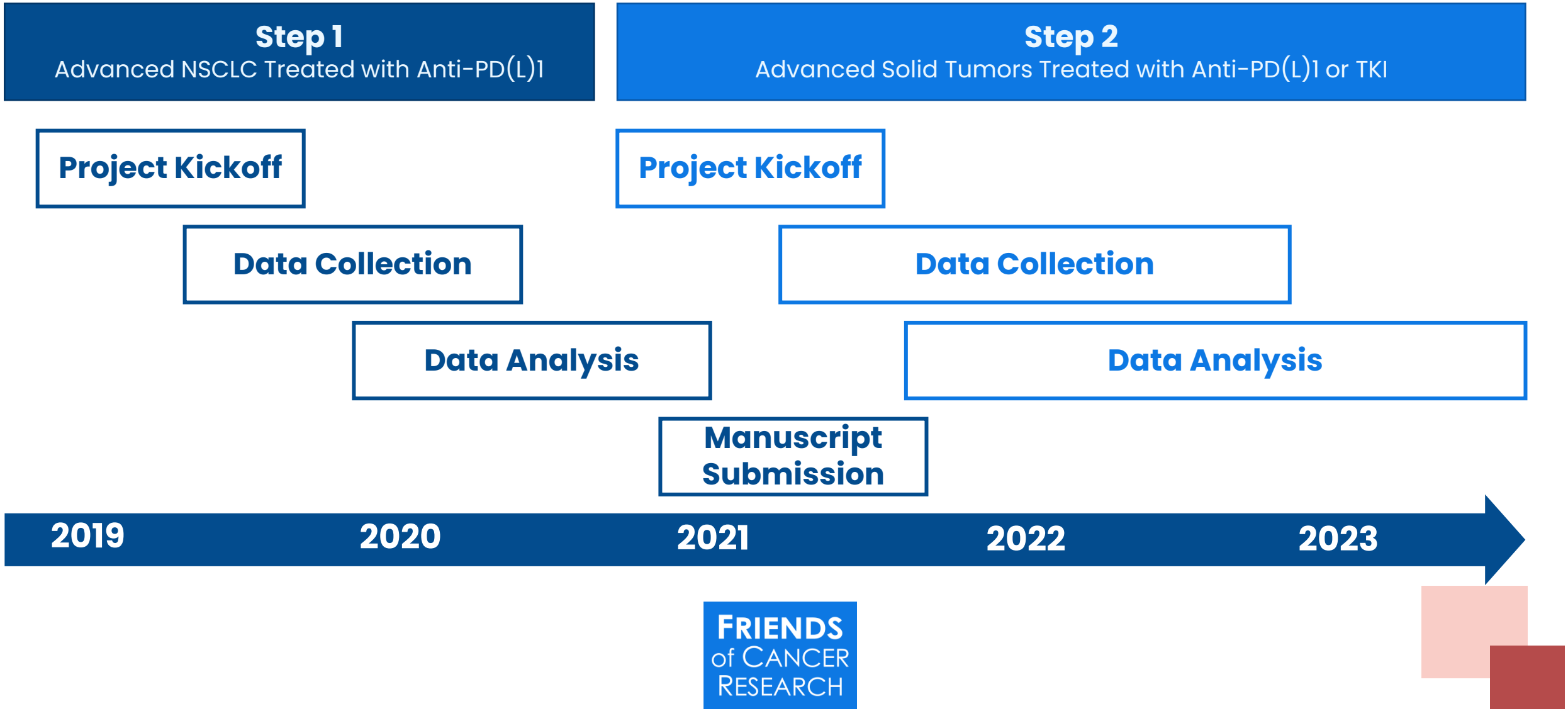
ctDNA for Monitoring Treatment Response (ctMoniTR) Project

Do changes in ctDNA levels accurately reflect the therapeutic effect of cancer therapies?



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ctMoniTR Project

Workflow	Step 1	Step 2
Outcomes	• Aligned on a methodology to combine data from multiple trials in lung cancer • Harmonized ctDNA data measured from different assays using different collection schedules • Manuscript forthcoming	• Update Step 1 methodology for combining data to account for additional treatment settings and tumor types • Harmonize ctDNA data from various uniformly collected datasets • Validate Step 1 findings
Approach	• Advanced stage NSCLC treated with PD-(L)1 inhibitors • Previously collected data from clinical trial and observational cohort studies	• Advanced solid tumors treated with PD-(L)1 inhibitors or TKI • Previously collected data from clinical trial and observational cohort studies

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ctMoniTR Step 1 Project Overview

Objectives

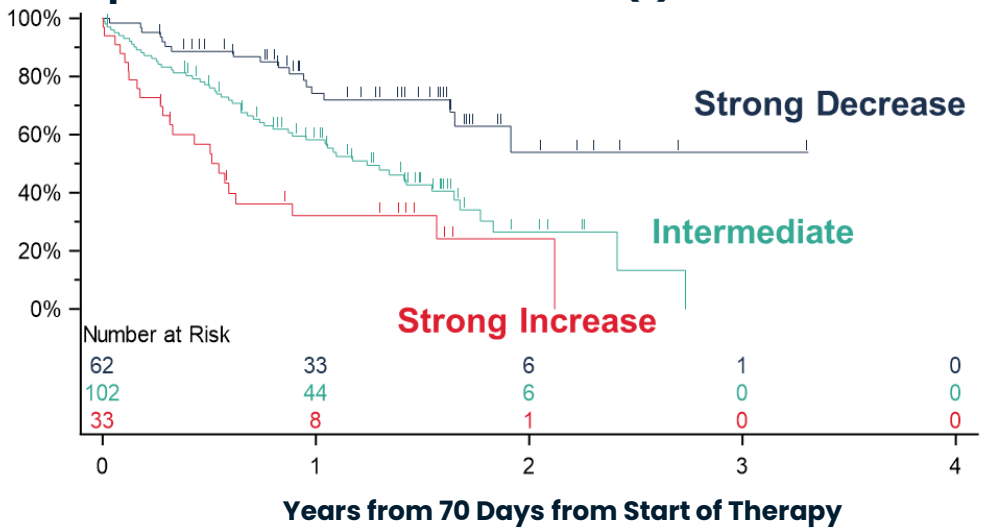
1. Investigate the feasibility of harmonizing ctDNA
2. Align on a methodology to combine clinical data from multiple trials
3. Characterize associations between ctDNA values and tumor response

Key Findings

1. Reductions in ctDNA are strongly associated with better clinical outcomes across multiple measures including OS and PFS
2. Baseline ctDNA levels alone were not predictive of clinical outcomes
3. Disparate datasets can be harmonized through statistical methods and other approaches

Strength of association remains after accounting for clinical covariates, demographics & smoking status

Overall Survival by ctDNA Max VAF 3-Level Change Groups in Patients With Anti-PD(L)1 treated NSCLC



Log-rank Pairwise p-value	Decrease	Intermediate	Increase
Decrease	-		
Intermediate	<0.001	-	
Increase	<0.001	0.014	-

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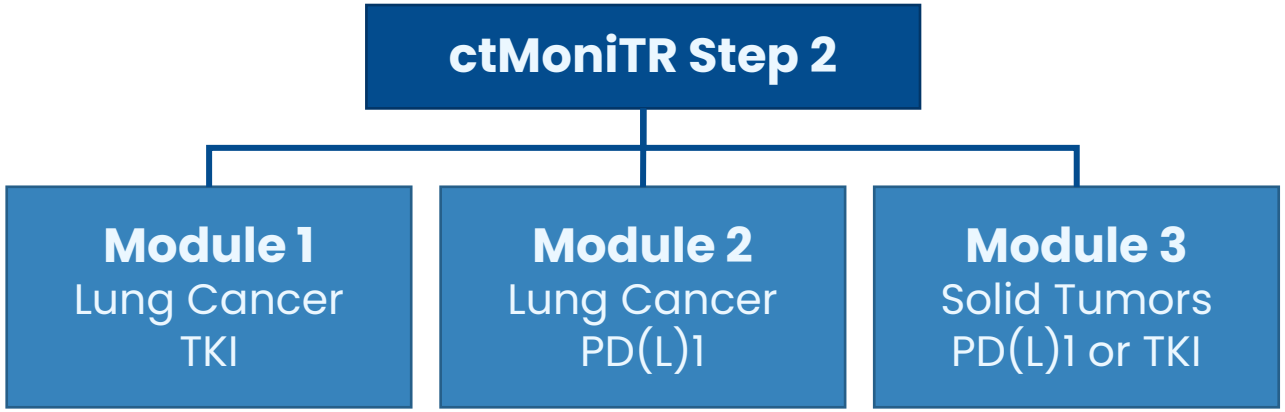
ctMoniTR Step 2 Project Overview

Objectives:

- Determine how long after treatment initiation an association between changes in ctDNA and clinical response can be detected
- Explore the extent to which ctDNA can complement RECIST
- Characterize whether changes in ctDNA are a prognostic indicator
- Examine ctDNA as a potential drug development tool or intermediate endpoint



22 clinical trials
3,000 patients
8 tumor types
16 different therapies

Provides an opportunity for generalizability but also represents a challenge in terms of complexity

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