On the Right TRACK: Operationalizing a National, Patient-Centric Fully Remote Precision Trial offering Comprehensive Genomic Profiling and a Molecular Tumor Board for Rare Cancers

TRACK TargetCancer Foundation
TARGET → RARE → CANCER → KNOWLEDGE

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TargetCancer Foundation

BACKGROUND

Patients with rare cancers are under-represented in precision medicine trials despite making up ~22% of cancer incidence. We created the TCF-001 TRACK (Target RAre Cancer Knowledge, NCT04504604) study to provide a home-based, patient-centered trial utilizing comprehensive genomic profiling (CGP) at enrollment and progression with review by a molecular tumor board (MTB).

MATERIALS AND METHODS

Patients with rare cancers (incidence<6/100,000) were enrolled and consented remotely (WCG IRB 1287011). Liquid (blood via mobile phlebotomy) and tissue biopsy samples were sent for CGP at Foundation Medicine. A fully remote MTB was convened following availability of each test. MTB notes and therapy recommendations were returned to patients and local physicians.

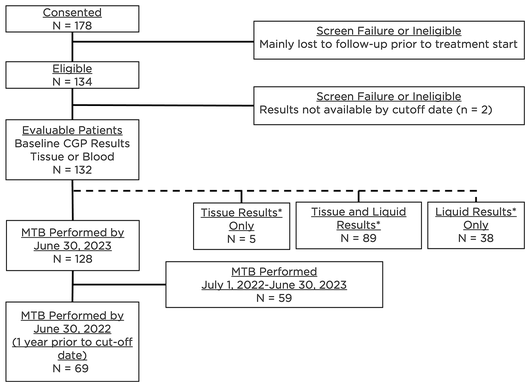

FIGURE 1: Patient Enrollment Flowchart. CGP indicates Comprehensive Genomic Profiling; MTB, Molecular Tumor Board.

**Genomic analyses limited to on-study results*

AFFILIATIONS

1. TargetCancer Foundation, Cambridge, **Massachusetts**, USA
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6. Department of Oncology, The Sidney Kimmel Comprehensive Cancer Center at The Johns Hopkins Hospital, Baltimore, **Maryland**, USA
7. Avera Cancer Institute, Sioux Falls, **South Dakota**, USA.
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9. Department of Pharmacy, The Sidney Kimmel Comprehensive Cancer Center at the Johns Hopkins Hospital, Baltimore, **Maryland**, USA
10. Rutgers New Jersey Medical School, Newark, **New Jersey**, USA
11. Medication Acquisition, Inc., San Diego, **California**, USA
12. Foundation Medicine, Inc., Boston, **Massachusetts**, USA
13. Sarah Cannon Research Institute, Nashville, **Tennessee**, USA
14. University of Nebraska, Omaha, Nebraska, USA (adjunct)
15. WIN Consortium for Precision Medicine

PATIENT CHARACTERISTICS

TABLE 1: All evaluable patients with on-study tissue and/or liquid CGP results.

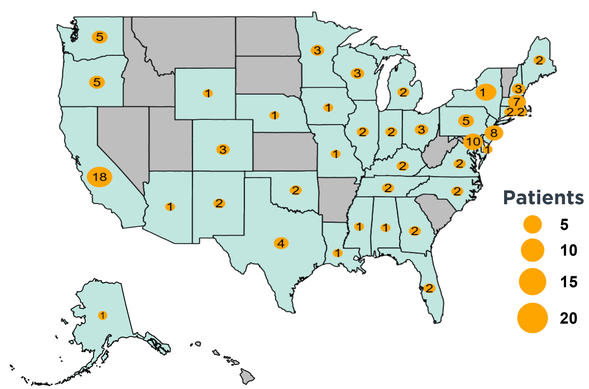
Characteristic	Overall (n=128)
Age, years, median [IQR]	56.0 [45.8, 63.3]
Male, n (%)	49.0 (38.3%)
Tumor Type, n (%)	
Cholangiocarcinoma	62 (48.4%)
Soft Tissue Tumor	24 (18.8%)
Gastrointestinal Tumors	21 (16.4%)
Others	21 (16.4%)
MSI Status, n (%)	
MS Stable	45 (35.2%)
MSI-H	1 (0.8%)
MSI unknown	80 (62.5%)
MSI-Equivocal	2 (1.6%)
TMB Score, median [IQR] (n = 51)	2.5 [1.3, 2.5]
bTMB Score, median [IQR] (n= 126)	1.3 [0.0, 2.5]

MSI = microsatellite instability; (b)TMB = (blood) tumor mutational burden; IQR = interquartile range.

A total of 132 eligible patients with evaluable results were enrolled. Tissue and liquid biopsy results were available in 89 patients; tissue only in 5; liquid only in 38. 128 patients had an MTB before the June 30, 2023 cut-off date. There were >40 rare/ultra-rare cancers, including cholangiocarcinoma (62) and soft tissue tumors (24).

GEOGRAPHIC DISTRIBUTION OF PATIENTS

FIGURE 2: Geographic Distribution of Eligible Patients. Out of the 134 eligible patients, 38 states are represented. An additional patient was found to reside in Canada after enrollment (not shown).



GENOMIC LANDSCAPE IN TISSUE AND LIQUID

FIGURE 4: Landscape of Genetic Alterations in On-Study Tissue Samples. A total of 61 patients with on-study tissue samples are shown, grouped by tumor type.

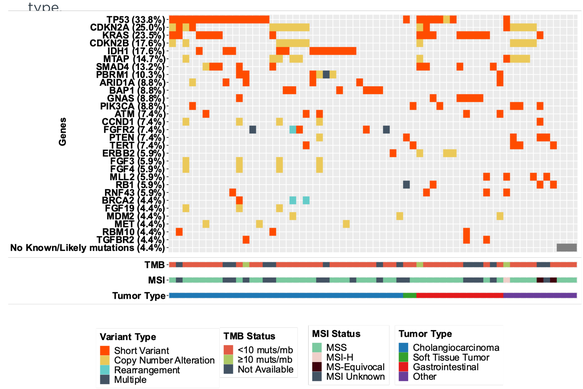
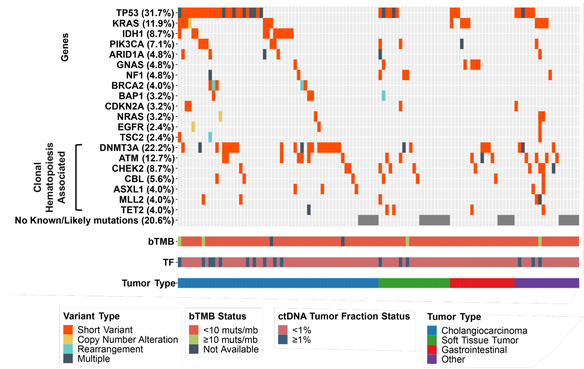
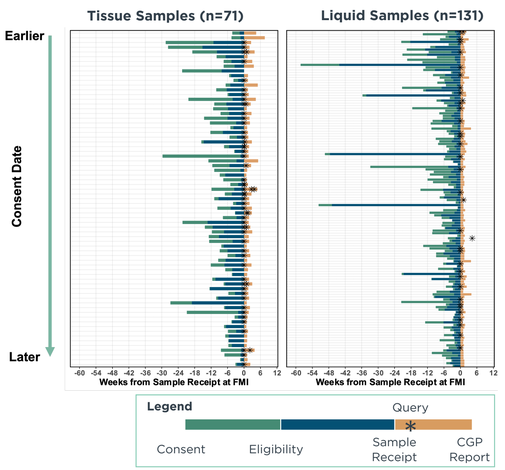


FIGURE 5: Landscape of Genetic Alterations in On-Study Liquid Samples. A total of 118 patients with on-study liquid samples are shown, grouped by tumor type. Genes associated with clonal hematopoiesis are separated below.



CHALLENGES IN A DECENTRALIZED TRIAL

FIGURE 3: Turn-around-time from Patient Consent to CGP Report Date.



Liquid biopsy results were available more quickly than tissue (median processing time, 9.1 vs 13.3 days); time from submission to processing was shorter for blood than tissue (2.4 vs 4.9 weeks). TRACK staff encountered 0.94 queries/sample (e.g., missing date of birth, etc.). MTB recommendations based on CGP were generated for 87.5% of the 128 patients presented.

TISSUE/LIQUID CONCORDANCE

No patients had identical molecular alterations. The median number of pathogenic alterations per tissue sample was 3 (range: 0-14) and liquid was 2 (range: 0-40). Three patients had no pathogenic alterations on tissue or liquid CGP. The sensitivity of liquid biopsy for pathogenic alterations found in tissue was 89.3% (25/28) for patients with ctDNA tumor fraction (TF) ≥1% and 28.1% (43/153) for TF <1%.

CONCLUSIONS AND LESSONS LEARNED

- A fully remote, advocacy driven, national precision genomics trial is feasible for managing rare cancers.
- The lack of designated on-site clinical research coordinators in a decentralized model leads to numerous queries (from Foundation Medicine back to TRACK team) that require resolution by trial and/or laboratory staff.
- Concordance between liquid and tissue samples is high when ctDNA TF is ≥1%.
- CGP with expert MTB review can identify potentially targetable alterations and inform therapeutic options.
- For more information about TRACK (NCT04504604), contact: info@targetcancerfoundation.org