Utilizing Targeted Enhanced-Whole-Genome Sequencing in Precision Oncology for the Treatment of Solid Tumors: A Clinical Perspective

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Background

Understanding the genomic landscape is essential for effective cancer management and treatment. Targeted panel sequencing (TPS) and whole exome sequencing (WES) have been key in identifying known mutations but cover only limited genetic regions, potentially missing significant insights. Recent advancements and cost reductions in whole-genome sequencing (WGS) provide a comprehensive alternative, examining the entire genomic landscape and capturing both common and rare mutations, including those in non-coding regions that may influence cancer management. This shift enhances cancer treatment precision by offering a more complete genetic profile, paving the way for personalized medicine.

Methods

This study retrospectively analyzed the genomic profiles and clinical data from the first 52 consecutive patients in Hong Kong and the US who underwent the CancerVision test as part of routine clinical management. The study adhered to exemption criteria per 45 CFR 46, category 4, under the Office for Human Research Protections Regulations, along with all participants consenting to genomic testing. Clinical data were provided by the referring physicians.

Tumor specimens were collected during standard care procedures and paired with matched normal blood samples. Genome sequencing, analysis, and interpretation were executed using the CancerVision platform, a target-enhanced whole genome assay (**Figure 1**), at Inocras, a CAP-accredited and CLIA-certified facility. DNA libraries were prepared using Watchmaker DNA Library Prep Kits (Watchmaker Genomics, Boulder, CO, USA) and sequenced on the Illumina NovaSeq 6000 or NovaSeq X Plus systems (Illumina Inc., San Diego, CA, USA), achieving an average depth of 40x for tumor samples and 20x for normal in WGS. For enhanced target coverage, tumor DNA libraries were captured using xGen Custom Hybridization Probes (IDT, Inc., Coralville, IA, USA) with a target size of 2.76 Mb, leading to an average sequencing depth of 500x.

The CancerVision test is validated for comprehensive oncologic genomic profiling, demonstrating 99.8% sensitivity for single nucleotide variants (SNVs) and 99.2% for insertions/deletions (indels), with positive predictive values of 99.3% and 98.7% for SNVs and indels, respectively. The clinical utility of the CancerVision test was assessed by evaluating its impact on targeted therapy selection, clinical trial eligibility, and diagnostic clarity.

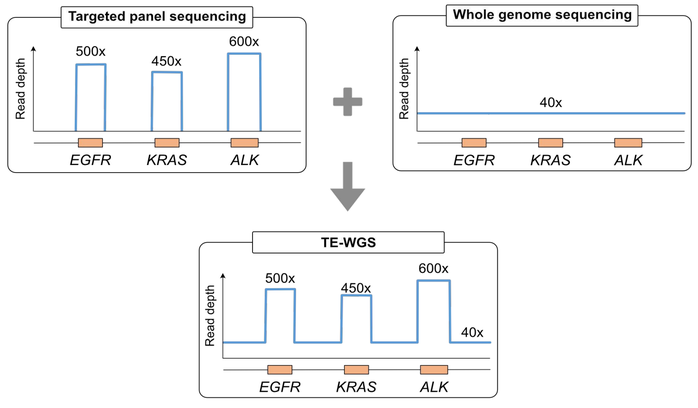

Figure 1: Target-Enhance Whole-Genome Sequencing (TE-WGS). This cartoon depicts TE-WGS, which combines a 40x coverage WGS backbone with a focused exploration of over 500x key biomarker genes.

Results

Patient Characteristics		
Age in years	Median	60
	Range	22-88
Sex	Male	22(42%)
	Female	30(58 %)
Tumor Type		n=52
	Breast cancer	3(6%)
	Colon cancer	14(27%)
	Glioblastoma	4(8%)
	Lung	6(12%)
	Prostate cancer	2 (4%)
	Rectal cancer	2(4%)
	Sarcoma	6(12%)
	Other	15(29%)

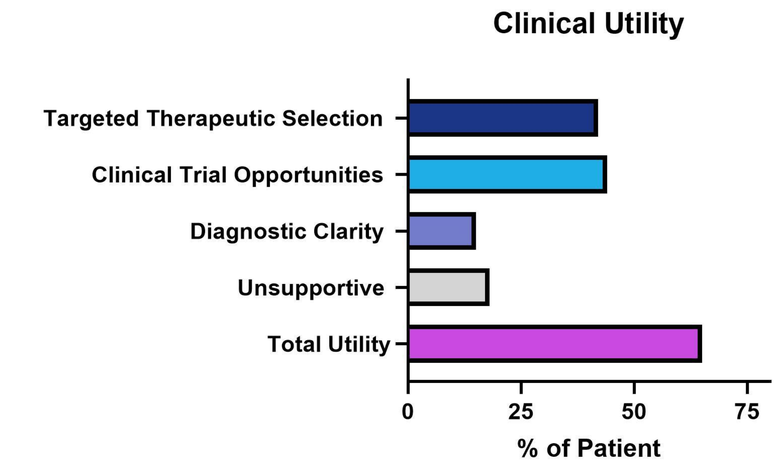

Figure 2: Total Clinical Utility represents the number of patients with genomic finding information Targeted Therapeutic Selection, Clinical Trial Opportunities, and/or Diagnostic clarity. Some patients are reported in more than one category of actionability

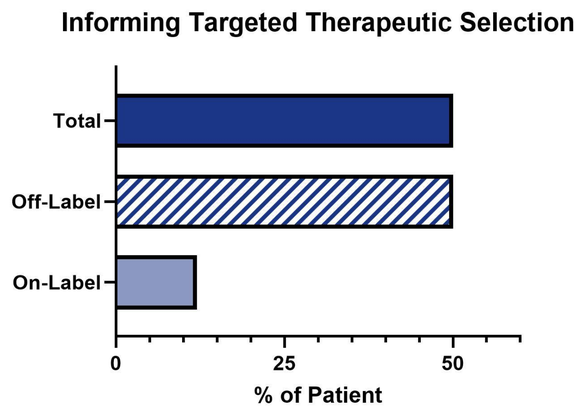

Figure 4: Targeted Therapeutic Selection indicates the number of patients with actionable findings for either on-label or off-label US FDA-approved therapies. Patients eligible for both on-label and off-label therapies are counted only once, as reflected in the total bar.

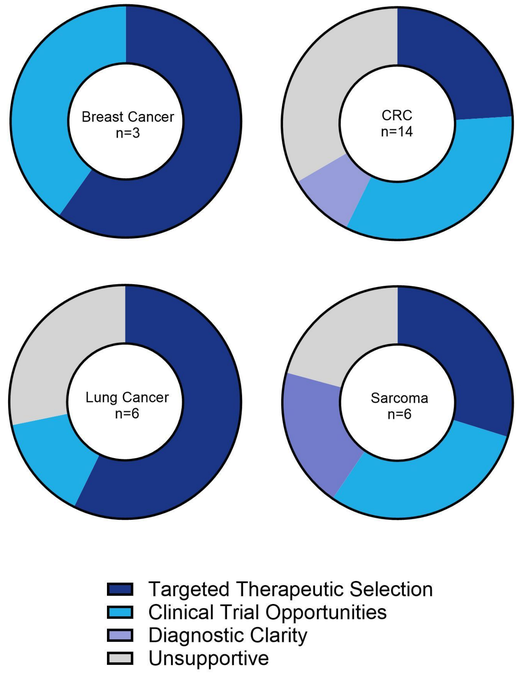

Figure 4: Clinical Utility by Disease State -The distribution of clinical utility categories across four cancer types: Breast Cancer (n=3), Colorectal Cancer (CRC, n=14), Lung Cancer (n=6), and Sarcoma (n=6). Clinical utility is categorized into Targeted Therapeutic Selection, Clinical Trial Opportunities, and Diagnostic Clarity. Each segment of the pie represents the proportion of patients within that cancer type who benefited from each category of actionable genomic findings. Some patients are reported in more than one category of actionability

Conclusion: CancerVision significantly enriches the genomic information accessible to clinicians, enhancing personalized treatment strategies in precision oncology through comprehensive and actionable genomic profiling.