Uncovering a Rare BRAF p.V600E Mutation in Breast Cancer Through Whole-Genome Sequencing: A Precision Medicine Approach

WonChul Lee[1],Ryul Kim[1], Ji-Yeon Kim[2], Erin Connolly-Strong[1], Yoon-La Choi[3], Young Seok Ju[1,4], Yeon Hee Park[2]

1. Inocras Inc., San Diego, California, United States 2. Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine 3. Department of Pathology and Translational Genomics, Samsung Medical Center, Sungkyunkwan University School of Medicine
4. Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology, Daejeon, South Korea

Introduction

Understanding the genomic landscape is critical for effective cancer management. Targeted panel sequencing, which typically focuses on frequently mutated genes in specific cancer types, may miss rare but clinically significant mutations. Recent advancements and cost reductions in whole-genome sequencing (WGS) provide a comprehensive alternative, allowing for the detection of common and rare mutations, including those in non-coding regions that may influence cancer progression and treatment response. WGS enhances cancer treatment precision by offering a comprehensive view of the genomic alterations driving disease.

Methods

A 41-year-old female presented with abdominal distension, weight loss, and jaundice. Diagnostic imaging and biopsy confirmed hormone receptor-positive (ER+/PR+/HER2-) breast cancer with metastases to the liver, peritoneum, and lymph nodes. Despite standard treatments, including hormone inhibitors and chemotherapy, her cancer progressed. Initial genetic testing for common mutations associated with breast cancer was negative, complicating treatment decisions. Given the limited response to standard therapies, comprehensive genomic testing using target-enhanced whole-genome sequencing (TE-WGS) (CancerVision, INOCRAS, San Diego, CA) was performed to identify potentially actionable mutations.

Results

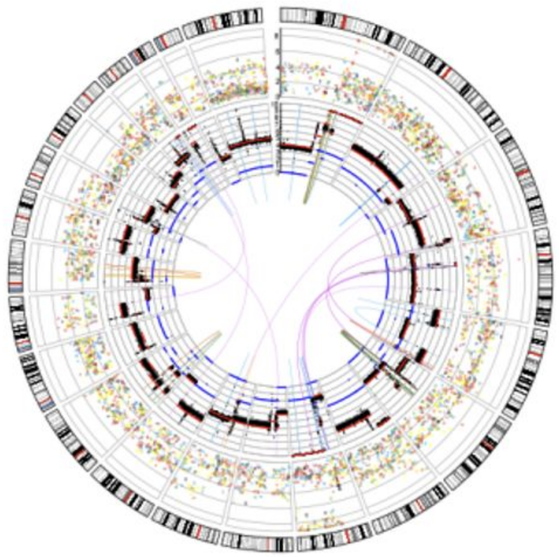

Figure 2. TE-WGS Genomic Findings Presented as a Circos Plot
Circos plot illustrating genome-wide alterations detected by TE-WGS, including structural variants, copy number variations, and mutational signatures.

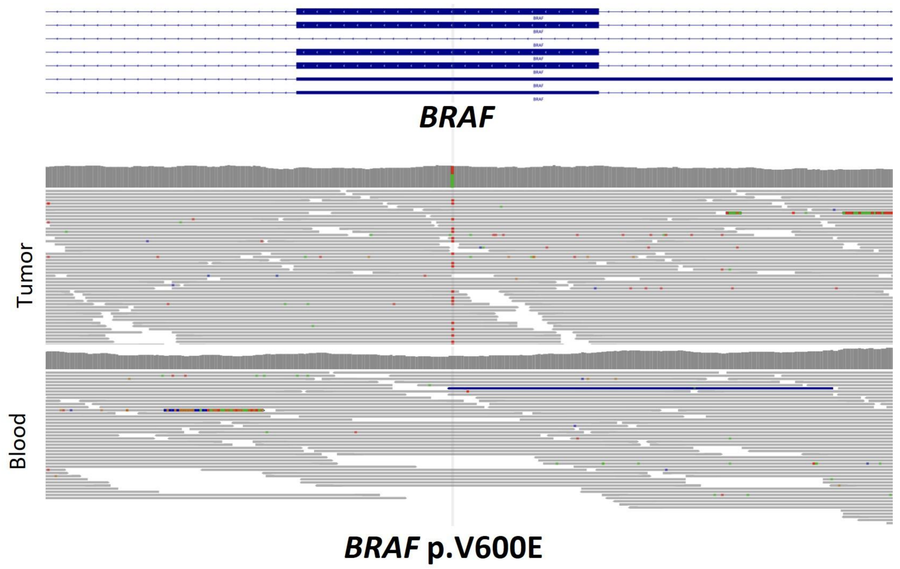

Figure 3. Genomic Visualization of *BRAF* p.V600E Mutation
Genome-wide sequencing and read alignment depicting the *BRAF* p.V600E variant in both tumor and blood samples. The visualization highlights the somatic nature of the mutation, with distinct variant reads in tumor tissue compared to normal blood. While *BRAF* p.V600E is a well-established driver in melanoma and colorectal cancer, its occurrence in breast cancer is exceedingly rare (0.11%). Its identification provided a critical therapeutic target, enabling the patient's enrollment in a precision oncology trial.

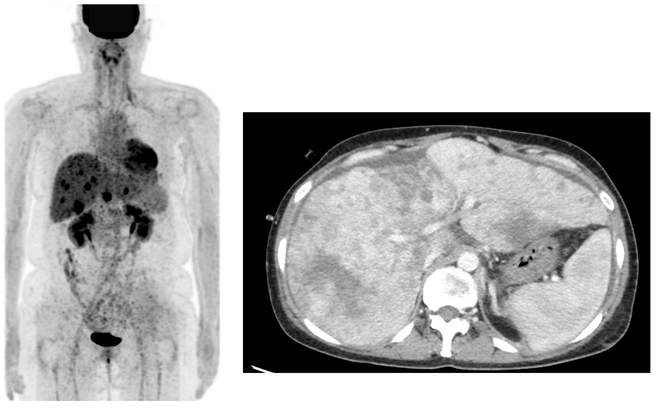

Figure 1. Imaging Findings : PET-CT scans demonstrating extensive metastases to the liver, peritoneum, and lymph nodes in a 41-year-old patient with hormone receptor-positive breast cancer. Disease progression despite standard therapy prompted further genomic investigation.

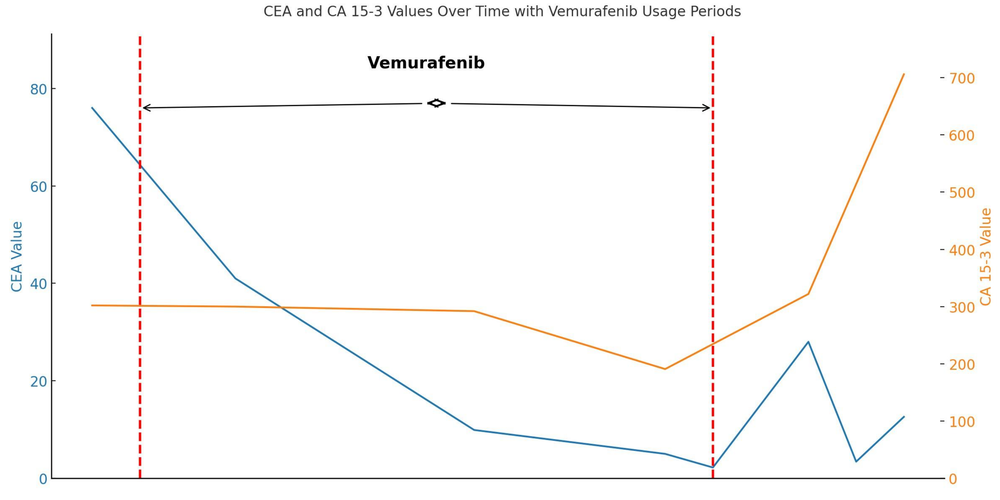

Figure 4. Longitudinal Tumor Marker Response to Vemurafenib Treatment
Graph illustrating dynamic changes in tumor markers (CEA, CA15-3) over the course of vemurafenib therapy. A rapid and sustained decline in biomarker levels correlates with clinical and radiologic tumor regression, indicating a therapeutic response. This case underscores the utility of WGS in detecting rare but actionable mutations, enabling precision-targeted intervention in an otherwise treatment-resistant breast cancer.

Conclusion: WGS potentially expands therapeutic possibilities by uncovering rare mutations, enabling precision-driven cancer care