CASE STUDY

Adopting a comprehensive genomic profiling (CGP) solution that meets the ordering oncologists' needs

"The FDA-cleared IVD solution offered immense value to my lab as it enabled a verification instead of full validation, a clear path to reimbursement and eliminated the need of a third-party vendor to generate reports."

Director of Genomic Pathology
at a premier integrated academic health system

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Summary

Implementing a comprehensive molecular profiling solution that addresses all of the relevant biomarkers—including those of emerging importance such as TMB—delivers accurate and actionable findings. This, in turn, empowers laboratories to gain the confidence of the treating oncologists, equipping them with the necessary insights to bring optimal care and the most effective treatments to patients.

The Laboratory

A part of a clinically integrated network of hospitals

This hospital network, situated in a large metropolitan area, offers specialty services in molecular diagnostics and cytogenetics, as part of a molecular profiling for solid tumors using a panel-based approach.

With the increasing number of actionable biomarkers and genomic signatures needed to comprehensively profile different tumor types, the panel that was at the core of our laboratory-developed molecular profiling test needed to expand in order to support our oncologists' needs.

KEY TAKEAWAYS

- Staying current with emerging biomarkers is a key challenge faced by diagnostic laboratories
- Tumor mutational burden (TMB) has been identified as a predictive biomarker associated with patient treatment response
- Adopting an FDA-cleared IVD enables laboratories, to deliver comprehensive reports while enabling operational efficiencies and path to reimbursement

labcorp

Labcorp Oncology offers a comprehensive test menu to assist in the diagnosis and management of patients with breast cancer throughout their continuum of care.

Tumor mutational burden (TMB): A key driver

In recent years, TMB has emerged as a predictive biomarker associated with a patient's response to checkpoint inhibitors. In the Phase II KEYNOTE-158 study, patients who had been previously treated for recurrent or metastatic cancers with high TMB status showed an improved objective response rate.[1] This genomic signature, defined as the number of somatic mutations per megabase (Mb) of interrogated genomic sequence, has been shown to be reliably estimated using broad next-generation-sequencing- based approaches.[2] This genomic signature, defined as the number of somatic mutations per megabase (Mb) of interrogated genomic sequence, has been shown to be reliably estimated using broad next-generation-sequencing- based approaches.[2]

With the growing interest in this emerging biomarker in addition to others already associated with approved therapies, oncologists are needing broader, more comprehensive reports that provide them with as much information to not only determine the best treatment course for their patient, but also to know the potential treatment response.

The solution

The FDA-cleared PGDx elio™ tissue complete assay

Driven by the need for a more comprehensive solution that includes TMB, we adopted the PGDx elioTM tissue complete solution. This assay-to- tiered-variant report solution enables a large, comprehensive FDA-cleared panel that detects SNVs, amplifications like ERBB2, and rearrangements in ALK, RET, and NTRK 2/3, and most importantly, reports on TMB and microsatellite instability or MSI.

Next-generation sequencing libraries are then sequenced on the NextSeq 550Dx platform and data is analyzed using the in vitro diagnostic (IVD) pipeline, generating an IVD summary report that is simple and easy to understand.

This tiered variant report, which follows the standards and guidelines for the interpretation of sequence variants,[3] provides both tier 1 variants with evidence of clinical significance and tier 2 variants with potential significance

The final report is then uploaded into the patient's electronic medical record, providing a comprehensive molecular profiling solution for solid tumors.

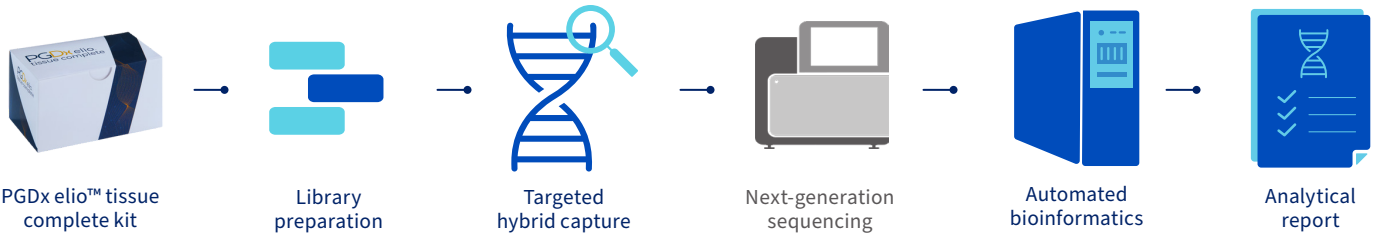

Fig 1. The PGDx elio tissue complete assay-to-report workflow

PGDx elio™ tissue complete
IVD Report

PGDx Personal Genome Diagnostics ™

Sample Name: PGDX31109T1_TMB2_X2

Tumor Type:	Other	**Run Quality Result:**	PASS	**Assay Name:**	PGDx elio tissue complete (03)
Sample Type:	Specimen	**Sample Quality Result:**	PASS	**Assay Version:**	2.3.0.0
Details:	(blank)	**Control Quality Result:**	PASS	**Platform Version:**	v1.6.0-9
Report Date:	2022-06-18	**Overall Case Quality Result:**	PASS	**Flow Cell ID:**	H3L27BGXM

Please refer to the Complete Case Record (CCR) for details on quality metrics

Summary of Results

Variant Category	Observation(s)
Variants with Evidence of Clinical Significance	4
Variants with Potential Clinical Significance	17

Variants with Evidence of Clinical Significance§

Genomic Signatures		
Signature	**Status/Score**	**Indications with Supporting Evidence**
Microsatellite Analysis	MSS	Solid Tumor
TMB Muts/Mb (Sequenced)	18.5	Pan-cancer

Sequence Mutation Analysis				
Gene	**Alteration**	**Consequence**	**MAF (%)**	**Indications with Supporting Evidence**
EGFR	Exon 19 deletion (E746_A750del)	In-frame Deletion	12.1	NSCLC
IDH1	R132S	Missense	12.3	CNS
MET	n/a	Splice site acceptor	18.3	NSCLC
PIK3CA	Q546E	Missense	8.2	Breast

Amplification Analysis		
Gene	**Alteration**	**Indications with Supporting Evidence**
No Amplifications with Evidence of Clinical Significance were detected.		

Translocation Analysis			
Gene	**Alteration**	**Partner**	**Indications with Supporting Evidence**
No Translocations with Evidence of Clinical Significance were detected.			

Fig 2. Sample IVD summary report

Addressing the need for TMB status reporting

With the increasing importance to report TMB alongside other biomarkers to help inform potential treatment response, it was critical to understand how the PGDx elio tissue complete test's TMB scoring and reporting matches up against the established comparator.

In a study performed by Deak et al[4] reported in the Journal of Molecular Diagnostics,[4,5] the team was able to establish a high concordance across the TMB scores generated by the PGDx elio tissue complete assay and the comparator NGS-based send-out assay, with a Pearson correlation coefficient of >0.95 and an area under the curve of 0.98.

Furthermore, based on linear regression, the team was able to demonstrate a correspondence between the comparator's TMB score of 10 mutations per megabase (Muts/Mb) and the PGDx elio tissue complete TMB score of 16 Muts/Mb (Figure 3). The difference in score thresholds is due to a combination of characteristics unique to each assay, including gene content, panel size (~1.3 Mb elio tissue complete vs. ~0.8 Mb FoundationOne® for TMB calculation), reporting rules, and filtering strategies such as germline call exclusion.[6]

This strong concordance data provides ordering oncologists the confidence in making treatment decisions based on accurate and comprehensive biomarker status, including TMB, to enable better patient outcomes.

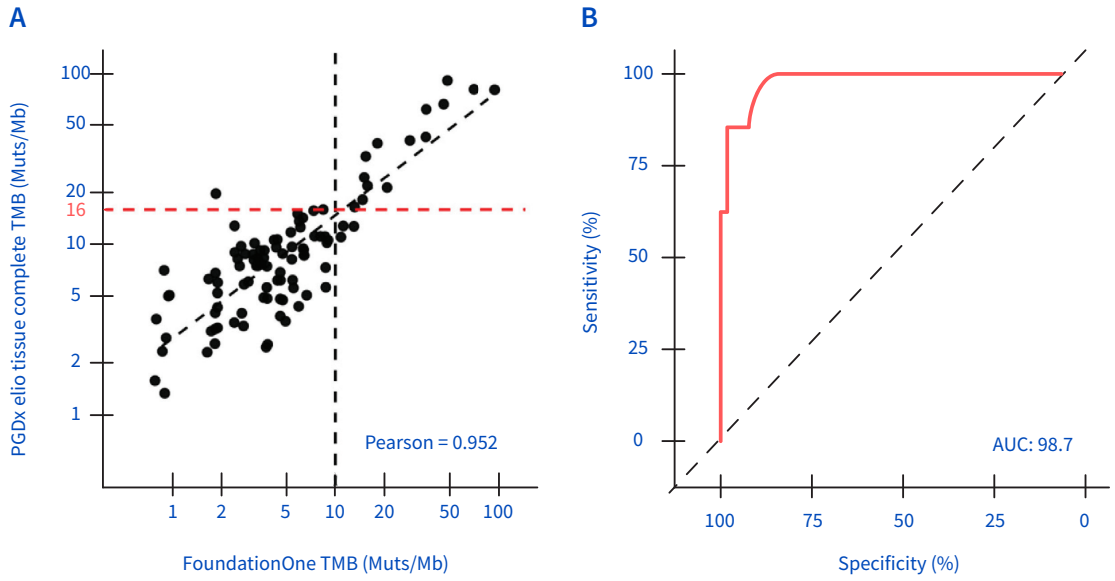

Fig 3. Concordance for reported TMB values

References

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