Paradigm PCDx™

Comprehensive Genomic Profiling, in record time

Accurate.

Clinically Proven.

Fast.

Paradigm

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Comprehensive genomic profiling, in record time

PCDx Comprehensive Genomic Profiling (CGP) provides precise information about the targetable cancer pathways in the tumor to allow for more effective clinical decision-making.

Challenges presented by current CGP solutions

Obtaining quality results on small tissue specimens

A large percentage of tumor biopsies that are received by molecular laboratories have either a limited amount of tissue (e.g. FNAs) or low tumor cellularity (e.g. samples with 5-10% tumor). These present practical challenges when attempting to run comprehensive genomic testing for many patients unless an accurate test such as PCDx is run.

Rapid turnaround time

Advanced stage cancer patients typically progress rapidly. Often these patients are unable to obtain their next course of therapy due to worsening of condition.[1,2] There is a clinical need to obtain your testing results as fast as possible.

Clinically meaningful results

Tissue should be tested to maximize potential treatment options. A large number of reports are generated citing either unactionable genomic findings or inapplicable clinical trials. This creates practical challenges and frustration to the treating clinician when deciding what to do next.

1. Von Hoff, D. D., et al., *Pilot study using molecular profiling of patients' tumors to find potential targets and select treatments for their refractory cancers.* Journal of Clinical Oncology, (2010) 28(33), 4877–83.

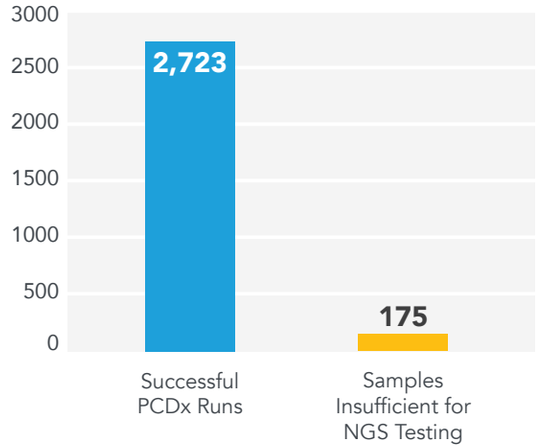
2, 3. Kalyan C. Mantripragada, et al., *Clinical Trial Accrual Targeting Genomic Alterations After Next-Generation Sequencing at a Non-National Cancer Institute–Designated Cancer Program.* Journal of Oncology Practice (2016) 12:4, e396-e404.

PCDx advantages

Comprehensive genomic profiling on small tissue specimens

With only 1/3rd of the sample failure rate of other leading NGS providers[3], Paradigm's success rate in profiling tumors with PCDx is 94%.[4] Through our proprietary library creation methods and other laboratory techniques that provide us with an average depth of coverage of >5000x, we obtain comprehensive genomic profiling results on small tissue specimens with limited tumor (e.g. 5-10%), including fine needle aspirates (FNAs).

Data on ~2900 sequential samples submitted for PCDx



- **123 PCDx Cases** Run and Reported with insufficient DNA and mRNA
- **52 PCDx cases** cancelled prior to testing due to insufficient tissue
- **94%** Sample Success Rate

Fastest turnaround time

Paradigm delivers clinical results to our clients in 4 to 5 business days from receipt of the tissue sample. Our laboratory processes have been engineered to ensure a reduced time to next therapy and continuity of clinical care.

Day 1
Sample is received and pathology confirms initial diagnosis with H&E.

Day 2
Tumor DNA & RNA are extracted, purified and quantified.

Day 3
DNA & RNA library creation.

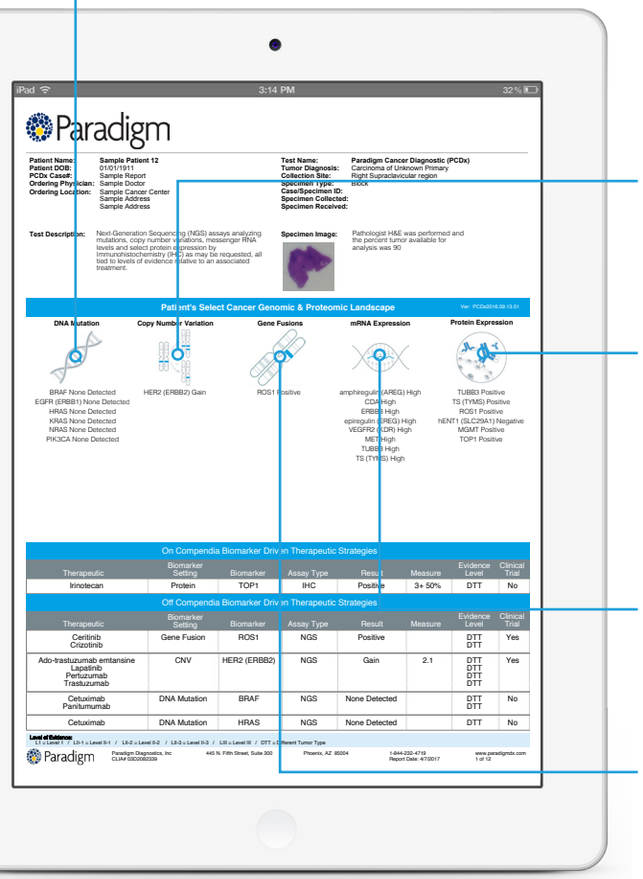
Day 4
Sequencing and IHC analysis.

Day 5
Clinical interpretation of results, quality assurance performed and clinical report delivered.

4, 6. Paradigm's sample rejection rate is approximately ~6% vs. 18% as seen for other leading NGS platforms (Matripragada et al. Journal of Oncology Practice. 2016). Paradigm internal data set and analysis on first 2700 patients run on the PCDx platform where only 175 patients had insufficient tissue for analysis.

Clinically proven & actionable

Paradigm PCDx is a comprehensive genomic profiling (CGP) test that interrogates the key drivers of cancer: **DNA, RNA and Protein**.



DNA Mutations

Changes in the DNA sequence, including insertions, deletions and base substitutions. Somatic mutation analysis has become standard of practice for solid tumors in order to identify therapeutic sensitizing and resistance mutations (e.g., EGFR, KRAS, BRAF).

Copy Number Variations

CNVs are alterations of the DNA of the cancer genome that result in the cell having abnormal copies of one or more sections of the DNA. These alterations can have a significant impact on response to therapy (e.g., HER2).

Protein Expression

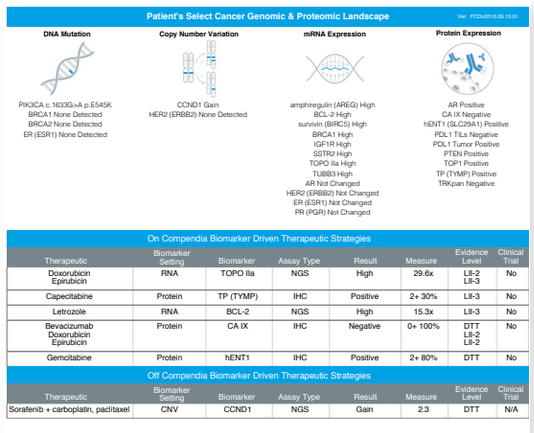
Changes in the protein expression as measured by IHC have been utilized for many years as the gold-standard to quantitate the actual translation of altered gene products. Our ability to interrogate key protein markers (e.g. PD-L1, HER2, AR, MGMT, TOP1) provides insights on potential response to hormonal manipulations, cytotoxic, targeted, and immuno-oncology agents as well as emerging clinical trials.

mRNA Expression

Gene expression is the process by which information from a gene is used in the synthesis of a functional protein. Sequencing-based mRNA expression analysis enables the significant multiplexing of biomarker targets (e.g., ER, ERCC1).

Rearrangements & Gene Fusions

Somatic rearrangements are usually result in the formation of a fusion gene, derived from two disrupted normal genes, from which a fusion transcript and protein is generated. (e.g., EML4-ALK)



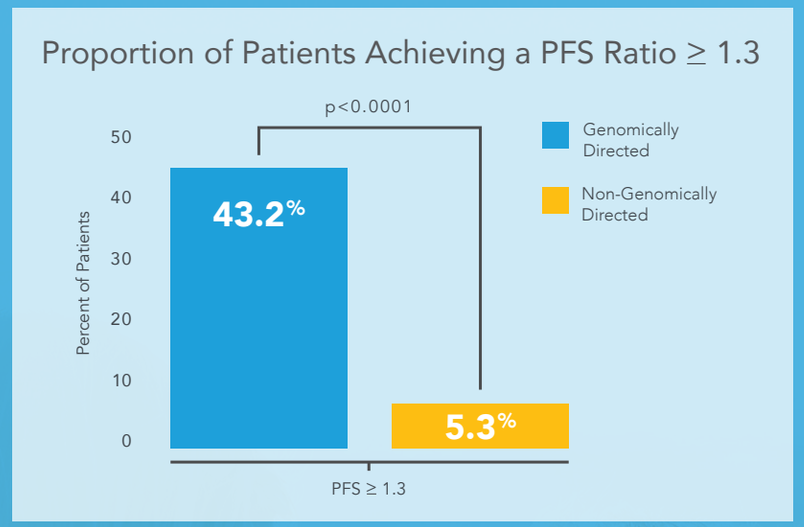
PCDx provides associations for the most drug therapies.

PCDx associates with >80 single agent drugs and combination therapies including:

- Standard Chemotherapies
- Hormonal Therapies
- Targeted Agents (TKIs and MABs)
- Immunotherapies
- Clinical Trials.

Supported by published clinical data

In an independent clinical study, genomically directed therapy guided by Paradigm PCDx improved progression free survival as compared to non-genomically guided therapy.[5]



Patients treated with genomically guided therapy had a superior median PFS compared to those treated with non-genomically guided therapy (86 days vs. 49 days, p=0.005, H.R.=0.55, 95% C.I.:0.37- 0.84).

5, 7. Radovich, M., et al., *Clinical benefit of a precision medicine based approach for guiding treatment of refractory cancers*. Oncotarget, (2016) 7(35), 56491–56500.

Accurate.

- 5000x average depth of coverage
- Low sample rejection (QNS) rates (6% vs. 18%)[6]

Clinically Proven.

- Analyzes Tumor DNA, RNA & Protein
- Prospective data published showing improvement in Progression Free Survival (PFS)[7]
- Provides associations to >80 single agent and combination therapies
- Full PCDx results possible from >5% tumor; including FNAs

Fast.

- Results delivered in 4 to 5 business days
- Reduces time to next therapy
- Ensures continuity of clinical care

PCDx can help identify the best cancer treatment options for you today.

Start getting better results, faster.

For more information, please contact Client Services at 844-232-4719 or visit paradigmdx.com

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