Leveraging Real-World Testing Data to Unlock the Promise of Precision Medicine

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Many patients are alive today who would not be if they had to rely on the one-size-fits-all treatment options that were not significantly increasing survival before the advent of precision medicine (PM). The power of PM derives from the data that characterize each individual patient. Having these specific datasets makes it possible to deliver precision treatments to patients most likely to benefit. Such precision requires accurate data. Much of the patient data and, therefore, information available are delivered through diagnostic testing. In an ideal PM universe, patients will receive the right test at the right time in order to identify the right treatment. However, despite the promise of PM, the adoption of companion diagnostic tests is typically delayed an average of four-and-a-half years following the launch of the associated precision drug.

Delays in Test Adoption Limit Potential of PM Treatments

Delays in test adoption are evidence that the current state of the precision testing ecosystem is suboptimal for realizing the potential of PM treatments. The lag time in test adoption indicates a clear knowledge and communication gap among many stakeholders, including prescribers, labs, *in vitro* diagnostic (IVD) manufactures, payers, and pharma companies. A cornerstone to addressing this gap involves data that are accurate and wisdom that can be drawn from the data to drive behavior changes.

At Diaceutics, we believe we are smart with our data. As a data analytics and implementation service provider in precision diagnostic commercialization, Diaceutics specializes in addressing that knowledge and communication gap among stakeholders in PM. We have had a special vantage point over precision testing during the past 14 years, incorporating analyses of real-world testing data and myriad experiences with purpose built in-market interventions to deliver better testing. Our beliefs today are simple: a radical improvement to the precision testing ecosystem can deliver equal or greater patient outcome benefit to that experienced with therapeutics alone — together, test and therapy are transformative, and the future incentives and capabilities to achieve this are now emerging.

What is Precision Testing?

An accurate assessment of precision testing begins with defining what precision testing is. In order to achieve more real-world data insights, we refined our definition of precision testing to include not just companion diagnostics but also complementary and conduit diagnostic tests — each of which key PM treatments depend on. (Companion diagnostics are required tests while complementary tests are not required. Both are included in the therapy label to guide in the selection of appropriate patients. Conduit tests are screening, diagnostic, or monitoring tests that help direct patients to the "right drug or therapeutic dose." They may or may not appear in the label.) Using this definition, we propose to assess the state of precision testing today by taking a disease-level view of non–small cell lung cancer (NSCLC) in the United States.

How far has precision testing in NSCLC come in the United States since the arrival of EGFR and ALK testing and precision treatments more than a decade ago? Consider the issues that still hold back progress, including disease-level diagnostic issues holding back PM, to explain why this results in more than 50% of cancer patients continuing to miss out on the precision treatments that can save their lives. This focused perspective will help illustrate the problems in the precision testing ecosystem as NSCLC reveals the major complex dynamics at work today in PM, including delayed diagnosis despite availability of new high-value precision treatments, evolving understanding of disease, fragmented stakeholders, siloed investment, wasted investment, imperfect information flows, and the absence of a standard optimal approach to precision testing for all NSCLC patients.

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Breakthroughs in extracting and analyzing real-world testing data (some driven by Diaceutics), versus merely a focus on oncologists' prescribing behavior, have opened up the ability to better understand and segment patients' diagnostic and treatment journeys. Segmenting physicians with high NSCLC caseloads by testing behavior helps us understand current and future education needs at an individual physician level. Understanding physicians' testing versus prescribing behavior will also identify more urgent key areas for improvement (e.g., the continued prescribing of PM treatments to 10% of patients with NSCLC without relevant test).

The Role of Smart Data

The role of smart data in addressing current issues in the precision testing ecosystem and achieving the potential of PM can be appreciated by looking at the effect of PM in the treatment of NSCLC, for which PM has made significant inroads during the last decade.

Among these advances are the improvements in precision testing with the shift toward next-generation sequencing (NGS) testing, as well as the development of six actionable biomarkers for NSCLC (i.e. EGFR, ALK, ROS1, PD-L1, BRAF, and NTRK) and their inclusion within NGS panels today. NGS continues to be adopted by those testing labs offering the most common biomarkers. For example, 67% of labs in the United States offering EGFR testing (the most established NSCLC companion biomarker) are now using NGS methods.

Among the aforementioned actionable biomarkers, NTRK in particular highlights advances in the treatment of NSCLC (and solid tumors). Following the recent FDA approval of larotrectinib for solid tumors with NTRK gene fusions, NSCLC can now be treated with pan cancer drugs, signaling the arrival of yet another new testing horizon potentially eliminating the lag that comes with sequential indication approvals.

Similarly, the development and commercialization of liquid biopsy tests including all the key NSCLC biomarkers — including those listed above (except for PD-L1) — are now delivering actionable test results to patients who might otherwise miss out on treatment because of the well-documented difficulties with tumor sampling.

The fruits of non-competitive, collaborative support for testing within a disease area are clearly evident in the success of PD-L1 testing, in particular, in NSCLC. During the last four years we have seen the power of multiple pharma competitors simultaneously promoting PD-L1 testing in general as a companion diagnostic to their treatment (with varying degrees of buy-in). This disinterested promotion not only increased the volume of precision testing but also decreased — by half — the time it normally takes to get 80% of patients tested with a new biomarker (our definition of the optimal testing rate) from seven years to three years.

The Diaceutics' 6th Annual Pharma Precision Medicine Readiness Report published in October 2019 (the first of three in our *Axis for Change* manifesto) sought to shine a timely and reflective light on the broken precision testing ecosystem holding back patient access to precision therapy. In that 30,000-foot report, we suggested that while the march toward better precision treatments continues, the balkanization of precision testing that has evolved along organizational and national boundaries is not serving the needs of patients or industry. Further, we postulated that the real promise of precision testing will not be addressed by current diagnostic business models or incremental improvement, which hallmarked the first era of PM.

In our next report (available soon), we argue for an *Axis for Change*, altering the playing field and radically accelerating every patient's diagnostic journey towards precision therapy. Specifically, we identify the current four-and-a-half-year average time for full test diffusion as an unmet need for an open diagnostic commercialization platform.

At Diaceutics, we wish to enable collaboration among stakeholders around a new systems-level approach we believe can reduce patient diagnostic journeys from four-and-a-half years to months — by establishing an open diagnostic commercialization platform that enables an optimized approach to biomarker diffusion and new standards of diagnostic care for every patient. PV

Diaceutics PLC *is the precision diagnostic commercialization company for global pharmaceutical companies.*
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