Precision medicine in oncology: a promise worth keeping

On June 26, 2000, President Bill Clinton announced the completion of the first survey of the entire human genome and remarked:

> With this profound new knowledge, humankind is on the verge of gaining immense, new power to heal. Genome science will have a real impact on all of our lives – and even more, on the lives of our children. It will revolutionize the diagnosis, prevention and treatment of most, if not all, human diseases.\(^1\)

Thirteen years later, advances in genomics and proteomics (the study of proteins) indeed have triggered a movement beyond conventional “one size fits all” clinical approaches toward greater precision in the understanding and assessment of disease and the treatment of patients. In particular, molecular diagnostic testing allows patients to be stratified into subgroups based upon their susceptibility to disease or response to a particular medicine. Additionally, “targeted” drugs are being developed to treat disease by specifically attacking the pathways associated with identifiable markers of pathogenesis. This “personalized medicine” approach holds incredible promise – not only of improved patient care and disease prevention, but also the potential to lower healthcare costs.\(^2\)

To be sure, healthy skepticism exists about whether precision medicine will lead to more effective and affordable care. While we have made incredible technical advances, the complexity of disease biology has challenged the premise of rapid cure development. Moreover, associating biological and environmental risk factors to real world outcomes will be breathtakingly complex. Delicate policy issues, such as individual privacy, will have to be navigated. Additionally, the health system, including providers, infrastructure, reimbursement, and care delivery models, is not currently set up to optimize individualized care.

Oncology will continue to pace the advancement of precision medicine

While precision medicine may be more marathon than sprint, the oncology space has been and will continue to be at the forefront of its advancement. Increased understanding of cancer biology demands it. For example, “we now know that breast cancer is not one disease but is made up of at least 10 different molecular subtypes, each of which responds to treatment in markedly different ways because they are not the same disease at the molecular level.”\(^3\) Developers have responded to this complexity by designing drugs for specific subgroups of patients. Since Genentech’s Herceptin and companion HER-2 test received FDA approval in 1998, more and more drugs depend on the use of a diagnostic to meet their labeled safety and effectiveness claims.\(^4\) A 2010 study estimated that more than 60% of all drugs in preclinical development rely

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2. President’s Council of Advisors on Science and Technology (PCAST), *Priorities for Personalized Medicine* (Washington, DC, September 2008).
on biomarker data.\textsuperscript{5} While this is an important step towards precision medicine in oncology, significant technical, regulatory, and reimbursement challenges exist, especially with respect to the development and commercialization of cancer-biomarker tests.

**Challenges to sustained development of molecular diagnostics for oncology**

Reliable and effective diagnostics are critical to the future of cancer treatments. Based on the results of a diagnostic assay, healthcare providers and payers need to be able to determine whether a patient will benefit from a particular treatment. However, whether one considers companion diagnostics in their current “one test/one drug” form or as panels of multiple biomarkers, challenges threaten their innovation and utility. These challenges include:

- **The lack of an integrated framework for the valuation of therapeutics and their companion diagnostics.** Greater clarity and alignment across regulators, payers, industry, patients and providers on the definition of the value of a diagnostic and a shared understanding on the assessment and reward of that value is needed. Differences in how the therapeutic and diagnostic industries approach their respective business strategies make the development of an integrated shared value framework difficult.

- **The lack of an integrated system for tracking outcomes and downstream impact of diagnostics to determine their effectiveness and capture their true value.** There is a need for uniformity of evidence and real world validation of the effectiveness and impact of diagnostics on downstream outcomes in order to foster the safest climate for patients who rely upon their efficacy. In large part, regulators currently lack the authority to require evidence of improved clinical outcomes, i.e., clinical utility.\textsuperscript{6} Payers who lack proof of the ability of a diagnostic test to create better clinical or financial outcomes may be de-incentivized to cover their use.

- **The lack of a standardized regulatory review and quality control process for diagnostics.** Currently there are several regulatory pathways to market authorization in the United States including pre-market approval or clearance through the FDA as well as the Clinical Laboratory Improvement Amendments (CLIA) laboratory certification process for laboratory developed tests through CMS. These pathways have distinct evidence and labeling requirements, time to market, quality programs, and financial consequences.\textsuperscript{7} The result is that assays for the same biomarker(s) may have followed different clinical development pathways and regulatory approval mechanisms. The lack of harmonization across multiple regulatory pathways creates confusion over which path, if any, to take and introduces uncertainty over the quality of available tests.

- **An infrastructure that fails to incentivize the creation of new and innovative diagnostics.** The current regulatory framework creates a “free rider” problem in which the first company to succeed may enter the market earliest but will have taken all the risks, thereby effectively underwriting the qualification of that biomarker for competitors to use in reducing development costs, reducing regulatory


\textsuperscript{7} Personalized Medicine Coalition, “Personalized Medicine Regulation: Pathways For Oversight Of Diagnostics,” (Washington, DC: Personalized Medicine Coalition, 2010).
risks, and increasing speed to market. Moreover, reimbursement of molecular diagnostics through Current Procedure Terminology (CPT) codes is largely based upon the cost of a type of test rather than the clinical value of an individual test.

Creating a sustainable model for predictive oncology therapeutics and diagnostics

Tapestry Networks has convened the multi-stakeholder Sustainable Predictive Oncology Therapeutics and Diagnostics Working Group (SPOT/Dx WG) to address these challenges and consider new approaches to advance precision medicine in oncology. The group brings together key thought leaders and decision makers from the public and private sectors, including clinical and policy experts, regulators, third-party payers, patient advocates, and industry leaders. Working together through 2014, participants are committed to improving patient outcomes by equipping healthcare leaders with the tools to advance the diagnosis and treatment of cancer, clinical decision-making, and the regulatory/reimbursement infrastructure required to support a sustainable shift toward precision medicine.

The SPOT/Dx WG will identify two or three opportunity areas within this broader mission, understand what is needed to carry recommendations in these areas forward, and develop a pilot plan(s) to test/validate these recommendations. Key questions the group is considering include:

?- How to define the value that companion diagnostics and therapies deliver to the US healthcare system? What are the best approaches to measuring that value in the context of treatment decisions?

?- What are the key barriers to commercializing a common predictive panel of prospectively identified biomarkers?

?- What accommodations would be necessary to develop a panel of predictive markers that were discovered later in development?

All outputs from the SPOT/Dx WG will be shared openly to help progress the field and to encourage additional forms of public-private partnership.

About Tapestry Networks

Tapestry Networks’ mission is to advance society’s ability to govern and lead across the borders of sector, geography, and constituency. We form working partnerships that include the public and private sector, as well as civil society. The participants in our initiatives are leaders from key stakeholders who realize the status quo is neither desirable nor sustainable. Tapestry Networks is built on the premise that relatively small groups of well-positioned leaders, seeking a goal that transcends their own parochial interests and benefits everyone, can make progress toward that goal through the collaborative network-based approaches that Tapestry designs and leads. Please visit www.tapestrynetworks.com.

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