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Making Cancer Personal: A Roadmap

Personalized oncology holds out the promise of transforming cancer treatment. This represents a significant opportunity for healthcare industry players, and, importantly, may be considered a test case for personalized medicine more broadly. But this vision of personalized treatment will require the creation of a massive molecular-associations database.

With personalized oncology, treatments are matched to patients based on objectively measurable characteristics, such as tumor biomarkers. The building blocks of personalized oncology today are single tests such as companion diagnostics that address specific clinical questions (e.g., whether the patient is a candidate for a particular treatment). While useful, this one-test/one-decision model falls short of addressing patient needs.

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Oncology is not a simple genetic disease: Tumors are marked by their biological complexity, heterogeneity and genetic instability. A treatment regimen that shrinks one person's tumor may have no impact on another person's, and even within the same individual a treatment may appear to work while missing a cluster of resistant cells with a different genetic make-up. The promise of personalized oncology is that it could address such complexity over the disease's course.

The key to this transformative future is the creation of a massive molecular-associations database (and surrounding care delivery infrastructure). Creating such a database will require marrying longitudinal molecular, clinical and outcomes data from routine patient care. That will require surmounting the significant challenges of bringing together a lot of quality longitudinal data from a variety of places in a standardized form. Once such a database exists, however, it would be a living resource that is able to refine existing associations, and discover new ones, with real-world implications for patient care.

In this piece, we offer a road map that describes the various obstacles to creating holistic personalized oncology solutions and offer suggestions for how to overcome them.

A Vision For Personalized Oncology

Characterizing the molecular basis of disease and using the information for patient management is increasingly driving oncology care. Companion diagnostics and other personalized medicine diagnostics (such as Genomic Health's OncotypeDx for breast cancer) provide a partial view of a tumor's molecular

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composition and are used sporadically during the patient's journey to inform specific clinical decisions. This represents the one-test/one-decision model. But while these tests may be validated clinically, evidence is often based on trial data gleaned from only hundreds, or sometimes thousands, of patients, which may not be large enough to see more nuanced effects (e.g., subpopulation and regional variance).

Imagine a future where comprehensive molecular profiles are generated and tracked over time and married with longitudinal clinical and outcomes data for all patients with significant tumors. In essence, this could create a massive dataset of molecular associations with the scale and level of detail surpassing what any traditional clinical trial is able to provide.

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Such a dataset holds out the promise of guiding clinical decision-making (including identifying treatments for patients with limited options) as well as R&D efforts for new therapies. Furthermore, each new patient added to the dataset would enrich it, reinforcing and refining those associations. Armed with this more holistic resource, oncologists could create personalized treatment plans that evolve over the course of disease. That is the crux of where personalized oncology – and personalized medicine, more generally – is headed.

Breaking Through the Barriers

While many of the pieces for personalized oncology are already in place, the key to a more holistic model is the creation of a standardized, integrated and scaled dataset of longitudinal molecular, clinical and outcomes data that yields associations. This will require investments in tools, infrastructure and training, as well as new ways of thinking, particularly around economic incentives.

Key barriers include:

- **Creation of a standardized, integrated and scaled molecular-associations dataset.** Longitudinal molecular, clinical and outcomes data exist in silos, but are most valuable together. Standardization across many dimensions (e.g., specimen collection and processing, data structure, analysis and interpretation) will be critical to ensure effective dataset cross-talking. The dataset must be able to yield validated associations of meaningful impact to support patient care decisions.

- **Adoption of new diagnostic tools.** These new tools must be capable of profiling tumors upon diagnosis and monitoring them over time. This includes molecular profiling tools (e.g., NGS, mass spectrometry), liquid biopsy tools for circulating tumor DNA and tumor cell analysis (e.g., digital PCR, cell capture and analysis) and imaging tools.

- **Creation of healthcare information technology infrastructure.** Pieces of this infrastructure exist, but it must become capable of integration and analysis of disparate data sets. Big Data analytics from other data-intensive industries may be helpful.

- **Training of healthcare stakeholders.** Pathologists, oncologists, molecular geneticists and the like all need to become effective decision-makers within an increasingly data-rich environment. They need to understand when and how to use and implement the envisioned tools for maximum benefit. This may require a different way of looking at the practice of medicine that may not appeal to all doctors.

- **Aligning incentives.** In order to build a holistic solution all players must share the economic burden and take a long-term view. Incentive gaps, such as payers refusing to cover tests that benefit secondary insurers, such as pharmacy benefit managers (PBMs), must be addressed.

Innovative companies, care providers, academic institutions and governments must continue to invest in tools, health care IT infrastructure and training. We believe that these capabilities, while not there yet, will be able to support the holistic model in the long run. Aligning incentives is more challenging. That's especially the case in fragmented care situations where a payer/provider does not own the downstream impact of their patient management decisions and policies. Some payers (especially those that take on the full financial risk of a patient), however, may be able to differentiate themselves by taking a more holistic and long-term perspective.

While not to minimize the other challenges discussed above, in our view, building the standardized, integrated and scaled molecular-associations dataset remains the most challenging for several reasons. Simply put, you need to gather a lot of quality longitudinal data from a multitude of places in a standardized form on the assumption that it will yield useful associations.

The Importance of Data

Different types of data are held in different places – doctors have clinical data, insurers have outcomes data – yet those datasets are most valuable when they can be integrated. Some datasets, such as patient background and secondary literature, may be readily available. Others, such as the patient's molecular profile or claims information, are more difficult to access (especially longitudinally). One of the trickiest is tracking treatments and outcomes over time especially as patients move from one care setting to another (as is often the case when a patient seeks care in both community and academic settings). HIPAA privacy rules – and patients' valid privacy concerns – may also undermine efforts to create comprehensive datasets.

Since the data is most valuable in aggregate, the lack of incentives for sharing is a major barrier to personalized oncology. While some integrated providers are beginning to see value in a more holistic solution, patients also need to be prodded to share data. Questions remain about the type of incentives, both clinical and monetary, that could foster such sharing, as well as how to align those incentives for the long-term payoff.

While many have access to select data, select players appear to be well positioned to leverage their existing data – particularly the hard-to-get longitudinal treatment and outcomes data – into something that goes beyond where medical practice is today. These players include: integrated care providers, such as Kaiser Permanente, that are both payers and providers of healthcare; and large community oncology practices, such as US Oncology Network and RainTree Oncology Services, that have the massive scale and digital backbone required, and are now setting up partnerships that could allow them to incorporate claims and molecular data.

While it's unclear how long it will take to reach the utopian state of personalized oncology, and there already have been major missteps along the way, we believe it ultimately is

Table 1

The key to personalized medicine is data

In the table below, we lay out the different data sets required for a comprehensive approach to personalized medicine, and the difficulty of acquiring the information in each of them.

Data categories	Examples	Difficulty to acquire
Patient background	Demographics Medical and treatment history Family history Comorbidities	Easy (patient record/EMR)
Molecular profile	Routine diagnosis (e.g. imaging, basic pathology) Molecular diagnosis (e.g. genomic profile, biomarker screen)	Moderate (available from laboratory, but may be dispersed across labs and not digitized or standardized)
Treatment history	Therapy (e.g. agent, stop/start, duration) Surgery Other interventions	Moderate (patient record/EMR, but may be dispersed across care settings)
Outcomes	Therapy response Survival Quality of life Remission/recurrence	Difficult (non-standardized and lacking longitudinal view, especially when patients change care settings)
Secondary literature	Treatment guidelines Regulatory guidance Payer policies Clinical trial data/availability	Easy (available and increasingly digitized)
Claims/financials	Prescription claims Utilization	Moderate (available from insurer, but may be dispersed across carriers)

achievable. Visionary executives will need to find ways to break through the barriers set out above.

The payoff for those who can crack the code will be not only longer and better lives for millions of cancer sufferers, but competitive advantages and economic gains in a vast and growing market. Equally important, getting this right for cancer could offer valuable insights for better health management across a variety of diseases.

Table 2

The ways in which two oncology networks are building a personalized approach

Two large oncology networks—RainTree Oncology and US Oncology—are creating new treatment models that attempt to marry their rich patient longitudinal data with molecular profiles and insurance claims.

Network	Description	Molecular profiling data partner	Claims data (pharmacy claims)	Patient outcomes data
RainTree Oncology Services	Community oncology alliance with about 800 physicians in almost 50 practices nationwide	Life Technologies (ThermoFisher)	Express Scripts	Network physicians use a standardized electronic medical records (EMR) system
US Oncology Network	Integrated network of community oncology practices with more than 1,000 oncologists in 370 locations and 80 cancer centers; acquired by McKesson in 2010	Foundation Medicine	McKesson	Network physicians