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Collecting Real World Evidence to Evaluate Clinical Utility of Molecular Testing

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The New York Times

Opinion

Are We Being Misled About Precision Medicine?

Doctors and hospitals love to talk about the cancer patients they've saved, and reporters love to write about them. But deaths still vastly outnumber the rare successes.

By Liz Szabo
Ms. Szabo is a health reporter for Kaiser Health News.

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Some experts, like Dr. David Hyman of Memorial Sloan Kettering Cancer Center in New York, say that such testing should be available to everyone with advanced cancer, because no one can predict which patients will have results that make them eligible for beneficial treatment. When patients respond to these drugs, they tend to do very well, and some survive much longer than expected.

But Dr. Hyman acknowledged precision medicine "is not addressing the needs of the majority of cancer patients."

"There are very few instances in which we can look at a genomic test and pick a drug off the shelf and say, 'That will work,'" said Dr. Nikhil Wagle, a cancer specialist at Dana-Farber Cancer Institute in Boston who helped develop precision-medicine tests. "That's our goal in the long run, but in 2018 we're not there yet."

A Retrospective Analysis of Precision Medicine Outcomes in Patients With Advanced Cancer Reveals Improved Progression-Free Survival Without Increased Health Care Costs

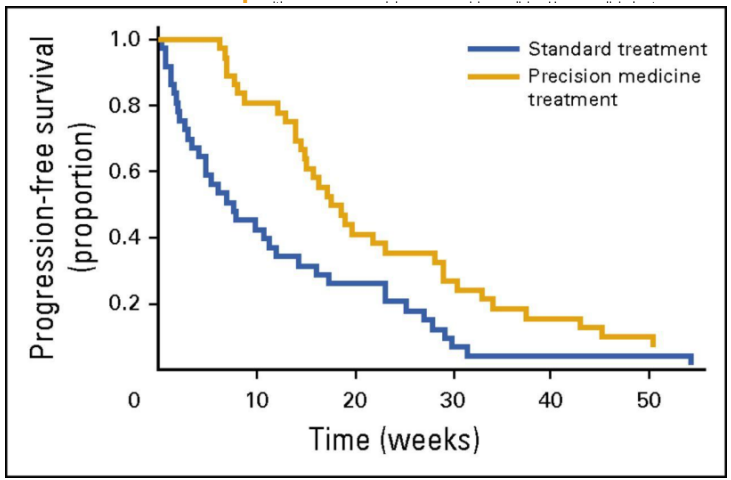
Derrick S. Haslem, MD, S. Burke Van Norman, BS, Gail Fulde, MS, Andrew J. Knighton, PhD, Tom Belnap, PhD, Allison M. Butler, MS, Sharanya Rhagunath, PhD, David Newman, MS, Heather Gilbert, MD, Brian P. Tudor, MD, Karen Lin, MD, Gary R. Stone, RN, MBA, David L. Loughmiller, MS, Pravin J. Mishra, PhD, Rajendu Srivastava, MD, James M. Ford, MD, and Lincoln D. Nadauld, MD, PhD

Intermountain Healthcare, Saint George and Salt Lake City; University of Utah School of Medicine, Salt Lake City, UT; Duke University School of Medicine, Durham, NC; and Stanford University School of Medicine, Stanford, CA

Abstract

Purpose

The advent of genomic diagnostic technologies such as next-generation sequencing has recently enabled the use of genomic information to guide targeted treatment in patients



Aurora Health Care
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Reportable Actionability Versus Pragmatic Actionability: Implementing Precision Medicine at Three Large Health Systems

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Henry Ford Health System
hoag

RESULTS (cont.)

24.4% (174/713) of MP reports were followed by a treatment order that matched to at least one reported actionable treatment. The translation from a MP-reported actionable finding to a prescribed treatment order was 28.1% (105/374) at AHC, 20.9% (9/43) at HFHS, and 20.3% (60/296) at HMHP, which has borderline statistical significance (p=0.0563) for differences between sites. Of the 713 MP reports analyzed, there was an average of 7.8 therapy recommendations per MP report. When limiting the analysis to patients who received a targeted therapy recommendation, the number of recommendations per report dropped to 3.4, and only 14% of patients with a positive targeted therapy recommendation had a matching treatment order. The match rate of individual therapy recommendations to ordered therapies was consistent between targeted therapies (4%) and chemotherapies (5%). There were no significant rate differences in actionability between the two molecular testing vendors examined.

Health system	# of MP reports with positive actionability	# of MP reports with treatment order matching therapy recommendation	% of MP reports with matching treatment order
Aurora	374	105	28.1%
Henry Ford	43	9	20.9%
Hoag	296	60	20.3%

Table 2. MP reports were followed by a lab-recommended therapy in 24.4% of cases across these three health systems, on average.

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We have a responsibility learn from every patient's experience. This is particularly true in precision medicine.

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NCI-MATCH

PRECISION MEDICINE TRIAL

Key Considerations:

Pragmatic

Retrospective and Prospective

Reduce Care Team Burden

Preserve Access

White Paper Proposal 2:

Identifying Innovative Methods and Standards for Data Collection on Evolving Uses in the Real World

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What is the context of use of the molecular test?

Component	Description	Purpose and Utilization for Decision-Making
Disease Characteristics	Primary Cancer Type Stage at Diagnosis Current Clinical Stage / Metastatic Disease Status Prior Lines of Therapy	Clinical characteristics of patient population and impact on clinical endpoints
Diagnostic Test	Test Vendor Test Type Genes and Variant Types Tested Genomic Results Quality Measures (as defined in Table 1)	Understand the testing performed

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Will require cooperation from testing labs to provide interoperable reports

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Does the molecular test impact clinical care decisions?

Component	Description	Purpose and Utilization for Decision-Making
Change in Care	*Following physician receiving molecular test results…* Intent to Change Treatment (including stop/start of treatment; inclusive of targeted therapies, immunotherapy, clinical trials) Change in Treatment (as measured by successful fill / administration) Difference Between Intent to Change and Change (assess whether obstacles in therapy procurement or trials enrollment effected molecular test impact)	Understand whether testing led to a change in care decisions and patient management

Does the molecular test improve outcomes?

Component	Description	Purpose and Utilization for Decision-Making
Clinical Outcomes	Overall Survival Progression Free Survival Proxies (e.g. Time on Treatment, Time to Treatment Discontinuation, Time to Next Treatment) Tolerability / Toxicity (Time to First Hospitalization, Adverse Event Frequency) Objective Response Rate Proxies	Assess impact of testing-driven decisions on clinical outcomes
Non-Clinical Outcomes	Patient Reported Outcomes (including Quality of Life, Symptoms, Physical Function, Impact on Social Roles)	Assess impact of testing-driven decisions on patient experience

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Non-Clinical Outcomes	Patient Reported Outcomes (including Quality of Life, Symptoms, Physical Function, Impact on Social Roles)	Assess impact of testing-driven decisions on patient experience

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