Precision Medicine: Strategies for Improving Cancer Care Team Communication

Bibliography

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Bibliography

Contents

Introduction

Recent advances in the application of molecularly-targeted therapies in cancer continue to revolutionize the approach to patient care. Oncologists around the country are applying principles of "biomarker-driven medicine" and tailoring therapies based on specific tumor characteristics to optimize outcomes in patients with cancer. At the same time, molecular testing processes are becoming increasingly complex, especially in community cancer programs where resources and staff are more limited when compared to major academic research centers. To ensure that cancer programs in the community have guidance around the molecular testing processes, the Association of Community Cancer Centers (ACCC), launched a multi-phased initiative in 2012 titled, Molecular Testing in the Community Oncology Setting.

Testing and Results

A report template for molecular genetic tests designed to improve communication between the clinician and laboratory.
Scheuner MT, Hilborne L, Brown J, Lubin IM; members of the RAND Molecular Genetic Test Report Advisory Board.

Genet Test Mol Biomarkers. 2012 Jul;16(7):761-9.

AIM:
Errors are most likely to occur during the pre- and postanalytic phases of the genetic testing process, which can contribute to underuse, overuse, and misuse of genetic tests. To mitigate these errors, we created a template for molecular genetic test reports that utilizes the combined features of synoptic reporting and narrative interpretation.

METHODS:
A variation of the Delphi consensus process with an expert panel was used to create a draft report template, which was further informed by focus group discussions with primary care physicians.

RESULTS:
There was agreement that molecular genetic test reports should present information in groupings that flow in a logical manner, and most participants preferred the following order of presentation: patient and physician information, test performed, test results and interpretation, guidance on next steps, and supplemental information. We define data elements for the report as "required," "optional," "possible," and "not necessary"; provide recommendations regarding the grouping of these data elements; and describe the ideal design of the report template, including the preferred order of the report sections, formatting of data, and length of the report.

DISCUSSION:
With input from key stakeholders and building upon prior work, we created a template for molecular genetic test reports designed to improve clinical decision making at the point of care. The template design should lead to more effective communication between the laboratory and ordering clinician. Studies are needed to assess the usefulness and effectiveness of molecular genetic test reports generated using this template.

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Patient name:	Ordering clinician:
Date of birth:	Patient age:
Lab accession No.:	Requisition date:
Patient sex:	Date of report:
Patient ethnicity/race:	
Patient clinical history:	
Patient family history:	

Test Performed:
Test indication:
Specimen type: Date collected:

Test Result:
Interpretation:

The results and interpretation, and guidance and supplemental information below, were reviewed and approved by:

_____   _____
John Doe, PhD, Director, The Genetics Laboratory   Date

Guidance
- General suggestions for management & prevention (includes mention of genetic consultation)
- *Patient-specific suggestions for management & prevention*
- Laboratory contact phone number to address questions, if available

Supplemental Information
- Clinical/epidemiological aspects of condition/disorder
- Genetic aspects of condition/disorder
- Test method description
- Test method analytic validity and limitations
- Information resources for clinicians
- Information resources for patients
- General disclaimer
- *Cite references for report facts*

FIG. 1.   There are five sections in the genetic test report template demarcated by lines on the page, including patient and ordering clinician information, the test performed, the test results and interpretation, guidance, and supplemental information. The increased font size and bolded font are used for items of particular importance, such as results and interpretation. Use of bullets and bolded headings helps organize content. The optional items in each section are shown in italics.

Biomarker testing for breast, lung, and gastroesophageal cancers at NCI designated cancer centers.

Schink JC, Trosman JR, Weldon CB, Siziopikou KP, Tsongalis GJ, Rademaker AW, Patel JD, Benson AB 3rd, Perez EA, Gradishar WJ.

BACKGROUND:
Molecular biomarkers, a cornerstone of precision oncology, are critical in breast, gastroesophageal, and non-small cell lung cancer management (BC, GEC, NSCLC). Testing practices are intensely debated, impacting diagnostic quality and affecting pathologists, oncologists and patients. However, little is known about testing

approaches used in practice. Our study described biomarker practices in BC, GEC, and NSCLC at the leading US cancer centers.

METHODS:

We conducted a survey of the National Cancer Institute (NCI) designated centers on BC, GEC, and NSCLC biomarker testing. We used simple frequencies to describe practices, two-sided Fisher's exact test and two-sided McNemar's test for cross-cancer comparison. All statistical tests were two-sided.

RESULTS:

For BC human epidermal growth factor receptor 2 (HER2), 39% of centers combine guidelines by using in situ hybridization (ISH) and immunohistochemistry (IHC) concurrently, and 21% reflex-test beyond guideline-recommended IHC2+. For GEC HER2, 44% use ISH and IHC concurrently, and 28% reflex-test beyond IHC2+. In NSCLC, the use of IHC is limited to 4% for epidermal growth factor receptor (EGFR) and 7% for anaplastic lymphoma kinase (ALK). 43.5% test NSCLC biomarkers on oncologist order; 34.5% run all biomarkers upfront, and 22% use a sequential protocol. NSCLC external testing is statistically significantly higher than BC ($P < .0001$) and GEC ($P < .0001$). NSCLC internally developed tests are statistically significantly more common than BC ($P < .0001$) and GEC ($P < .0001$).

CONCLUSIONS:

At the NCI cancer centers, biomarker testing practices vary, but exceeding guidelines is a common practice for established biomarkers and emerging practice for newer biomarkers. Use of internally developed tests declines as biomarkers mature. Implementation of multibiomarker protocols is lagging. Our study represents a step toward developing a biomarker testing practice landscape.

Effective communication of molecular genetic test results to primary care providers.

Scheuner MT, Edelen MO, Hilborne LH, Lubin IM; RAND Molecular Genetic Test Report Advisory Board.

PURPOSE:

We evaluated a template for molecular genetic test reports that was developed as a strategy to reduce communication errors between the laboratory and ordering clinician.

METHODS:

We surveyed 1,600 primary care physicians to assess satisfaction, ease of use, and effectiveness of genetic test reports developed using our template and reports developed by clinical laboratories. Mean score differences of responses between the reports were compared using t-tests. Two-way analysis of variance evaluated the effect of template versus standard reports and the influence of physician characteristics.

RESULTS:

There were 396 (24%) respondents. Template reports had higher scores than the standard reports for each survey item. The gender and specialty of the physician did not influence scores; however, younger physicians gave higher scores regardless of report type. There was significant interaction between report type and whether physicians ordered or reviewed any genetic tests (none versus at least one) in the past year, $P = 0.005$.

CONCLUSION:

For each survey item assessing satisfaction, ease of use, and effectiveness, physicians gave higher ratings to genetic test reports developed with the template than standard reports used by clinical laboratories. Physicians least familiar with genetic test reports, and possibly having the greatest need for better communication, were best served by the template reports.

Germline BAP1 mutations misreported as somatic based on tumor-only testing.

Abdel-Rahman MH, Rai K, Pilarski R, Davidorf FH, Cebulla CM.

We present three unrelated patients with germline mutations in BAP1 misreported as somatic mutations. All had strong family histories of cancer. One of these patients presented with an invasive breast cancer with the tumor tissue showing partial loss of the mutant rather than the wild type allele, suggesting that the germline BAP1 mutation didn't contribute to breast cancer development in this patient. This data highlights the importance of sequencing matching germline and tumor DNA for proper assessment of somatic versus germline mutation status. In patients with somatic mutations reported from laboratories carrying out tumor-only genomic testing, the possibility that a variant may be a germline mutation should be considered, especially if the personal and/or family history suggests hereditary cancer predisposition. Since tumor-only testing can reveal germline mutations, ethical issues for patients being tested should be considered including proper consent and genetic counseling.

Guidance for laboratories performing molecular pathology for cancer patients.

Cree IA, Deans Z, Ligtenberg MJ, Normanno N, Edsjö A, Rouleau E, Solé F, Thunnissen E, Timens W, Schuuring E, Dequeker E, Murray S, Dietel M, Groenen P, Van Krieken JH; European Society of Pathology Task Force on Quality Assurance in Molecular Pathology; Royal College of Pathologists.

Molecular testing is becoming an important part of the diagnosis of any patient with cancer. The challenge to laboratories is to meet this need, using reliable methods and processes to ensure that patients receive a timely and accurate report on which their treatment will be based. The aim of this paper is to provide minimum requirements for the management of molecular pathology laboratories. This general guidance should be augmented by the specific guidance available for different tumour types and tests. Preanalytical considerations are important, and careful consideration of the way in which specimens are obtained and reach the laboratory is necessary. Sample receipt and handling follow standard operating procedures, but some alterations may be necessary if molecular testing is to be performed, for instance to control tissue fixation. DNA and RNA extraction can be standardised and should be checked for quality and quantity of output on a regular basis. The choice of analytical method(s) depends on clinical requirements, desired turnaround time, and expertise available. Internal quality control, regular internal audit of the whole testing process, laboratory accreditation, and continual participation in external quality assessment schemes are prerequisites for delivery of a reliable service. A molecular pathology report should accurately convey the information the clinician needs to treat the patient with sufficient information to allow for correct interpretation of the result. Molecular pathology is developing rapidly, and further detailed evidence-based recommendations are required for many of the topics covered here.

Integrating genomics into clinical oncology: ethical and social challenges from proponents of personalized medicine.

McGowan ML, Settersten RA Jr, Juengst ET, Fishman JR.

INTRODUCTION:
The use of molecular tools to individualize health care, predict appropriate therapies, and prevent adverse health outcomes has gained significant traction in the field of oncology under the banner of "personalized medicine" (PM). Enthusiasm for PM in oncology has been fueled by success stories of targeted treatments for a variety of cancers based on their molecular profiles. Though these are clear indications of optimism for PM, little is known about the ethical and social implications of personalized approaches in clinical oncology.
OBJECTIVE:
The objective of this study is to assess how a range of stakeholders engaged in promoting, monitoring, and providing PM understand the challenges of integrating genomic testing and targeted therapies into clinical oncology.
METHODS AND MATERIALS:
The study involved the analysis of in-depth interviews with 117 stakeholders whose experiences and perspectives on PM span a wide variety of institutional and professional settings.
RESULTS:
Despite their considerable enthusiasm for this shift, promoters, monitors, and providers of PM identified 4 domains that provoke heightened ethical and social concerns: (1) informed consent for cancer genomic testing, (2) privacy, confidentiality, and disclosure of genomic test results, (3) access to genomic testing and targeted therapies in oncology, and (4) the costs of scaling up pharmacogenomic testing and targeted cancer therapies.
CONCLUSIONS:
These specific concerns are not unique to oncology, or even genomics. However, those most invested in the success of PM view oncologists' responses to these challenges as precedent setting because oncology is farther along the path of clinical integration of genomic technologies than other fields of medicine. This study illustrates that the rapid emergence of PM approaches in clinical oncology provides a crucial lens for identifying and managing potential frictions and pitfalls that emerge as health care paradigms shift in these directions.

NCCN Work Group Report: Emerging Issues in Tissue Allocation

DeMartino JK.

Expanding research interests in molecular profiling over the past several years have led researchers in academia and pharmaceutical and biotechnology companies to significantly increase their need for access to tissue specimens collected through clinical care and clinical trials. As a result, tissue allocation has become a growing issue for many clinical and translational investigators. High-quality biospecimens are needed by all stakeholders in order to have scientifically accurate studies and results. At the center of the process are the patients, who have increasingly become active partners in the clinical research enterprise as individuals and through highly sophisticated patient advocacy organizations. All stakeholders must recognize that human specimens, including tissue, represent a valuable and unique resource that must have proper acquisition, handling, custodianship, and consent for use in accordance with best practices for biospecimen resources.

Next-generation sequencing: ready for the clinics?

Desai AN, Jere A.

Next-generation sequencing (NGS) has transformed genomic research by decreasing the cost of sequencing and increasing the throughput. Now, the focus is on using NGS technology for diagnostics and therapeutics. In this review, we discuss the possible clinical applications of NGS and the potential of some of the current systems to transition to the clinic. Clinical use of NGS technologies will enable the identification of causative mutations for rare genetic disorders through whole-genome or targeted genome resequencing, rapid pathogen screening and cancer diagnosis along with the identification of appropriate therapy. Routine clinical use of NGS technologies is appealing, but mandates high accuracy, simple assays, small inexpensive instruments, flexible throughput, short run times and most importantly, easy data analysis as well as interpretation. A number of NGS systems launched recently have least some of these characteristics, namely, small instruments, flexible throughput and short run time, but still face a few challenges. Moreover, simplified data analysis tools will need to be developed to minimize the requirement of sophisticated bioinformatics support in clinics. In summary, for successful transition of NGS to clinic, a sustained collaboration between research labs, clinical practitioners and vendors offering sequencing based genetic tests is required.

Oncologists' and cancer patients' views on whole-exome sequencing and incidental findings: results from the CanSeq study.

Gray SW, Park ER, Najita J, Martins Y, Traeger L, Bair E, Gagne J, Garber J, Jänne PA, Lindeman N, Lowenstein C, Oliver N, Sholl L, Van Allen EM, Wagle N, Wood S, Garraway L, Joffe S.

PURPOSE:
Although targeted sequencing improves outcomes for many cancer patients, it remains uncertain how somatic and germ-line whole-exome sequencing (WES) will integrate into care.
METHODS:
We conducted surveys and interviews within a study of WES integration at an academic center to determine oncologists' attitudes about WES and to identify lung and colorectal cancer patients' preferences for learning WES findings.
RESULTS:
One-hundred sixty-seven patients (85% white, 58% female, mean age 60) and 27 oncologists (22% female) participated. Although oncologists had extensive experience ordering somatic tests (median 100/year), they had little experience ordering germ-line tests. Oncologists intended to disclose most WES results to patients but anticipated numerous challenges in using WES. Patients had moderately low levels of genetic knowledge (mean 4 correct out of 7). Most patients chose to learn results that could help select a clinical trial, pharmacogenetic and positive prognostic results, and results suggesting inherited predisposition to cancer and treatable noncancer conditions (all ≥95%). Fewer chose to receive negative prognostic results (84%) and results suggesting predisposition to untreatable noncancer conditions (85%).
CONCLUSION:
The majority of patients want most cancer-related and incidental WES results. Patients' low levels of genetic knowledge and oncologists' inexperience with large-scale sequencing present challenges to implementing paired WES in practice.

Ordering molecular genetic tests and reporting results: practices in laboratory and clinical settings.

Lubin IM, Caggana M, Constantin C, Gross SJ, Lyon E, Pagon RA, Trotter TL, Wilson JA, McGovern MM.

J Mol Diagn. 2008 Sep;10(5):459-68.

Previous studies have suggested that patient care may be compromised as a consequence of poor communication between clinicians and laboratory professionals in cases in which molecular genetic test results are reported. To understand better the contributing factors to such compromised care, we investigated both pre- and postanalytical processes using cystic fibrosis mutation analysis as our model. We found that although the majority of test requisition forms requested patient/family information that was necessary for the proper interpretation of test results, in many cases, these data were not provided by the individuals filling out the forms. We found instances in which result reports for simulated diagnostic testing described individuals as carriers where only a single mutation was found with no comment pertaining to a diagnosis of cystic fibrosis. Similarly, reports based on simulated scenarios for carrier testing were problematic when no mutations were identified, and the patient's race/ethnicity and family history were not discussed in reference to residual risk of disease. Remarkably, a pilot survey of obstetrician-gynecologists revealed that office staff, including secretaries, often helped order genetic tests and reported test results to patients, raising questions about what efforts are undertaken to ensure personnel competency. These findings are reviewed in light of what efforts should be taken to improve the quality of test-ordering and result-reporting practices.

Rethinking Patient-Physician Communication of Biopsy Results-The Waiting Game.

Krishnan N, Fagerlin A, Skolarus TA.

JAMA Oncol. 2015 Nov 1;1(8):1025-6.

[no abstract]

Translating genomics in cancer care.

Bombard Y, Bach PB, Offit K.

J Natl Compr Canc Netw. 2013 Nov;11(11):1343-53.

There is increasing enthusiasm for genomics and its promise in advancing personalized medicine. Genomic information has been used to personalize health care for decades, spanning the fields of cardiovascular disease, infectious disease, endocrinology, metabolic medicine, and hematology. However, oncology has often been the first test bed for the clinical translation of genomics for diagnostic, prognostic, and therapeutic applications. Notable hereditary cancer examples include testing for mutations in BRCA1 or BRCA2 in unaffected women to identify those at significantly elevated risk for developing breast and ovarian cancers, and screening patients with newly diagnosed colorectal cancer for mutations in 4 mismatch repair genes to reduce morbidity and mortality in their relatives. Somatic genomic testing is also increasingly used in oncology, with gene expression profiling of breast tumors and EGFR testing to predict treatment response representing commonly used examples. Health technology assessment provides a rigorous means to inform clinical and policy decision-making through systematic assessment of the evidentiary base, along with precepts of clinical effectiveness, cost-effectiveness, and consideration of risks and benefits for health care delivery and society. Although this evaluation is a fundamental step in the translation of any new therapeutic, procedure, or diagnostic test into clinical care, emerging developments may threaten this standard. These include "direct to consumer" genomic risk assessment services and the challenges posed by incidental results generated from next-generation sequencing (NGS) technologies. This article presents a review of the evidentiary standards and knowledge base supporting the translation of key cancer genomic technologies along the continuum of validity, utility, cost-

effectiveness, health service impacts, and ethical and societal issues, and offers future research considerations to guide the responsible introduction of NGS technologies into health care. It concludes that significant evidentiary gaps remain in translating genomic technologies into routine clinical practice, particularly in efficacy, health outcomes, cost-effectiveness, and health services research. These caveats are especially germane in the context of NGS, wherein efforts are underway to translate NGS results despite their limited accuracy, lack of proven efficacy, and significant computational and counseling challenges. Further research across these domains is critical to inform the effective, efficient, and equitable translation of genomics into cancer care.

Standards and Guidelines: General

Delivering precision medicine in oncology today and in future-the promise and challenges of personalised cancer medicine: a position paper by the European Society for Medical Oncology (ESMO).

Ciardiello F, Arnold D, Casali PG, Cervantes A, Douillard JY, Eggermont A, Eniu A, McGregor K, Peters S, Piccart M, Popescu R, Van Cutsem E, Zielinski C, Stahel R.

Ann Oncol. 2014 Sep;25(9):1673-8.

Excerpts from article:

Disclosure of results from genetic testing that are clinically and analytically valid can be positive, helping patients take control of their lives.

Providing feedback opportunities might also contribute to involving and educating patients and patients' advocacy groups, and there is wide public interest in being informed of such results [30]. Nonetheless, there is not enough research studying cancer patients' preferences and expectations concerning genetic testing [30]. Continuing research and discussions to develop ethical and legal frameworks and establish counselling recommendations on disclosing information from genetic testing to cancer patients and their relatives are required. Furthermore, patients' involvement in this process will be essential to further improve the translation of genetic testing data to the benefit of cancer patients.

Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology.

Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, Grody WW, Hegde M, Lyon E, Spector E, Voelkerding K, Rehm HL; ACMG Laboratory Quality Assurance Committee.

Genet Med. 2015 May;17(5):405-24.

The American College of Medical Genetics and Genomics (ACMG) previously developed guidance for the interpretation of sequence variants.(1) In the past decade, sequencing technology has evolved rapidly with the advent of high-throughput next-generation sequencing. By adopting and leveraging next-generation sequencing, clinical laboratories are now performing an ever-increasing catalogue of genetic testing spanning genotyping, single genes, gene panels, exomes, genomes, transcriptomes, and epigenetic assays for genetic disorders. By virtue of increased complexity, this shift in genetic testing has been accompanied by new challenges in sequence interpretation. In this context the ACMG convened a workgroup in 2013 comprising

representatives from the ACMG, the Association for Molecular Pathology (AMP), and the College of American Pathologists to revisit and revise the standards and guidelines for the interpretation of sequence variants. The group consisted of clinical laboratory directors and clinicians. This report represents expert opinion of the workgroup with input from ACMG, AMP, and College of American Pathologists stakeholders. These recommendations primarily apply to the breadth of genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. This report recommends the use of specific standard terminology-"pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign"-to describe variants identified in genes that cause Mendelian disorders. Moreover, this recommendation describes a process for classifying variants into these five categories based on criteria using typical types of variant evidence (e.g., population data, computational data, functional data, segregation data). Because of the increased complexity of analysis and interpretation of clinical genetic testing described in this report, the ACMG strongly recommends that clinical molecular genetic testing should be performed in a Clinical Laboratory Improvement Amendments-approved laboratory, with results interpreted by a board-certified clinical molecular geneticist or molecular genetic pathologist or the equivalent.

Standards and Guidelines: Breast Cancer

Breast cancer: updated guideline recommendations for HER2 testing.

Rakha EA, Ellis IO.

Nat Rev Clin Oncol. 2014 Jan;11(1):8-9.

The recently updated HER2 testing guidelines by ASCO and the College of American Pathologists (CAP) are a significant step towards personalized medicine. It is excellent news that such great effort has been put into standardizing biomarker assessment. Undoubtedly, these recommendations will improve the analytical validity of HER2 testing, its clinical utility and the communication among health-care providers.

Current HER2 Testing Recommendations and Clinical Relevance as a Predictor of Response to Targeted Therapy.

Ballinger TJ, Sanders ME, Abramson VG.

Clin Breast Cancer. 2015 Jun;15(3):171-80.

Clinical decision-making in the treatment of breast cancer depends on an accurate determination and understanding of human epidermal growth factor receptor 2 (HER2) status. The guidelines for HER2 testing were recently updated in late 2013, but limitations continue to exist in the interpretation and clinical application of results when the tumor specimens do not fall neatly into positive or negative categories with immunohistochemistry and fluorescence in situ hybridization testing. The issues, including discordance between pathologists or laboratories, polysomy, and genetic heterogeneity, present challenging situations that are difficult to translate into clinical significance. The present review discussed the changes in the updated American Society of Clinical Oncology/College of American Pathologists guidelines, the clinical relevance of complex issues in HER2 testing, and the implications of the results on the response to HER2-targeted therapies. Great advances have been made in the treatment of HER2-positive breast cancer; however, the challenge remains to determine the best testing analysis that will identify patients who will benefit the most from these therapies.

The updated ASCO/CAP guideline recommendations for HER2 testing in the management of invasive breast cancer: a critical review of their implications for routine practice.

Rakha EA, Starczynski J, Lee AH, Ellis IO.

Histopathology. 2014 Apr;64(5):609-15. doi: 10.1111/his.12357.

The American Society of Clinical Oncology and the College of American Pathologists have issued joint updated comprehensive guideline recommendations for human epidermal growth factor receptor 2 (HER2) testing in breast cancer. The update not only provides guidelines for the test performance parameters, with the aim of improving test accuracy, reproducibility, and precision, but also provides comprehensive recommendations on the post-analytical interpretation of the results, and requires improved communication among healthcare providers. The updated guidelines are targeted at testing laboratories, pathologists, oncologists, surgeons, and, indirectly, other healthcare providers. Although the guidelines contribute to the improved analytical validity and clinical utility of laboratory assays required for successful molecularly targeted therapy in the era of personalized medicine, the implications of such recommendations have to be acknowledged. Certain recommendations, particularly those related to repeating the test and pathological concordance, have lower levels of supportive evidence than existing key recommendations, and the associated workload implications will be challenging to support in most healthcare systems. In this commentary, we critically address the key updated recommendations and their impact on service provision and patient care.

Standards and Guidelines: Lung Cancer

Broad, Hybrid Capture-Based Next-Generation Sequencing Identifies Actionable Genomic Alterations in Lung Adenocarcinomas Otherwise Negative for Such Alterations by Other Genomic Testing Approaches.

Drilon A, Wang L, Arcila ME, Balasubramanian S, Greenbowe JR, Ross JS, Stephens P, Lipson D, Miller VA, Kris MG, Ladanyi M, Rizvi NA.

Clin Cancer Res. 2015 Aug 15;21(16):3631-9.

PURPOSE:
Broad, hybrid capture-based next-generation sequencing (NGS), as a clinical test, uses less tissue to identify more clinically relevant genomic alterations compared with profiling with multiple non-NGS tests. We set out to determine the frequency of such genomic alterations via this approach in tumors in which previous extensive non-NGS testing had not yielded a targetable driver alteration.
EXPERIMENTAL DESIGN:
We enrolled patients with lung adenocarcinoma with a ≤ 15 pack-year smoking history whose tumors previously tested "negative" for alterations in 11 genes (mutations in EGFR, ERBB2, KRAS, NRAS, BRAF, MAP2K1, PIK3CA, and AKT1 and fusions involving ALK, ROS1, and RET) via multiple non-NGS methods. We performed hybridization capture of the coding exons of 287 cancer-related genes and 47 introns of 19 frequently rearranged genes and sequenced these to deep, uniform coverage.
RESULTS:
Actionable genomic alterations with a targeted agent based on NCCN guidelines were identified in 26% [8 of 31: EGFR G719A, BRAF V600E, SOCS5-ALK, HIP1-ALK, CD74-ROS1, KIF5B-RET (n = 2), CCDC6-RET]. Seven of these patients either received or are candidates for targeted therapy. Comprehensive genomic profiling using this method also identified a genomic alteration with a targeted agent available on a clinical trial in an additional 39% (12 of 31).
CONCLUSIONS:

Broad, hybrid capture-based NGS identified actionable genomic alterations in 65% [95% confidence interval (CI), 48%-82%] of tumors from never or light smokers with lung cancers deemed without targetable genomic alterations by earlier extensive non-NGS testing. These findings support first-line profiling of lung adenocarcinomas using this approach as a more comprehensive and efficient strategy compared with non-NGS testing.

Genotyping and genomic profiling of non-small-cell lung cancer: implications for current and future therapies.

Li T, Kung HJ, Mack PC, Gandara DR.

J Clin Oncol. 2013 Mar 10;31(8):1039-49.

Substantial advances have been made in understanding critical molecular and cellular mechanisms driving tumor initiation, maintenance, and progression in non-small-cell lung cancer (NSCLC). Over the last decade, these findings have led to the discovery of a variety of novel drug targets and the development of new treatment strategies. Already, the standard of care for patients with advanced-stage NSCLC is shifting from selecting therapy empirically based on a patient's clinicopathologic features to using biomarker-driven treatment algorithms based on the molecular profile of a patient's tumor. This approach is currently best exemplified by treating patients with NSCLC with first-line tyrosine kinase inhibitors when their cancers harbor gain-of-function hotspot mutations in the epidermal growth factor receptor (EGFR) gene or anaplastic lymphoma kinase (ALK) gene rearrangements. These genotype-based targeted therapies represent the first step toward personalizing NSCLC therapy. Recent technology advances in multiplex genotyping and high-throughput genomic profiling by next-generation sequencing technologies now offer the possibility of rapidly and comprehensively interrogating the cancer genome of individual patients from small tumor biopsies. This advance provides the basis for categorizing molecular-defined subsets of patients with NSCLC in whom a growing list of novel molecularly targeted therapeutics are clinically evaluable and additional novel drug targets can be discovered. Increasingly, practicing oncologists are facing the challenge of determining how to select, interpret, and apply these new genetic and genomic assays. This review summarizes the evolution, early success, current status, challenges, and opportunities for clinical application of genotyping and genomic tests in therapeutic decision making for NSCLC.

Excerpts from article:

Last, but not least, clinical implementation of genotyping and genomic tests in NSCLC demands a close collaboration between multidisciplinary health care professionals, including, but not limited to, surgeons, pulmonologists, radiologists, pathologists, translational scientists, medical oncologists, insurers, and regulatory agencies. It is also vitally important to engage patients with NSCLC, the prime target of personalized cancer therapy, to help them understand the growing importance of molecular testing and to motivate them to participate in the process in appropriate ways.

Molecular pathology of non-small cell lung cancer: a practical guide.

Aisner DL, Marshall CB.

Am J Clin Pathol. 2012 Sep;138(3):332-46. doi: 10.1309/AJCPFR12WJKCEEZZ.

The traditional distinction between small cell lung cancer and non-small cell lung cancer (NSCLC) is no longer sufficient for treatment planning. It is advised to handle small diagnostic specimens prudently because they are often the only specimen available for molecular analysis. Pathologists are experiencing pressure to subclassify lung carcinoma based on extremely small tumor samples, because NSCLC tumor subtyping is now essential to determine molecular testing strategies. Evaluation for EGFR mutations and ALK rearrangements are now

considered to be the standard of care in advanced-stage pulmonary adenocarcinomas. Immunohistochemical stains can aid in subclassifying NSCLC, but performing these ancillary studies can significantly reduce the quantity of tissue available for molecular tests, requiring careful balancing of these 2 needs. The pathologist plays a pivotal role in facilitating clear and timely communication between the clinical oncology care team and the molecular laboratory to ensure that the appropriate tests are ordered and optimal material is submitted for testing.

Molecular Testing for Treatment of Metastatic Non-Small Cell Lung Cancer: How to Implement Evidence-Based Recommendations.

Levy BP, Chioda MD, Herndon D, Longshore JW, Mohamed M, Ou SH, Reynolds C, Singh J, Wistuba II, Bunn PA Jr, Hirsch FR.

The recent discovery of relevant biomarkers has reshaped our approach to therapy selection for patients with non-small cell lung cancer. The unprecedented outcomes demonstrated with tyrosine kinase inhibitors in molecularly defined cohorts of patients has underscored the importance of genetic profiling in this disease. Despite published guidelines on biomarker testing, successful tumor genotyping faces significant hurdles at both academic and community-based practices. Oncologists are now faced with interpreting large-scale genomic data from multiple tumor types, possibly making it difficult to stay current with practice standards in lung cancer. In addition, physicians' lack of time, resources, and face-to-face opportunities can interfere with the multidisciplinary approach that is essential to delivery of care. Finally, several challenges exist in optimizing the amount and quality of tissue for molecular testing. Recognizing the importance of biomarker testing, a series of advisory boards were recently convened to address these hurdles and clarify best practices. We reviewed these challenges and established recommendations to help optimize tissue acquisition, processing, and testing within the framework of a multidisciplinary approach.

IMPLICATIONS FOR PRACTICE:

Although several professional societies have incorporated biomarker testing recommendations into clinical practice guidelines for the diagnosis and management of non-small cell lung cancer (NSCLC), health care providers still face considerable challenges when establishing and implementing these standards. Developing and instituting protocols to ensure that all appropriate patients are tested for molecular biomarkers requires communication among the various specialists involved in the care of patients with NSCLC. This report provides insights into key challenges and recommendations for molecular testing of patients with metastatic NSCLC, summarized from a multidisciplinary team of experts spanning academic, community, and integrated health systems.

Using multiplexed assays of oncogenic drivers in lung cancers to select targeted drugs.

Kris MG, Johnson BE, Berry LD, Kwiatkowski DJ, Iafrate AJ, Wistuba II, Varella-Garcia M, Franklin WA, Aronson SL, Su PF, Shyr Y, Camidge DR, Sequist LV, Glisson BS, Khuri FR, Garon EB, Pao W, Rudin C, Schiller J, Haura EB, Socinski M, Shirai K, Chen H, Giaccone G, Ladanyi M, Kugler K, Minna JD, Bunn PA.

IMPORTANCE:
Targeting oncogenic drivers (genomic alterations critical to cancer development and maintenance) has transformed the care of patients with lung adenocarcinomas. The Lung Cancer Mutation Consortium was formed to perform multiplexed assays testing adenocarcinomas of the lung for drivers in 10 genes to enable clinicians to select targeted treatments and enroll patients into clinical trials.

OBJECTIVES:
To determine the frequency of oncogenic drivers in patients with lung adenocarcinomas and to use the data to select treatments targeting the identified driver(s) and measure survival.
DESIGN, SETTING, AND PARTICIPANTS:
From 2009 through 2012, 14 sites in the United States enrolled patients with metastatic lung adenocarcinomas and a performance status of 0 through 2 and tested their tumors for 10 drivers. Information was collected on patients, therapies, and survival.
INTERVENTIONS:
Tumors were tested for 10 oncogenic drivers, and results were used to select matched targeted therapies.
MAIN OUTCOMES AND MEASURES:
Determination of the frequency of oncogenic drivers, the proportion of patients treated with genotype-directed therapy, and survival.
RESULTS:
From 2009 through 2012, tumors from 1007 patients were tested for at least 1 gene and 733 for 10 genes (patients with full genotyping). An oncogenic driver was found in 466 of 733 patients (64%). Among these 733 tumors, 182 tumors (25%) had the KRAS driver; sensitizing EGFR, 122 (17%); ALK rearrangements, 57 (8%); other EGFR, 29 (4%); 2 or more genes, 24 (3%); ERBB2 (formerly HER2), 19 (3%); BRAF, 16 (2%); PIK3CA, 6 (<1%); MET amplification, 5 (<1%); NRAS, 5 (<1%); MEK1, 1 (<1%); AKT1, 0. Results were used to select a targeted therapy or trial in 275 of 1007 patients (28%). The median survival was 3.5 years (interquartile range [IQR], 1.96-7.70) for the 260 patients with an oncogenic driver and genotype-directed therapy compared with 2.4 years (IQR, 0.88-6.20) for the 318 patients with any oncogenic driver(s) who did not receive genotype-directed therapy (propensity score-adjusted hazard ratio, 0.69 [95% CI, 0.53-0.9], P = .006).
CONCLUSIONS AND RELEVANCE:
Actionable drivers were detected in 64% of lung adenocarcinomas. Multiplexed testing aided physicians in selecting therapies. Although individuals with drivers receiving a matched targeted agent lived longer, randomized trials are required to determine if targeting therapy based on oncogenic drivers improves survival.

Nursing

Clinical practice on the horizon: personalized medicine.

Chadwell K.

With the advent of the human genome project, we have never known so much about the uniqueness of individuals. Personalized medicine is poised to use this genetic and genomic information along with the impact of environment and clinical presentation to provide healthcare from an individual perspective. This offers the opportunity to improve our ability to diagnose and predict disease, provide earlier intervention, identify new treatment regimens, and address the safety and efficacy of drug use. The impact of personalized medicine to our current model of healthcare delivery is tremendous, and although strides have been made, there are still challenges and barriers to overcome before personalized medicine can be fully implemented. Advanced practice nurses may not be fully aware of the personalized medicine initiative or may not be well versed on genetic and genomic content, which is a key concept of personalized medicine. The role of advanced practice nurses is an integral part of the healthcare system, and as such, they are poised to be key providers and contributors to personalized medicine. The personalized medicine initiative is discussed along with examples of genetic and genomic information that lend to our understanding, diagnosis, and treatment of disease, as well as the role and responsibilities of advanced practice nurses. Resources for personalized medicine and genetic and genomic content are provided.

Information technology and precision medicine.

Carney PH.

OBJECTIVES:
To provide oncology nurses with an overview of clinical decision support (CDS) and explore opportunities for genomic CDS interventions. The nation's first personalized cancer decision support tool, My Cancer Genome, is presented as an exemplar of a novel CDS tool.

DATA SOURCES:
Published nursing and medical literature and the internet for an exemplar.

CONCLUSION:
CDS is a sophisticated health information technology that can translate and integrate genomic knowledge with patient information, providing recommendations at the point of care.

IMPLICATIONS FOR NURSING PRACTICE:
Nurses, as key stakeholders, must have an understanding of CDS interventions and their application to fully participate in all stages of CDS development and implementation.

Nursing genomics: practice implications every nurse should know.

Umberger R, Holston EC, Hutson SP, Pierce M.

Twenty-first century nurse clinicians, scientists, and educators must be informed of and become proficient in genetic competencies to provide the best available evidenced-based patient care. This article presents a historical context and basic applications of genetics, along with the attendant legal and ethical issues, to provide a framework for understanding genetics and the genomics applications used in clinical nursing practice. The implications of genomics are relevant to all areas of nursing practice, including risk assessment, education, clinical management, and future research.

Nursing implications of personalized and precision medicine.

Vorderstrasse AA, Hammer MJ, Dungan JR.

OBJECTIVES:
Identify and discuss the nursing implications of personalized and precision oncology care.

DATA SOURCES:
PubMed, CINAHL.

CONCLUSION:
The implications in personalized and precision cancer nursing care include interpretation and clinical use of novel and personalized information including genetic testing; patient advocacy and support throughout testing, anticipation of results and treatment; ongoing chronic monitoring; and support for patient decision-making. Attention must also be given to the family and ethical implications of a personalized approach to care.

IMPLICATIONS FOR NURSING PRACTICE:
Nurses face increasing challenges and opportunities in communication, support, and advocacy for patients given the availability of advanced testing, care and treatment in personalized and precision medicine. Nursing education and continuing education, clinical decision support, and health systems changes will be necessary to provide personalized multidisciplinary care to patients, in which nurses play a key role.

Precision medicine in oncology standard of care.

Adams L.

OBJECTIVES:
To review the histologic subtypes and staging of non-small cell lung cancer and metastatic melanoma, as well as the molecular markers used to direct standard therapy.

DATA SOURCES:
Book chapters and journal articles from medical and nursing literature, as well as published clinical guidelines.

CONCLUSION:
Patients with metastatic non-small cell lung cancer and metastatic melanoma have had a paucity of treatment options, most fraught with toxicity with limited benefit. Increased understanding of tumor genetics and molecular markers has expanded the treatment options for these patients, often providing them with durable responses and improved quality of life.

IMPLICATIONS FOR NURSING PRACTICE:
To provide education and support to their patients, nurses caring for these patients need to understand the role that genetics and molecular markers play in directing these therapies.

Prognostic information in breast cancer care: helping patients utilize important information.

Rosenzweig MQ, Rust D, Hoss J.

The Oncology Nursing Society's (ONS's) position on quality cancer care states that "quality cancer care incorporates the individual with cancer (and the family) as fully informed partners and decision makers" (ONS, 1997). Patients diagnosed with breast cancer are inundated with information, and oncology nurses help these patients receive quality cancer care by providing and explaining information related to their diagnosis and treatment. This information allows patients to participate in meaningful collaborative decision making. Prognostic tumor markers have provided information that can determine the natural history of breast cancer, identify women with high-risk or aggressive tumors, and help to establish a disease prognosis.

Patients

Attitudes of patients with cancer about personalized medicine and somatic genetic testing.

Gray SW, Hicks-Courant K, Lathan CS, Garraway L, Park ER, Weeks JC.

PURPOSE:
Dramatic advances in genomic technology stand to revolutionize cancer care; however, little is known about patients' understanding and acceptance of personalized medicine and widespread genetic testing (GT).

PATIENTS AND METHODS:
We conducted a formative, semi-structured interview study with a random sample of patients with lung, colorectal, and breast cancers to assess awareness of personalized medicine and GT and attitudes about somatic GT. Willingness to undergo GT was elicited through hypothetic scenarios.

RESULTS:
Sixty-nine patients participated; 71% were women; 42% were black; median age was 59 years; and 42% had an education level ≥ college. We found that a majority of patients either were not aware of the term "personalized medicine" or defined it in unexpected ways. Although many patients identified relevant benefits of somatic testing (eg, informs treatment), many patients also expressed significant concerns (ie, psychological harm and discrimination). A majority of patients expressed a willingness to undergo somatic (predictive, 96%, prognostic, 93%) and germline (cancer risk without incidental information, 87%; cancer risk with incidental information, 81%; pharmacogenetic, 91%) testing; however, far fewer patients expressed a willingness to undergo full genome sequencing (62%). Reluctance was attributed to concerns over incidental findings, information overload, and the lack of a clear benefit.

CONCLUSION:
Many patients relayed misunderstandings about somatic testing and a reluctance to undergo full sequencing; oncologists must carefully consider how they present testing to patients so that concerns over discrimination and psychological harm do not hinder test uptake. More work is needed to identify effective ways to communicate complex genomic concepts to patients and research participants.

Attitudes toward molecular testing for personalized cancer therapy.

Yusuf RA, Rogith D, Hovick SR, Peterson SK, Burton-Chase AM, Fellman BM, Li Y, McKinney C, Bernstam EV, Meric-Bernstam F.

BACKGROUND:
This study assessed attitudes of breast cancer patients toward molecular testing for personalized therapy and research.

METHODS:
A questionnaire was given to female breast cancer patients presenting to a cancer center. Associations between demographic and clinical variables and attitudes toward molecular testing were evaluated.

RESULTS:
Three hundred eight patients were approached, and 100 completed the questionnaire (a 32% response rate). Most participants were willing to undergo molecular testing to assist in the selection of approved drugs (81%)

and experimental therapy (59%) if testing was covered by insurance. Most participants were white (71%). Even if testing was financially covered, nonwhite participants were less willing to undergo molecular testing for the selection of approved drugs (54% of nonwhites vs 90% of whites, odds ratio [OR] = 0.13, P = .0004) or experimental drugs (35% vs 68%, OR = 0.26, P = .0072). Most participants (75%) were willing to undergo a biopsy to guide therapy, and 46% were willing to undergo research biopsies. Nonwhite participants were less willing to undergo research biopsies (17% vs 55%, OR = 0.17, P = .0033). Most participants wanted to be informed when research results had implications for treatment (91%), new cancer risk (90%), and other preventable/treatable diseases (87%).

CONCLUSIONS:
Most patients were willing to undergo molecular testing and minimally invasive procedures to guide approved or experimental therapy. There were significant differences in attitudes toward molecular testing between racial groups; nonwhites were less willing to undergo testing even if the results would guide their own therapy. Novel approaches are needed to prevent disparities in the delivery of genomically informed care and to increase minority participation in biomarker-driven trials.

Cancer patients acceptance, understanding, and willingness-to-pay for pharmacogenomic testing.

Cuffe S, Hon H, Qiu X, Tobros K, Wong CK, De Souza B, McFarlane G, Masroor S, Azad AK, Hasani E, Rozanec N, Leighl N, Alibhai S, Xu W, Issa AM, Liu G.

Pharmacogenet Genomics. 2014 Jul;24(7):348-55.

BACKGROUND:
Pharmacogenomics is gaining increasing importance in the therapeutics of cancer; yet, there is little knowledge of cancer patients' attitudes toward the use of pharmacogenomic testing in clinical practice. We carried out this study to explore cancer patients' acceptance, understanding, and willingness-to-pay for pharmacogenomic testing.
MATERIALS AND METHODS:
A broad cross-section of gastrointestinal, lung, breast, and other cancer patients were interviewed in terms of their acceptance of pharmacogenomic testing using hypothetical time, efficacy, and toxicity trade-off and willingness-to-pay scenarios.
RESULTS:
Among the 96% of 123 adjuvant patients accepting chemotherapy under optimal conditions, 99% wanted pharmacogenomic testing that could identify a subset of patients benefiting from chemotherapy, accepting median incurred costs of $2000 (range $0-25,000) and turnaround time for test results of 16 days (range 0-90 days). Among the 97% of 121 metastatic patients accepting chemotherapy, 97.4% wanted pharmacogenomic testing that could detect the risk of severe toxicity, accepting median incurred costs of $1000 (range $0-10,000) and turnaround time for results of 14 days (range 1-90 days). The majority of patients wanted to be involved in decision-making on pharmacogenomic testing; however, one in five patients lacked a basic understanding of pharmacogenomic testing.
CONCLUSION:
Among cancer patients willing to undergo chemotherapy, almost all wanted pharmacogenomic testing and were willing-to-pay for it, waiting several weeks for results. Although patients had a strong desire to be involved in decision-making on pharmacogenomic testing, a considerable proportion lacked the necessary knowledge to make informed choices.

Developing patient-friendly genetic and genomic test reports: formats to promote patient engagement and understanding.

Haga SB, Mills R, Pollak KI, Rehder C, Buchanan AH, Lipkus IM, Crow JH, Datto M.

Genome Med. 2014 Jul 31;6(7):58.

With the emergence of electronic medical records and patient portals, patients are increasingly able to access their health records, including laboratory reports. However, laboratory reports are usually written for clinicians rather than patients, who may not understand much of the information in the report. While several professional guidelines define the content of test reports, there are no guidelines to inform the development of a patient-friendly laboratory report. In this Opinion, we consider patient barriers to comprehension of lab results and suggest several options to reformat the lab report to promote understanding of test results and their significance to patient care, and to reduce patient anxiety and confusion. In particular, patients' health literacy, genetic literacy, e-health literacy and risk perception may influence their overall understanding of lab results and affect patient care. We propose four options to reformat lab reports: 1) inclusion of an interpretive summary section, 2) a summary letter to accompany the lab report, 3) development of a patient user guide to be provided with the report, and 4) a completely revised patient-friendly report. The complexity of genetic and genomic test reports poses a major challenge to patient understanding that warrants the development of a report more appropriate for patients.

Genetic Knowledge Among Participants in the Coriell Personalized Medicine Collaborative.

Schmidlen TJ, Scheinfeldt L, Zhaoyang R, Kasper R, Sweet K, Gordon ES, Keller M, Stack C, Gharani N, Daly MB, Jarvis J, Christman MF.

J Genet Couns. 2015 Aug 27.

Genetic literacy is essential for the effective integration of genomic information into healthcare; yet few recent studies have been conducted to assess the current state of this knowledge base. Participants in the Coriell Personalized Medicine Collaborative (CPMC), a prospective study assessing the impact of personalized genetic risk reports for complex diseases and drug response on behavior and health outcomes, completed genetic knowledge questionnaires and other surveys through an online portal. To assess the association between genetic knowledge and genetic education background, multivariate linear regression was performed. 4 062 participants completed a genetic knowledge and genetic education background questionnaire. Most were older (mean age: 50), Caucasian (90 %), female (59 %), highly educated (69 % bachelor's or higher), with annual household income over $100 000 (49 %). Mean percent correct was 76 %. Controlling for demographics revealed that health care providers, participants previously exposed to genetics, and participants with 'better than most' self-rated knowledge were significantly more likely to have a higher knowledge score ($p < 0.001$). Overall, genetic knowledge was high with previous genetic education experience predictive of higher genetic knowledge score. Education is likely to improve genetic literacy, an important component to expanded use of genomics in personalized medicine.

Racial/ethnic disparities in knowledge about one's breast cancer characteristics.

Freedman RA, Kouri EM, West DW, Keating NL.

Cancer. 2015 Mar 1;121(5):724-32.

BACKGROUND:
Understanding tumor characteristics is likely important, but little is known about breast cancer patients' knowledge of their own disease. The authors assessed women's knowledge about their tumor characteristics, whether racial/ethnic disparities in knowledge exist, and whether education and health literacy influence associations.

METHODS:
A population-based cohort of women in Northern California with stage 0 through III breast cancers diagnosed from 2010 to 2011 (participation rate 68.5%) was surveyed. Among 500 respondents (222 non-Hispanic white women, 142 non-Hispanic black women, and 136 Hispanic women), racial/ethnic differences in knowledge about tumor characteristics (estrogen receptor [ER] status, human epidermal growth factor receptor 2 [HER2] status, stage, grade) and correctness of tumor information (with California Cancer Registry data for confirmation) were examined. Multivariate logistic regression was used to assess the probability of: 1) knowing tumor stage, receptor status, and grade; and 2) correctly answering questions about tumor information by race/ethnicity. The impact of education and health literacy on findings was examined in sequential models.

RESULTS:
Overall, 32% to 82% of women reported knowing each of the 4 tumor characteristics of interest, and 20% to 58% correctly reported these characteristics. After adjustment, black and Hispanic women were less likely than white women to know and have correct responses for stage, ER status, and HER2 status (all P<.05). Education and health literacy were significantly associated with knowing and having correct information about some characteristics, but these variables did not eliminate most of the racial/ethnic differences observed.

CONCLUSIONS:
Patient's knowledge about their own breast cancer was generally poor, particularly for minority women. Further study of how this knowledge may impact receipt of care and outcomes is warranted.

Racial differences in attitudes toward personalized medicine.

Diaz VA, Mainous AG 3rd, Gavin JK, Wilson D.

Public Health Genomics. 2014;17(1):1-6. doi: 10.1159/000354785.

BACKGROUND/AIMS:
Patient concerns regarding personalized medicine may limit its use. This study assesses racial differences in attitudes toward personalized medicine, evaluating variables that may influence these attitudes.

METHODS:
A convenience sample of 190 adults (≥18 years) from an academic primary care practice was surveyed regarding awareness and acceptance of personalized medicine, plus concerns and benefits regarding its use. Logistic regressions predicting awareness, acceptance and concerns were performed, controlling for race, gender, marital status, education, children, internet use, and self-reported discrimination.

RESULTS:
The sample was 35% non-Hispanic white (NHW) and 34.7% male. More NHW participants expressed acceptance of personalized medicine than non-Hispanic black (NHB) participants (94.4 vs. 81.9%, p = 0.0190). More NHBs were concerned about the use of genes without consent (57.3 vs. 20.6%, p < 0.0001), sharing genetic information without consent (65.0 vs. 35.6%, p < 0.0001), discrimination based on genes (62.4 vs. 34.3%, p = 0.0002), and lack of access due to cost (75.0 vs. 48.0%, p = 0.0002). In logistic regressions, NHBs (OR = 7.46, 95% CI = 3.04-18.32) and those self-reporting discrimination (OR = 2.87, 95% CI = 1.22-6.78) had more concerns about the misuse of genes and costs associated with personalized medicine.

CONCLUSION:
Racial differences exist in attitudes toward personalized medicine and may be influenced by self-reported discrimination. Further study to understand factors influencing the acceptance of personalized medicine could help encourage its use.

Testing personalized medicine: patient and physician expectations of next-generation genomic sequencing in late-stage cancer care.

Miller FA, Hayeems RZ, Bytautas JP, Bedard PL, Ernst S, Hirte H, Hotte S, Oza A, Razak A, Welch S, Winquist E, Dancey J, Siu LL.

Developments in genomics, including next-generation sequencing technologies, are expected to enable a more personalized approach to clinical care, with improved risk stratification and treatment selection. In oncology, personalized medicine is particularly advanced and increasingly used to identify oncogenic variants in tumor tissue that predict responsiveness to specific drugs. Yet, the translational research needed to validate these technologies will be conducted in patients with late-stage cancer and is expected to produce results of variable clinical significance and incidentally identify genetic risks. To explore the experiential context in which much of personalized cancer care will be developed and evaluated, we conducted a qualitative interview study alongside a pilot feasibility study of targeted DNA sequencing of metastatic tumor biopsies in adult patients with advanced solid malignancies. We recruited 29/73 patients and 14/17 physicians; transcripts from semi-structured interviews were analyzed for thematic patterns using an interpretive descriptive approach. Patient hopes of benefit from research participation were enhanced by the promise of novel and targeted treatment but challenged by non-findings or by limited access to relevant trials. Family obligations informed a willingness to receive genetic information, which was perceived as burdensome given disease stage or as inconsequential given faced challenges. Physicians were optimistic about long-term potential but conservative about immediate benefits and mindful of elevated patient expectations; consent and counseling processes were expected to mitigate challenges from incidental findings. These findings suggest the need for information and decision tools to support physicians in communicating realistic prospects of benefit, and for cautious approaches to the generation of incidental genetic information.

What do providers, payers and patients need from comparative effectiveness research on diagnostics? The case of HER2/Neu testing in breast cancer.

Trosman JR, Weldon CB, Schink JC, Gradishar WJ, Benson AB 3rd.

AIMS:
Comparing effectiveness of diagnostic tests is one of the highest priorities for comparative effectiveness research (CER) set by the Institute of Medicine. Our study aims to identify what information providers, payers and patients need from CER on diagnostics, and what challenges they encounter implementing comparative information on diagnostic alternatives in practice and policy.
MATERIALS & METHODS:
Using qualitative research methods and the example of two alternative protocols for HER2 testing in breast cancer, we conducted interviews with 45 stakeholders: providers (n = 25) from four academic and eight nonacademic institutions, executives (n = 13) from five major US private payers and representatives (n = 7) from two breast cancer patient advocacies.
RESULTS:

The need for additional scientific evidence to determine the preferred HER2 protocol was more common for advocates than payers (100 vs 54%; p = 0.0515) and significantly more common for advocates than providers (100 vs 40%; p = 0.0077). The availability of information allowing assessment of the implementation impact from alternative diagnostic protocols on provider institutions may mitigate the need for additional scientific evidence for some providers and payers (24 and 46%, respectively). The cost-effectiveness of alternative protocols from the societal perspective is important to payers and advocates (69 and 71%, respectively) but not to providers (0%; p = 0.0001 and p = 0.0001). The lack of reporting laboratory practices is a more common implementation challenge for payers and advocates (77 and 86%, respectively) than for providers (32%). The absence of any mechanism for patient involvement was recognized as a challenge by payers and advocates (69 and 100%, respectively) but not by providers (0%; p = 0.0001 and p = 0.0001).
CONCLUSION:
Comparative implementation research is needed to inform the stakeholders considering diagnostic alternatives. Transparency of laboratory practices is an important factor in enabling implementation of CER on diagnostics in practice and policy. The incongruent views of providers versus patient advocates and payers on involving patients in diagnostic decisions is a concerning challenge to utilizing the results of CER.