<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreword</td>
<td>3</td>
</tr>
<tr>
<td>Executive Summary</td>
<td>4</td>
</tr>
<tr>
<td>The Oncology Landscape: Trending Toward Precision Medicine in Cancer Care</td>
<td>7</td>
</tr>
<tr>
<td>Methodology</td>
<td>9</td>
</tr>
<tr>
<td>Precision Medicine in Oncology: Pathway to Progress?</td>
<td>10</td>
</tr>
<tr>
<td>Value of Innovation: In the Eye of the Beholder</td>
<td>11</td>
</tr>
<tr>
<td>Paying for Outcomes: Toward Value-Based Coverage and Reimbursement</td>
<td>16</td>
</tr>
<tr>
<td>Molecular Diagnostics: Making the Value Proposition</td>
<td>19</td>
</tr>
<tr>
<td>Clinical Adoption: Managing Information Overload</td>
<td>24</td>
</tr>
<tr>
<td>Conclusions</td>
<td>26</td>
</tr>
</tbody>
</table>
Foreword

Oncology care has always been personalized. For hundreds of years, physicians have strived to help patients grapple with the characteristics of the dreaded disease. What is different today is that advances in molecular science and technology are enabling us to be much more precise in how we prevent, diagnose, and treat cancer.

It is precision that promises improved patient outcomes and reduced health care costs. It is precision that offers a viable solution to the challenges facing our health care system, including the affordability and accessibility of new cancer interventions in our current economic environment.

We are at a critical turning point in our progress against cancer. As we know, these advances are occurring in an environment of intense pressure for fiscal restraint that could, if not managed properly, stifle progress. Reimbursement policies, for example, that support or impede innovative precision medicine technologies will play a major role in determining whether recent progress against cancer can be sustained.

The Precision Oncology Annual Trend Report: Perspectives From Payers and Providers, was commissioned to illuminate the perspectives of payers and oncologists on key issues. It reveals where their perspectives align and where they differ in order to identify the opportunities that may emerge through personalized medicine. This, in turn, will enable us to formulate potential solutions that may lead to more widespread adoption and improved clinical outcomes based on progress in science and technology.

This report is an important contribution to the field, reflecting some payers’ and oncologists’ belief that precision oncology interventions can improve patient outcomes in a cost-effective manner. Nonetheless, it also underlines that we face challenges. Among those highlighted in the report are defining the value of new interventions, collecting the requisite levels of evidence to satisfy different constituencies to justify investment in precision medicine, and using the data based on that evidence to inform clinical decision making.

The insights from this trend report will help define a path forward for many stakeholders in the health care community as we seek to promote innovation that benefits both patients and the health system.

Edward Abrahams, PhD
President
Personalized Medicine Coalition
Executive Summary

Progress against cancer is at a critical turning point. Advances in science and technology are changing the way in which the more than 200 types of cancer\(^1\) are identified, classified, and treated, and are forming the foundation of precision medicine in cancer care. But these opportunities are occurring at a time when the entire health care industry is under intense pressure to exercise fiscal restraint.\(^2\) The advance of precision medicine in cancer care may offer viable solutions to the challenges facing our health care system, including trade-offs between costs and quality, declining resources, and an aging population. Accordingly, the creation of coverage and reimbursement policies that support innovative precision medicine technologies may play a critical role in determining whether progress against cancer can be maintained in the current environment.

Payers and providers are the major stakeholder groups responsible for the widespread implementation and adoption of precision medicine approaches, and both are increasingly being challenged to manage these emerging technologies and products. An unpublished survey conducted by Novartis Oncology in 2011 found that 90% of payers interviewed did not believe they had the information needed to effectively manage new oncology drugs, regardless of the size and sophistication of the health care plans. Without the full engagement of these communities, the transformation to a new generation of precision medicine in cancer care may not succeed.

In order to address this information need, Novartis commissioned this inaugural report, *The Precision Oncology Annual Trend Report: Perspectives From Payers and Providers*, to reveal the perspectives of both payers and providers on key issues within the field of precision medicine in oncology. Understanding the perspectives of these major stakeholders will provide insight into adoption of precision medicine and identify potential pathways for change that may lead to improved clinical and economic outcomes.

Methodology

This trend report is based on data obtained from both a fielded survey and in-depth interviews with subject matter experts. All participants were selected to represent a mix of government, private, and large employer payers, payers from regional and national health plans (N=50 for survey; N=5 for interviews), as well as small and large group health care providers (sometimes referred to as “oncologists” in this report) from both community and large specialized clinics (N=50 for survey; N=5 for interviews) with geographic balance. The survey and in-depth interviews were conducted with complete transparency. (Note: this report uses the terms “survey” or “surveyed” to discuss findings from the 50 respondents, and “interview” or “interviewed” to discuss findings or comments from the 5 individuals who were interviewed.)
Key Findings

**Precision Oncology Is a Pathway to Progress**

The majority of payers and providers surveyed and interviewed believe that precision medicine in oncology is a viable solution to the challenges facing our health care system. Specifically, these stakeholders are in agreement that:

- Precision oncology interventions can improve patient outcomes—and in a cost-effective manner
- Higher short-term [direct] costs for increased biomarker-based diagnostic testing are worth the potential long-term savings in health care costs
- Precision medicine in oncology offers a solution to the rising costs of health care, mainly because these interventions can help to avoid waste in the system

The ability of precision medicine to improve patient outcomes in a cost-effective manner comes with the following caveat from payers: treatment decisions must be based on the results of the molecular diagnostic tests.

**Value Is in the Eye of the Beholder**

Most payers and oncologists surveyed and interviewed have different perspectives on the benefit-cost ratio of targeted cancer treatments that have been launched within the last 5 years. While the majority of payers surveyed believe that less than 25% of targeted cancer treatments have a price that is justified by the known health outcomes delivered, most providers surveyed believe that more than 25% of these treatments have a justified price point.

Payers and oncologists are in agreement that after overall survival and cost, the next most valuable attributes of a new cancer intervention are improved progression-free survival (PFS), improved quality of life, and fewer side effects/hospital visits. Although payers agree that quality-of-life improvements are valuable attributes of a new cancer intervention, quality of life is not a key attribute that payers consider when making coverage decisions for these interventions. According to payers interviewed, part of the challenge lies in the ability to define suitable quantitative metrics.
Payers rely on a number of resources when considering coverage decisions, including clinical trial data and comparative effectiveness research. But to help make the most informed coverage decisions for precision medicine interventions, payers surveyed stated that they need additional information beyond what existing value assessment approaches provide, including:

- Head-to-head studies/data between new agents and standard of care (not placebo)
- Economic data (eg, cost of overall care)
- Long-term, real-world clinical and economic data
- Clinical utility data for molecular diagnostic tests

Assessing the Value of Molecular Diagnostics

The lack of clinical utility data (the ability of test results to inform clinical decision making) for molecular diagnostic tests is the most common concern for payers and providers with respect to expanding coverage for, and incorporating these tests into clinical practice, respectively. Additionally, payers are concerned that providers will order molecular diagnostic tests, but will not use the test results to support treatment decisions. This concern was not supported by the providers’ viewpoint, however: the majority of oncologists surveyed almost always prescribe the molecular diagnostic test before treating patients with targeted agents—and almost always base their clinical decisions on the results of the test.

Most payers and oncologists surveyed and interviewed are in agreement that molecular diagnostic tests should have to demonstrate the same level of clinical evidence as therapeutics via randomized controlled trials, and that the US Food and Drug Administration (FDA) should regulate all laboratory-developed tests (LDTs).
The Oncology Landscape: Trending Toward Precision Medicine in Cancer Care

Overview

• This trend report provides the perspectives of both payers and oncologists on key issues within the field of precision medicine, and future editions will seek to report on changes in attitudes and practices over time.

• Precision medicine in cancer care may offer a viable solution to the challenges facing our health care system, and the field is becoming increasingly important to all stakeholders.

• Advances that are being made in this field, however, are occurring at a time when the entire health care industry is under intense pressure to exercise fiscal restraint.

• Understanding the perspectives of these major stakeholders will provide insight into barriers to adoption of precision medicine and identify potential pathways for change that may lead to improved clinical outcomes.

• The creation of policies that support the development, reimbursement, and widespread adoption of innovative precision oncology interventions may play a critical role in sustaining our efforts to improve patient outcomes at a time of health care cost containment.

Extraordinary advances in science and technology are changing the way we identify, classify, and treat the more than 200 types of cancer, and are forming the foundation of precision medicine in cancer care. There is a pronounced shift toward molecular targeted therapies and increased fragmentation of oncology as common cancers are being further classified into molecular subtypes based on their genetic characteristics. The promise of precision medicine in oncology is to individualize prevention and treatment strategies based on the molecular makeup of the patient and/or the patient’s tumor.

The field of precision medicine is becoming increasingly important to all stakeholders in the health care system. Physicians, payers, and industry are focused on optimizing patient outcomes, while addressing rising health care costs, by diagnosing disease more precisely in each individual and treating each patient with only the most appropriate therapy based on molecular subtype. Additionally, ineffective therapies can harm patients. In 2010, a 5-month study at an intensive care unit (ICU) of a comprehensive cancer center found that 22.9% of all ICU admissions were due to adverse drug reactions (ADRs). The average length of stay for each patient was 6.2 days and the mortality rate was 28%.

According to the FDA, more than 140 marketed drugs include a pharmacogenomic biomarker on their label that either recommends or requires genetic testing for optimal treatment; of these, more than 40 are oncology-specific. The number of biomarker-driven cancer therapies is expected to rise in coming years as 100% of the companies surveyed by the Tufts Center for the Study of Drug Development (CSDD) are utilizing biomarker data to drive drug discovery and development. Of 36 pharmaceutical and biotechnology companies surveyed by Tufts CSDD, 80% had established strategic partnerships related to personalized medicine, 70% had submitted biomarker data to the FDA, and 50% had clinical trials collecting DNA samples from trial participants.
“With precision medicines, the cost per benefit will be lower because we will not be treating the 80% of patients who will not respond, which is what we do today with most of our treatments.”

– Oncologist from a teaching hospital in New England

“The promise of precision medicine] is to...be more cost-effective in the use of these new targeted therapies.”

– Oncologist-Partner from a Minnesota Hematology-Oncology Practice

“Hopefully patients will not receive drugs if they have no capacity to benefit...that is where the waste is.”

– Medical Director from a Northeastern US Integrated Health System

In response to demands for an improved health care system that increases quality and reduces costs, many organizations (eg, American Society of Clinical Oncology’s CancerLinQ program®) and cancer centers (eg, Moffitt Cancer Center’s Total Cancer Care®) are embracing a learning health care system. The promise of this emerging innovative model is to aggregate, analyze, and apply evidence-based knowledge to improve patient care. A learning health care system seeks to “link research and care into a seamless process by using advances in information technology (IT) to continually and automatically collect and compile from clinical practice, disease registries, clinical trials, and other sources of information, the evidence needed to deliver the best, most up-to-date care that is personalized for each patient.”

Another trend in cancer care is the shift in medication delivery, away from intravenous delivery at the oncologist’s office and toward self-administered, oral therapy in the patient’s home. A National Comprehensive Cancer Network® (NCCN®) task force in 2008 estimated that more than 25% of the approximately 400 anticancer agents in development will be administered orally. This shift from intravenous to oral agents may require fewer office visits and may provide patients with a sense of being in charge of their treatment.

All these advances, however, are occurring at a time when the entire health care industry is under intense pressure to exercise fiscal restraint. The cost of cancer care will continue to escalate in the near future, partly due to an aging population, rising direct medical costs, and expanded access under health care reform. According to the National Institutes of Health, medical expenditures for cancer are projected to reach at least $158 billion in 2020—a 27% increase from 2010.

Precision medicine interventions for oncology, including targeted therapies and molecular diagnostics, are not immune to the current pressures facing the US and other health care systems—notably, the issue of affordability. Given the above-mentioned economic challenges, there is even greater pressure on payers to manage costs of care.

Precision medicine in cancer care may offer a viable solution to the challenges facing our health care system; however, challenges to the widespread implementation and adoption of precision medicine approaches remain. The creation of policies that support the development, reimbursement, and widespread adoption of innovative precision oncology interventions may play a critical role in sustaining our efforts to improve patient outcomes at a time of health care cost containment.
Thinking ahead...

Payers may want to assess their organization’s abilities to adapt to developments in precision medicine.

- Do we know the degree of alignment (or nonalignment) between our providers and us regarding the use of precision medicine technologies?

- Are our insurance (coverage and reimbursement) policies, regulations, and practices flexible enough to meet the needs of our payer, provider, and patient stakeholders? Do we need to anticipate new or modified regulatory filings in upcoming years?

- Do we have private and secure communication channels to support appropriate patient adherence to oral, outpatient therapies? Do existing systems work, or do we need to consider new ones?

Methodology

Payers and oncologists are increasingly being challenged to make coverage and treatment decisions, respectively, for emerging precision medicine interventions in spite of the above-mentioned challenges (ie, balancing quality, costs, evidence, oral administration of more oncology drugs, patient demographic shifts). This trend report seeks to reveal the perspectives of payers and oncologists on key issues within the field of precision medicine, and future editions will seek to report on changes in attitudes and practices over time. Understanding the perspectives of these major stakeholders will provide insight into barriers to adoption of precision medicine and identify potential pathways for change that may lead to improved clinical outcomes.

This trend report is based on data obtained from a fielded survey and from in-depth interviews with subject matter experts. Participants were selected to represent a mix of government, private, and large employer payers, payers from regional and national health plans (N=50 for survey; N=5 for interviews), as well as small and large group health care providers from both community and large specialized clinics (N=50 for survey; N=5 for interviews) with geographic balance. The survey and in-depth interviews were conducted with complete transparency. Secondary research was also conducted to provide a thorough landscape analysis. (Note: This report uses the terms “survey” or “surveyed” to discuss findings from the 50 respondents, and “interview” or “interviewed” to discuss findings or comments from the 5 individuals who were interviewed.)

“A biomarker can identify whom a drug is for and, even more importantly, whom it’s not for.”

- Director from a Northeastern US Integrated Health System
Precision Medicine in Oncology: Pathway to Progress?

Key Insights

Most payers and providers surveyed and interviewed believe:

• Precision medicine in oncology is a viable solution to the challenges facing our health care system
• Precision oncology interventions can improve patient outcomes in a cost-effective manner if treatment decisions are based on the results of molecular diagnostic tests
• The short-term direct costs of biomarker-based diagnostic testing are worth the potential long-term savings in health care costs, examples of which could include decreased hospitalization, increased work days, decreased (overall) health care utilization, decreased time to arrive at the appropriate therapy, and decreased diagnostic testing for patients identified as “precision medicine patients”

The majority of payers and providers surveyed and interviewed believe that precision medicine in oncology is a viable solution to the challenges facing our health care system (Figure 1). Specifically, they are in agreement that precision oncology interventions can improve patient outcomes in a cost-effective manner, and that the short-term direct costs of biomarker-based diagnostic testing are worth the potential long-term savings in health care costs. Some interviewees stated that the potential of these interventions to address rising health care costs lies in their ability to avert waste in the health care system.

The ability of precision medicine to improve patient outcomes in a cost-effective manner comes with the following caveat from payers: treatment decisions must be made based on the results of the molecular diagnostic tests.

“Precision medicine offers one solution to the rising costs of health care because it can avoid waste in the system...when you avoid waste, you save money.”

– Director of Pharmacy Operations from a New England HMO
**Thinking ahead...**

Payers may want to assess their organization’s abilities to adapt to new developments in precision medicine.

- **Should our organization consider “post authorization” tools to follow up as to how precision medicine information was actually factored into treatment decisions?**

---

**Value of Innovation: In the Eye of the Beholder**

---

**Key Insights**

What payers and providers surveyed and interviewed believe:

- Half of payers believe that all stakeholders together should define value; 60% of oncologists believe that only oncologists should define value

- While more than half of payers surveyed believe that less than 25% of targeted cancer treatments have a price that is justified by the known health outcomes delivered, more than half of providers surveyed believe that greater than 25% of these treatments have a justified price point

- The majority of payers and oncologists are in agreement that the value of innovative precision medicines should be measured continually, and not just at the time of FDA approval

---

In our current environment, a key question facing stakeholders—policymakers, payers, industry, providers—is how to sustain biomedical innovation and optimize patient outcomes while managing rising health care costs. A lack of consensus among stakeholders regarding what constitutes value in a new treatment creates challenges for both industry and payers, as decisions have to be made about which products to bring to market and how these products should be evaluated and reimbursed, respectively.

Payers are caught between 2 sets of stakeholders with (sometimes) competing interests: patients and providers, who may want access to new treatments regardless of cost; and employers, taxpayers, and underinsured patients or caregivers, who need to contain spiraling costs. Payers are therefore under intense pressure to rein in the cost of care without negatively impacting patient outcomes or taking treatment decisions out of the hands of practicing oncologists.

---

"In oncology, we are still not thinking of the benefits of a drug in terms of cost, but this may become a factor when some drugs will not be reimbursed...In other words, I don’t place much emphasis on cost for now.”

– Oncologist from a Teaching Hospital in New England

---

"We like certainty. And for that certainty we almost accept a higher premium price on the assumption that [precision medicines] will lead to better outcomes. We can define the population and the smaller it is, the more comfortable we feel we can manage it."

– Medical Director from a Northeastern US Integrated Health System
When asked who should ultimately determine whether an intervention provides value, payers and oncologists surveyed had differing perspectives (Figure 2). Half of the payers believe that all stakeholders, including oncologists, payers, patients, and government, should define value; 60% of oncologists, however, believe that only oncologists should define value.

Payers are often at odds with oncologists in terms of what constitutes a survival benefit in the context of cancer treatment. A 2008 Zitter Group survey found that while two-thirds of oncologists believe a treatment should extend life by 3 to 6 months to constitute a survival benefit, payers believe a treatment should extend survival by at least 10 months to constitute a survival benefit. The majority of payers and oncologists surveyed for this report also have different perspectives on the benefit-cost ratio of targeted cancer treatments that have been launched within the last 5 years (Figure 3). While more than half of payers surveyed believe that less than 25% of targeted cancer treatments have a price that is justified by the known health outcomes delivered, over half of providers surveyed believe that more than 25% of these treatments have a justified price point.
Improved survival and direct cost of therapy are the top attributes that payers consider when making coverage decisions (Figure 4). After overall survival and cost, payers and oncologists surveyed are in agreement that the next most valuable attributes of a new cancer intervention are improved progression-free survival, improved quality of life, and fewer side effects/hospital visits (ranked in that order; data not shown). Although payers agree that quality-of-life improvements are valuable attributes of a new cancer intervention, quality of life is not a key attribute that payers surveyed and interviewed consider when making coverage decisions for these interventions. According to those interviewed, part of the challenge lies in the ability to define suitable quantitative metrics.

“Quality of life is not as important in our decision making because it’s hard to measure.”
– Pharmacy Director from a Mountain State Integrated Health System

“Quality of life is very important to the patient and doctor. Quality of life is impacted by toxicities and comorbidities that are important in terms of how a patient looks and feels...and are also important [for cost control] because it takes a lot of effort to manage these things.”
– Oncologist from a Los Angeles Hematology-Oncology Practice
“Quality of life is important because it determines patient satisfaction with treatment, and payers are increasingly demanding improved satisfaction. Additionally, a good quality of life improves the relationship between doctor and patient and allows them to better deal with difficult decisions later on.”

– Oncologist-Partner from a Hospital-affiliated Oncology Practice

“Every patient is unique...and this is why existing value measurement approaches are not helpful for decision making.”

– Oncologist from a Teaching Hospital in New England

A number of evidence-generation approaches are being used by payers and oncologists to help assess the value of innovative technologies and care delivery, including clinical trial data, comparative effectiveness research (CER), cost-effectiveness analysis (CEA), and health technology assessments (HTAs). However, these value assessment tools only measure a single point in time and may become increasingly challenged by precision medicine in oncology.15

The majority of payers and oncologists surveyed rely most on the same 3 primary evidence-generation tools when making policy or treatment decisions, respectively, for precision oncology interventions: 1) clinical trial data, 2) clinical guidelines, and 3) peer-reviewed publications. Furthermore, most payers and oncologists are in agreement that the value of innovative precision medicines should be measured continually, and not just at the time of FDA approval (Figure 5).

| Figure 5 When should the value of innovative precision oncology interventions be measured? |
|---|---|
| Continuously | Oncologists: 50% Payers: 50% |
| After a defined period of use in the real-world setting | Oncologists: 20% Payers: 30% |
| At conclusion of phase 4 studies | Oncologists: 10% Payers: 10% |
| At the time of FDA approval | Oncologists: 10% Payers: 10% |

Percent of Respondents

Oncologists

Payers
At this point in time, the majority of payers and oncologists surveyed do not feel strongly either way that the Patient-Centered Outcomes Research Institute (PCORI) will prove to support advances in precision medicine in oncology, or whether precision medicine and comparative effectiveness research are mutually exclusive (Figure 6).

To help make the most informed coverage decisions for precision medicine interventions, payers surveyed need additional information beyond what existing value assessment approaches provide. Payers would also like more information on the following:

- Clinical utility data for molecular diagnostic tests
- Economic data (eg, cost per PFS, cost of overall care)
- Long-term, real-world clinical and economic data
- Head-to-head studies/data

**Thinking ahead...**

Payers may want to assess their organization’s abilities to adapt to new developments in precision medicine.

- Do our stakeholders have a common definition of success for the implementation and use of precision medicine....or a designated arbiter?
- Has our organization designated or defined evidence-based measures for precision medicine?
- Does our organization need to reach out to, and possibly work with, third-party organizations that could provide such evidence-based measures?

“[The value of innovative precision oncology technologies] should be measured continuously because we have to make decisions along that spectrum.”

– Medical Director from a New Jersey Health Plan

“We don’t want a model to tell us what is cost-effective. We want this information to be based on real-world data.”

– Medical Director from a Northeastern US Integrated Health System
In market response to increasing cost pressures, payers are moving away from *volume-based* and toward *value-based* coverage and reimbursement models. For example, a coverage model affects how the payer (e.g., employer or health plan) will initially cover and reimburse for the drug while collecting data about the drug’s performance. This information ultimately leads to better coverage decisions for specific patient subpopulations.16 Some coverage models also impact how much an insurer will pay the manufacturer for the drug.17 A payment model affects how the payer will pay providers (e.g., hospitals or physicians). Payments may be tied to quality metrics or cost targets.18 The goal of a value-based model is to align the level of reimbursement with the predetermined value achieved. According to payers surveyed, there are multiple coverage models being tested or implemented by payers for precision oncology interventions, including coverage with evidence development, outcomes-based risk sharing, and performance-linked reimbursement (Figure 7). Additionally, there are many payment models that are being tested or implemented by payer organizations for precision oncology interventions, the most common of which include fee for service, pay for performance, and episode or bundle payments (Figure 8).
Payers were asked what types of payment models are being tested or implemented by their organization for precision oncology interventions (respondents could choose more than 1 response). Other responses included “capitation,” “none,” “DIRPP” (drug intervention response predictions with paradigm—a probabilistic graphical model).

Fueled by a mutual interest in improving care quality and lowering costs, some payers and product sponsors are collaborating in evidence-generation programs to achieve this vision. Most payer organizations surveyed, however, are not currently engaged in such programs with product sponsors for precision medicine interventions, and most are not sure whether there will be an increase in these types of collaborations in the near future (Figure 9).

“We tried to work with [a pharmaceutical company] on a risk-based contract model for some of their products, but we could never come to agreement on what the measured outcomes were going to be.”

– Pharmacy Director from a Southwestern US Integrated Health System
Payers surveyed were divided regarding the point during the clinical development process at which product sponsors should begin to interact with payers (Figure 10). Almost half believe these interactions should begin during phase 2 or 3 clinical trials, whereas almost 40% believe these interactions should begin only after FDA approval.

“Some manufacturers actually engage us in phase 2 of drug development. Why? Because if this drug is coming out five or six years later, what a shame that we weren’t involved in helping them understand what the environment may look like in terms of defining what value needs to look like and the end points they should be considering. When they do come to market, hopefully they have what it takes to be covered.”

– Medical Director from a Northeastern US Integrated Health System

Thinking ahead...

Payers may want to evaluate their organization’s abilities to adapt to new developments in precision medicine.

• Are our coverage models and/or reimbursement models aligned with our organization’s overall goals with respect to precision medicine? Have we evaluated needs at all levels: customer, payer, provider, and patient?

• Should we seek collaboration with manufacturers, laboratories, or other organizations to help us characterize and use precision medicine information?
Molecular Diagnostics: Making the Value Proposition

Key Insights

• The majority of payers and oncologists surveyed agree that the biggest concern they have with respect to expanding coverage for molecular diagnostics and incorporating these tests into clinical practice, respectively, is the lack of data on the tests’ clinical utility.

• Most payers surveyed and interviewed are concerned that providers will order diagnostic tests, but will not use the test results to make treatment decisions.
  – However, the majority of oncologists surveyed almost always prescribe the molecular diagnostic test before treating patients with targeted agents, and almost always base their clinical decisions on the results of the test.

• Payers and oncologists interviewed would like molecular diagnostic tests to be incorporated into clinical guidelines.

• When asked about the level of evidence needed for molecular diagnostic tests, most payers and oncologists are in agreement that:
  – These tests should have to provide the same level of evidence as therapeutics, via randomized, controlled clinical trials.
  – FDA should regulate all LDTs.
  – FDA approval of these tests will increase the likelihood of clinical adoption.

• However, according to payers interviewed, reimbursement and clinical adoption may not be guaranteed even with proven clinical utility.
Targeted, more effective treatments will be unattainable unless providers have molecular information about their patient’s disease. The majority of payers and oncologists surveyed agree that the biggest concern they have with respect to expanding coverage for molecular diagnostics and incorporating these tests into clinical practice, respectively, is the lack of data on the tests’ clinical utility (Figure 11a and b). This finding is consistent with a recent survey demonstrating that 83% of payers cover diagnostics in breast cancer, specifically epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor 2 (HER2) testing, because of the validated clinical utility of these tests.20

“Sometimes we deal with biomarkers that are not definitive. If the test is negative, it means patients may not benefit as much, but you can’t say that they won’t benefit at all. We like to deal with certainty, and certainty is black and white; you get the therapy or you don’t.”

– Medical Director from a Northeastern US Integrated Health System
Additionally, most payers surveyed and interviewed are concerned that providers will order diagnostic tests, but will not use the test results to make treatment decisions. In these cases, the molecular diagnostic would only add cost to an already financially overburdened health care system. Consequently, when making coverage decisions for molecular diagnostics, payers surveyed claim that they must have clinical utility and validity data, and the test results must change patient management (Figure 12). Interestingly, the majority of oncologists surveyed almost always prescribe the molecular diagnostic test before treating patients with targeted agents—and almost always base their clinical decisions on the results of the test (Figure 13).

“There are so many molecular targets for which tests are being developed that may or may not lead to decisions about drug efficacy that it’s overwhelming…I think it’s becoming increasingly difficult for practicing oncologists to keep up with all of this material.”

– Oncologist from a Los Angeles Hematology-Oncology Practice
In addition to the lack of clinical utility data, a lack of evidence-based guidelines on the use of diagnostic tests is of almost equal concern for oncologists (Figure 11b). Payers and oncologists interviewed mentioned the need for these tests to be incorporated into clinical guidelines. In 2011, 90% of payers indicated that clinical guidelines influence their decision to cover an oncology diagnostic test, with American Society of Clinical Oncology (ASCO) and NCCN guidelines given equal preference.20

Payers require that precision medicine interventions demonstrate clinical- and cost-effectiveness similar to other clinical interventions. While the incorporation of molecular diagnostics into clinical practice may increase short-term costs, they may provide critical information that can change the course of treatment—and the course of the disease. Therefore, long-term cost savings for medical care may be possible if, for example, costly trial-and-error–based medicine is replaced with precision medicine.21 Additionally, the costs associated with treating patients who will not respond to treatment may be reduced22 and the rate of adverse events and unnecessary hospital admissions may also be reduced.23 For these reasons, the majority of payers and oncologists believe such tests are worth the potential long-term savings (Figure 1).

Most molecular-based tests are LDTs.24 Although a few LDTs are FDA approved (eg, MammaPrint® and AlloMap®), the majority of these tests are regulated under CMS’s authority in accordance with Clinical Laboratory Improvement Amendment rules.25 Given the considerable growth in volume and complexity of LDTs—and their growing role in informing critical health care decisions such as treatment selection, dosing, and exclusion—the FDA would like to end its policy of enforcement discretion for these tests and is moving to regulate all LDTs.26 The regulatory framework for LDTs will be risk-based according to intended use, and a phased-in, long-term approach is planned. When asked about the level of evidence needed for molecular diagnostic tests, most payers and oncologists are in agreement that these tests should have to provide the same level of evidence as therapeutics, via randomized controlled clinical trials (Figure 14). They also agree that the FDA should regulate all LDTs, and that FDA approval of these tests will increase the likelihood of clinical adoption (Figure 14). However, according to payers interviewed, reimbursement and clinical adoption may not be guaranteed even with proven clinical utility.

Note: MammaPrint is a registered trademark of Agendia BV, Amsterdam. AlloMap is a registered trademark of CareDX, Inc.
**Figure 14**

Payers and oncologists were asked to rate their level of agreement with each statement.

- I feel the FDA approval of a molecular diagnostic will increase the likelihood of clinical adoption.
- I support the FDA's decision to regulate all laboratory-developed tests (LDTs).
- I feel that diagnostic tests should have to provide the same level of evidence as therapeutics via randomized control trials.

**Thinking ahead...**

Payers may want to evaluate their organization's abilities to adapt to new developments in precision medicine.

- Do we have access to clinical utilization data from LDTs about precision medicine (via electronic medical records or other sources)?
- Are we satisfied with the standardization of LDT procedures and data?

“Unlike drugs, where FDA approval means we cover them, for diagnostic tests, FDA approval means we’ll look at them.”

– Medical Director from a New Jersey Health Plan
Clinical Adoption: Managing Information Overload

Key Insights
- The majority of oncologists surveyed feel that they have the information and resources they need to effectively make clinical decisions regarding precision medicines; however, payers need more resources.
- Most oncologists surveyed are somewhat to very confident in their level of genetic knowledge to inform clinical decision making.

The advent of vast amounts of clinical, genomics, and outcomes data—as well as rapid accumulation of evidence for these extremely complex technologies—is changing the landscape for understanding what is effective and what treatment approach should be followed. The widespread coverage and adoption of precision oncology interventions depends heavily on the degree to which the payer and provider communities are able to manage the volume of information.

Most oncologists feel that they have the information and resources they need to effectively make clinical decisions regarding precision medicines; however, payers need more resources (Figure 15). The majority of both payers and oncologists rely on peer-reviewed publications over all other resources to keep abreast of advances in precision medicine (Figure 16). Additionally, most oncologists are somewhat to very confident in their level of genetic knowledge to inform clinical decision making (Figure 17).

![Figure 15](image-url)
Payers and oncologists were asked what types of educational resources they use most frequently.

![Graph showing usage of educational resources]

Oncologists were asked how confident they are in their level of genetic knowledge to inform clinical decision making for innovative precision medicine products.

![Graph showing confidence levels]

Thinking ahead...

Payers may want to evaluate their organization’s abilities to adapt to new developments in precision medicine.

- Do we have an IT strategy in place to manage and utilize precision medicine to its full potential?
- Do we have managerial and/or training systems in place to manage and utilize precision medicine to its full potential?
Conclusions

The potential benefits of precision medicine in oncology are promising. Full implementation of precision medicine will challenge all stakeholders as they seek ways to create real-world clinical outcomes data, develop a transparent regulatory framework, and integrate molecular diagnostics into the reimbursement system.

As precision medicine in cancer care becomes a reality in mainstream clinical practice, payers and providers will have to work together, continuing to make policy and clinical decisions, respectively, on the rapidly growing numbers of complex molecular diagnostic tests, companion diagnostics, and biomarker-guided therapies. The ability of precision medicine interventions to improve patient outcomes in a cost-effective manner relies on both the clinical utility of the diagnostic test and the incorporation of test results into therapeutic decision making. To achieve this goal, payers and providers must determine whether the information yielded by each diagnostic test can effectively guide clinical decision making. Furthermore, correlating patient outcomes of a specific therapy with specific diagnostic test results should be reinforced and endorsed in treatment guidelines.

The art of medicine is still alive and well, so clinical evaluation by oncologists is still necessary. Payers will drive the need for quantitative measures, and simultaneously, for interventions that optimize quality and costs across a defined patient population. Advances in validating companion diagnostics, improvements in information technology, and growing skill among clinicians in the interpretation of clinical results will be key. All stakeholders will need to work together to achieve better patients outcomes.
References


