

Catch-22 for Cancer Tests

Why biomarker assays struggle for reimbursement

Personalized cancer medicine needs a solid foundation of proven, precise, and readily available molecular biomarker tests to guide treatment. As test makers struggle to build that foundation, one of their biggest challenges is that cost incentives aren't always fully in place to successfully deliver the tests.

"It's a vicious cycle," says Daniel Hayes, MD, professor of medicine at the University of Michigan and clinical director of the breast oncology program at the University of Michigan Comprehensive Cancer Center in Ann Arbor. "There is a disconnect between the clinical value and the economic value of tumor biomarker tests. Third-party payers wring their hands if a test costs more than \$50 or \$100, even if it might save you from treating a patient with a drug that costs \$100,000 a year and may have toxic side effects."

"We value therapeutics a lot more than we value diagnostics, although a bad biomarker is as bad as a bad drug," says Hayes, senior author on a recent commentary on challenges for tumor diagnostics (*Sci Transl Med* 2013;5:196cm6).

"Reimbursement for tests by payers is poor and at best uncertain," says Debra Leonard, MD, PhD, professor and chair of pathology at the University of Vermont College of Medicine in Burlington, and coauthor on the same commentary. "Clinical laboratories generally don't have NIH or other funding for a test validation clinical trial, so labs may validate a test with either relevant samples without known clinical outcomes or smaller sample sizes than might otherwise be optimal. Then the test is poorly valued, because the evidence review groups don't have the data to say the test is actually useful. You get into this recurring cycle of not knowing, before tests are put into clinical use, whether they affect clinical outcomes or not."

Given such uncertainties, reimbursement payments may not reflect a test's value or full costs of development and delivery, comments Gary Gustavsen, a program manager with Health Advances, a consultancy in Weston, MA, which works with many testing firms. "People say half-jokingly that this new industry carries the risks of drug development without the rewards of drug development," he says.

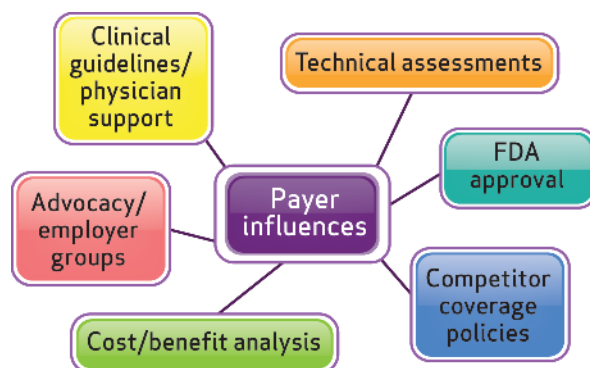
EARNING EVIDENCE

Cancer biomarker tests cover a very broad range, from Ki67 proliferation analyses to cancer recurrence assays, from companion diagnostics for targeted drugs to multigene panels bundled with decision support information, and from screening assays to recurrence monitoring tests. Payers struggle to evaluate this onslaught of products, which may arrive with little evidence of clinical usefulness.

"We often can't tell what kind of test is being used," says Lee Newcomer, MD, senior vice president of oncology services at UnitedHealthcare, an insurance provider in Minnetonka, MN. "We need to know what each and every test does and how to use them."

Biomarker testing "is an absolutely critical area of medicine for development," he adds, "but we can't skip the evidence part."

Factors Influencing Test Coverage



The Reimbursement Landscape for Novel Diagnostics, Health Advances

As health-care payers look to assess the value of new cancer diagnostics, many factors may affect their decision making on reimbursements for tests.

A 5-year follow-up to the RASTER study of Agendia's MammaPrint breast cancer recurrence assay offers a gold standard for evidence of enhanced treatment decision making, says Newcomer (*Int J Cancer* 2013;133:929-36). "Not all of the studies have to be randomized controlled trials, but they need to be done," he says.

Bas van der Baan, vice president of clinical affairs at Agendia in Irvine, CA, notes that his firm began collecting evidence of MammaPrint's clinical effectiveness when the product debuted in 2004, and the RASTER follow-up study was published in 2013. "This illustrates the investment to reach a level of evidence that needs to be accumulated to show that a test is clinically useful," he says. "For smaller cancer indications, that may not be economically viable."

Another category of tests, companion diagnostics for targeted therapies that have been approved by the FDA, might seem to offer a straightforward value proposition.

However, there are still devils in the details. "Companion diagnostics don't work very well from a patient care perspective," Leonard says. In lung cancer, for example, the small amount of tissue that may be adequate for both standard pathology and a multigene sequencing panel may be insufficient for standard pathology plus multiple individual companion diagnostic tests. "We actually need a combined test with all of the companion diagnostics in it that are relevant for a patient," Leonard says.

Multigene panels also can offer practical advantages in reproducibility and quality control over companion diagnostics run one at a time, she notes, "but the FDA hasn't approved such tests."

Given all the players and challenges in developing, delivering, and paying for new cancer tests, Gustavsen, Hayes, Leonard, and Newcomer call for a national dialogue that helps to establish clearer frameworks and economic incentives.

"We need to set the bar high and reward people who get across the bar," sums up Hayes. "That's not easy to do and therefore we need to increase the payoff, so that people do it right." —Eric Bender ■

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