Quest Diagnostics™

Why companion diagnostics are now **essential to cancer care**

Introduction

It's called precision medicine for a reason: companion and complementary diagnostic tests remove some of the uncertainty about which cancer drug or drug combination may be the most appropriate for a specific cancer in a specific patient.

The U.S. Food & Drug Administration (FDA) defines a companion diagnostic as "a medical device, often an *in vitro* device, which provides information that is essential for the safe and effective use of a corresponding drug or biological product."[1] Often, the drug and diagnostic are approved by the FDA simultaneously during development.

Fueling the ongoing development of companion diagnostics are cancer's rising costs and increasing prevalence, as more than 1.7 million new cases will be diagnosed in the US in 2018.[2] Currently, companion diagnostics are used for many different cancers to help identify specific genetic or somatic mutations in patient samples that are targets for specific therapies.

$80.2B

total healthcare costs for cancer in the US in 2015[3]

52%

of this cost is for hospital outpatient or doctor office visits[3]

The companion diagnostics market is projected to grow by 20% annually through 2023,[4] and as the industry advances, health systems and community cancer centers will play a major role. Keeping up—and staying ahead—will require investing in the right technologies and systems in order to bring the latest information and options to the point of care.

Collaboration will also be necessary as more health systems work with pharmaceutical companies and laboratories to research and evaluate the effectiveness of new therapies and corresponding diagnostics. And once these have proven successful, all players must come together to make companion diagnostic tests more accessible and affordable for more patients. Doing so will help health systems provide effective and cost-efficient patient management solutions, for improved patient outcomes.

Companion vs. complementary

What's the difference? Companion diagnostics are typically linked to a specific drug within its approved label. Complementary diagnostics are associated more broadly, not with a specific drug but with a class of drugs, and not confined to specific uses by labeling.[5]

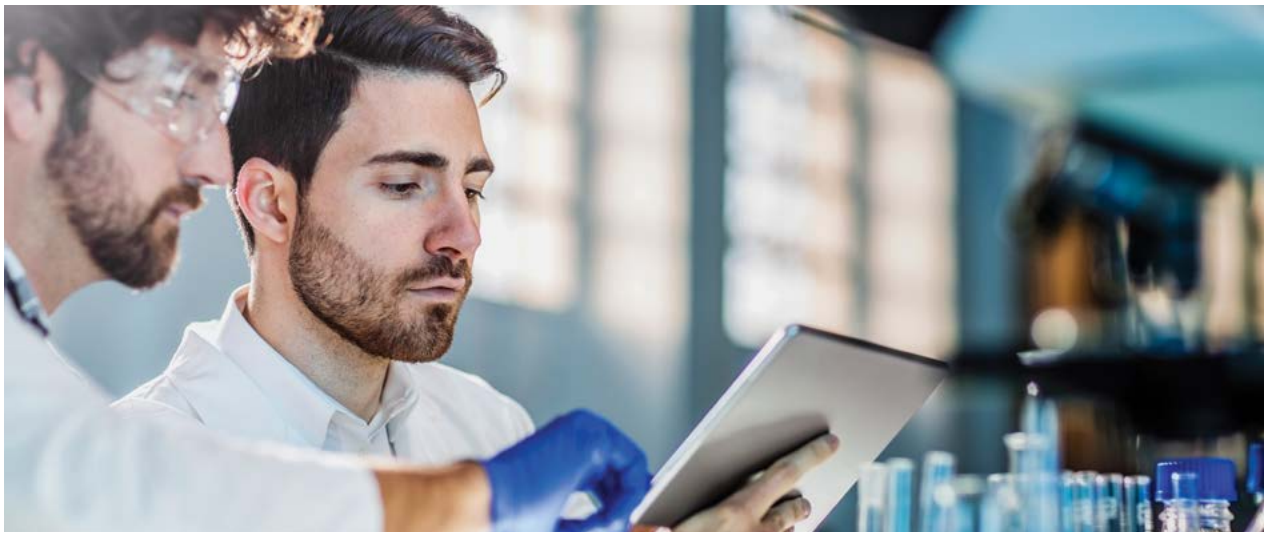
Companion diagnostics: a brief history

Genomic biomarkers have altered the way we treat cancer, revealing the unique features of each patient's tumor. Companion diagnostics that measure these biomarkers have become essential—simplifying decision-making, reducing uncertainty, and improving outcomes.[6]

Companion diagnostics got their start in 1998 with the approval of Herceptin (trastuzumab).[7] Scientists recognized that only those women whose breast tumors overexpressed the *HER2* receptor were benefiting from the drug.[7] The need to determine how much *HER2* was present and how much was necessary to respond to therapy prompted the development of a new in vitro diagnostic device to detect and quantify *HER2*. Thus, the first companion diagnostic, HercepTest™, was approved along with trastuzumab.[7]

Like the therapies they work with, all in vitro diagnostic tests are subject to FDA regulation. In 2014, the FDA issued "Guidance for Industry: In Vitro Companion Diagnostic Devices," to help organizations identify the need for companion diagnostics at an earlier stage in the drug development process and to plan for co-development of the drug and companion diagnostic test. The FDA followed this up with "Principles for Codevelopment of an In Vitro Companion Diagnostic Device with a Therapeutic Product" in 2016, to assist therapeutic product and in vitro diagnostics sponsors.

Since then, the FDA has worked with the diagnostic and pharmaceutical industries to ensure that companion diagnostics are approved in a timely manner along with their therapeutic partners—referred to as the co-development model.[7]



The current state of companion diagnostics

As they are most often developed in parallel with a drug, companion diagnostics have played an important role in therapy development—improving the likelihood that a drug succeeds in clinical trials.[6] Currently, there are more than 40 approved cancer treatment-related companion diagnostics.[8]

Sample list of cancer treatment-related companion diagnostics[9]

Companion diagnostic			Drug	Indication
Biomarker	Type	Year approved		
KRAS mutation	LDT	2006	Cetuximab, panitumumab	Colorectal cancer
	PMA	2012		
BRAF V600E mutation	PMA	2011	Vemurafenib	Melanoma
ALK fusion	PMA	2011	Crizotinib	Non-small cell lung cancer
EGFR mutation	LDT	2003	Gefitinib, erlotinib, afatinib	Non-small cell lung cancer
HER2 amplification	PMA	1998	Trastuzumab	Breast cancer
	PMA	2008		
BCR-ABL translocation	PMA	2005	Imatinib, dasatinib, nilotinib	Chronic myeloid leukemia

LDT = Laboratory developed test in CLIA-certified clinical laboratory
PMA = Pre-market approval by the FDA

New developments and approvals in companion diagnostics are occurring at a faster and faster rate. In 2016, for example, the FDA approved the first liquid biopsy—for non-small cell lung cancer—and in 2017, it granted its first approval for a next-generation sequencing-based diagnostic to identify patients with advanced ovarian cancer eligible for treatment with rucaparib.[10]

How companion diagnostics have improved cancer care

As a result of developments in both companion diagnostics and partner therapies, patients with cancer have better treatment options than ever before—and, in many cases, their quality of life has been substantially improved by target-based therapies compared with conventional cytotoxic therapies.[11]

Below is a sampling of findings and results.

- The discovery of the *BCR-ABL* gene fusion in chronic myeloid leukemia (CML) and the development of imatinib and its companion diagnostic improved the overall survival rates of CML patients to 90% over 5 years and 88% over 8 years[11]
- For *HER2*-positive breast cancer, the addition of trastuzumab to chemotherapy significantly slowed disease progression, increased the objective response rate (32% vs. 50%), prolonged survival time (median 20.3 vs. 25.1 months), and reduced the risk of cancer-related death by 20%[11]
- At least 8 clinical trials comparing frontline *EGFR TKI* treatment with standard platinum chemotherapy in patients with *EGFR*-mutated non-small cell lung cancer have shown that targeted treatment is better than standard chemotherapy, leading to a significant improvement in survival, which reached a plateau of 24 to 30 months[12]
- Pembrolizumab was approved for the treatment of patients with advanced solid tumors that have specific genomic changes, based on findings from 149 patients with MMR-deficient or MSI-H solid tumors—90 had colorectal cancer and 59 had one of 14 other types of cancer—who were enrolled in 5 clinical trials; tumors shrank in 40% of patients, and in 78% of those patients, tumor response lasted 6 months. In one of the studies that included patients with 12 different types of cancer, 21% of patients experienced a complete remission of cancer[13]

Looking ahead: multiple biomarkers

Though companion diagnostics have played a vital role in redefining how we treat cancer, more can be done. Currently, most companion diagnostics test for one biomarker at a time, which can result in missed information or lead to treatment delays.[6] Many are recognizing a need for diagnostics that can test for multiple biomarkers simultaneously.

In fact, the FDA has noted a trend toward more advanced tests that can detect dozens or even hundreds of genetic mutations in a single test—known as an oncopanel—rather than one test to detect a single genetic mutation.[2]

90% of oncologists in the US believe multi-biomarker diagnostics will be the standard of care within the next 3–5 years[14]

Advancing companion diagnostics: the role of health systems and community cancer centers

Health systems and cancer centers play a key role in the advancement of companion diagnostics, therapies, and cancer care, often serving as the connecting link between pharmaceutical companies, diagnostic laboratories, healthcare professionals, and patients.

Collaboration has been and will continue to be paramount for the development and approval of new drugs and diagnostic devices, which rely on the success of clinical trials. For example, The University of Texas MD Anderson Cancer Center engaged in a strategic clinical research collaboration with Merck to evaluate pembrolizumab over a 3-year period, focusing on gastroesophageal adenocarcinoma, pancreatic adenocarcinoma, and hepatocellular carcinoma tumors. The goal, according to MD Anderson's Cancer Medicine division head, is to accelerate the pace of discovery and help speed the delivery of new cancer treatments to patients who need them.[15] To that end, collaboration between health systems and other key players will also be necessary to make both diagnostic tests and treatments more accessible to more patients.

Health systems and cancer centers will lead the way in adopting new technologies and systems to bring more diagnostics—and treatments—to more people. This means making the right investments and building the right capabilities now to provide clinicians with real-time decision-support systems (i.e., bioinformatics).

Conclusion

Companion diagnostics—and partner therapies—are changing not just cancer care, but also patient outcomes, for the better. As companion diagnostics continue to evolve, health systems and community cancer centers will play a major role, connecting the dots between pharma, labs, providers, and patients, and making tests more accessible.

By supporting and advancing the evolution of targeted therapies with research, clinical trials, new technologies, and bioinformatics systems, health systems will help to ensure that, even as the number of cancer cases continues to grow, more patients receive the right treatment supporting more cures.

Advance precision medicine with oncology testing from Quest Diagnostics

Quest offers solutions and services to help you ensure effective cancer care, while supporting improved clinical and performance outcomes.

- A broad oncology test menu, including molecular testing, companion diagnostics, and pharmacogenomics tests
- Innovative bioinformatics solutions, including IBM Watson™ Genomics from Quest Diagnostics®
- Clinical expertise, including access to board-certified/fellowship-trained pathologists and genetic counselors

References

1. U.S. Food & Drug Administration. Companion diagnostics. Available at https://www.fda.gov/medicaldevices/productsandmedicalprocedures/invitrodiagnostics/ucm407297.htm. Accessed July 17, 2018.
2. National Institutes of Health: National Cancer Institute. Cancer statistics. Available at www.cancer.gov/about-cancer/understanding/statistics. Accessed May 21, 2018.
3. American Cancer Society. Cancer facts & figures 2018. Available at www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf. Accessed May 25, 2018.
4. Research and Markets. Global companion diagnostics market research report insights, opportunity analysis, market shares and forecast, 2017–2023.
5. Milne CP, Bryan C, Garafalo S, et al. Complementary versus companion diagnostics: apples and oranges? *Biomark Med.* 2015;9(1):25-34.
6. Miller V. The clinical value of a comprehensive approach to companion diagnostics. Foundation Medicine. 16 Oct 2017. Available at www.foundationmedicine.com/blog/the-clinical-value-of-a-comprehensive-approach-to-companion-diagnostics. Accessed July 17, 2018.
7. Mansfield EA. FDA perspective on companion diagnostics: an evolving paradigm. *Clin Cancer Res.* 2014;20;1453-1457.
8. U.S. Food & Drug Administration. List of cleared or approved companion diagnostic devices (in vitro and imaging tools). Available at www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm301431.htm.
9. Barrett JC, Frigault MM, Hollingsworth S, et al. Are companion diagnostics useful? *Clin Chem.* 2013;59:198-201.
10. The American Society of Clinical Oncology. The state of cancer care in America, 2017: a report by the American Society of Clinical Oncology. *J Oncol Pract.* 2017;13(4):256-e394.
11. Shin SH, Bode AM, Dong Z. Precision medicine: the foundation of future cancer therapeutics. *NPJ Precision Oncology.* 2017;1:12.
12. Rolfo C, Passiglia F, Ostrowski M, et al. Improvement in lung cancer outcomes with targeted therapies: an update for family physicians. *J Am Board Fam Med.* 2015;28(1):124-133.
13. American Society of Clinical Oncology. Advances in cancer treatment. Available at www.asco.org/research-progress/reports-studies/clinical-cancer-advances-2018/advances-cancer-treatment. Accessed July 18, 2018.
14. Lee J, Patel R, Ruch D. Companion diagnostics: the expanding reach of personalized medicine. *In Vivo.* 14 Mar 2017. Available at invivo.pharmaintelligence.informa.com/IV005045/Companion-Diagnostics-The-Expanding-Reach-Of-Personalized-Medicine. Accessed July 6, 2018.
15. MD Anderson. Merck and MD Anderson announce immuno-oncology research collaboration in solid tumors. 13 Aug 2015. Available at www.mdanderson.org/newsroom/2015/08/merck-and-md-anderson-announce-immuno-oncology-research-collabor.html.

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