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DIAGNOSTIC TESTING & Emerging Technologies

New Trends, Applications, and IVD Industry Analysis

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Two App Marketplaces Ramping Up Consumer Genomics Offerings

Two personal genome app marketplaces—Sequencing.com (San Francisco, Calif.) and Helix (San Carlos, Calif.)—are now up and running offering consumers a combined total of 55 products for purchase. While both companies are optimistic about the potentially explosive growth of the nascent industry, analysts still question the sustainability of initial demand, how regularly curious customers will engage with these apps, and how the marketplaces will overcome privacy concerns and the challenge of reliably, yet simply, communicating complex information.

"Genomics apps are very much an emerging market," Brandon Colby M.D., the founder and CEO of Sequencing.com, tells *DTET*. "We launched Sequencing.com not even a year ago and it has grown very rapidly because of demographics. Millions of people have had their genomes sequenced, and they want added value beyond that initial result. The full value has not been unlocked and they are trying to find it."

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Consortium Releases New Interoperability Standard for Lab IT Systems

With the release of a new information technology (IT) standard, the dream of true interoperability of electronic health care information has gotten one step closer to reality. The new standard, called LIVD maps in vitro diagnostic (IVD) test results directly to the Logical Observation Identifiers Names and Codes (LOINC) code set for identifying lab procedures and results.

In other words, LIVD enables the automated transfer of test results directly to laboratory information systems and electronic health records, without transmitting plain text or non-machine-readable PDF reports. Previously there was not a unique relationship between LOINC codes and each individual test.

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Two App Marketplaces Ramping Up Consumer Genomics Offerings, *from page 1*

Sequencing.com

In addition to providing tools to curious consumers, Sequencing.com seeks to solve many of the challenges early players in the sequencing field face. The company says it provides researchers a source of genetic data through customers ("altruists") who donate their genetic data and provides laboratories a secure storage solution for all of their genetic data.

Sequencing.com now has 35 apps, mostly developed by third parties, and is expecting to double the number of available apps in 2018, while reaching hundreds of thousands of users by the end of 2017 and approaching millions of users "rapidly" after that.

Users can import genetic data from companies like 23andMe, Ancestry.com, GeneDx, Illumina, National Geographic, and Sequencing.com converts the data into a format optimized for the specific purchased app. Or, if users have not yet had their DNA sequenced, Sequencing.com has a list of preferred providers offering testing services (like Dante Labs and Genomics Personalized Health).

Sequencing.com offers developers a "simple and fair" arrangement, with 75 percent of revenue going to the developer. The app developer sets prices with current apps ranging in price from free to $199.

While the company classifies early growth as "organic," it recently started partnering with laboratories, which is expected to substantially grow the user base. Laboratories inform their customer about sequencing.com and provide a user ID and password. Sequencing.com provides safe storage of the laboratory's genetic data and whenever a file is used to generate revenue (the laboratory's client buys an app through the marketplace), the laboratory receives royalties. Additionally, the company is exploring a subscription-pricing model in which clients receive updates on a regular basis as knowledge of genetic variants evolves.

Helix

Illumina-backed Helix, which launched in late July with 20 apps, operates slightly differently. A customer's first purchase on Helix.com requires a saliva collection kit that has a one-time cost of $80. The saliva sample is analyzed in Helix's CLIA- and CAP-accredited sequencing laboratory (in San Diego) using the proprietary Exome+ assay, which sequences all 22,000 protein-coding genes.

The data is securely stored and the user can then order products from marketplace. Helix securely shares the relevant portion of the DNA data with the app partner, when ordered by the user. Like Sequencing.com, Helix offers products covering ancestry, entertainment, family, fitness, wellness, health, and nutrition. Helix also offers customers access to independent genetic counseling before or after ordering any app, through Genome Medical .

Looking Forward

Last year, a survey by financial services firm UBS found that the majority

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> *"Our understanding of how DNA impacts health and wellness is advancing rapidly and we are moving towards an era where insights from your DNA will be essential to how you live and the decisions you make, from the moment you wake up until the minute you go to sleep."*
>
> — Robin Thurston, CEO, Helix

of 1,000 Americans questioned were aware of consumer genomic tests, but only five percent said they had been tested on their own initiative for nonclinical purposes. But substantially more—half of those questioned—reported being open to pursuing future testing.

"Our understanding of how DNA impacts health and wellness is advancing rapidly and we are moving towards an era where insights from your DNA will be essential to how you live and the decisions you make, from the moment you wake up until the minute you go to sleep," said Helix's CEO Robin Thurston in a statement. "The Helix marketplace makes this possible by providing an open platform for emerging and established businesses who can now build or enhance their products with DNA sequenced at our state-of-the-art CLIA- and CAP-accredited lab."

Colby says that there is "limitless growth potential" when developers focus on unique integration of genetic data into popular apps used daily (e.g., weather forecasts cross-referenced with genetic information may look at sunburn risk and in real-time remind you to use sunscreen).

The U.S. Food and Drug Administration (FDA) still has not offered final guidance on how it will regulate the growing mobile health market.

"Our app market is not a laboratory and it is not offering genetic testing," Colby explains. "We are a software platform that transforms data from existing genetic data. The same regulatory landscape [faced by 23andMe] would not apply because of the clear differentiation that we are not functioning as a laboratory and we are not licensed as a laboratory."

However, Colby adds, "if an app is specifically for clinical use—for diagnosis or treatment—then it may fall under the guise of the FDA, as it should.

Takeaway: The two consumer genomic app marketplaces, Sequencing.com and Helix, are optimistic that curiosity of the empowered health consumer will drive growth in this emerging market.

Celebrity Power to Drive Testing Extends Beyond 'Angelina Jolie Effect'

The power of celebrity impacts health decisions and drives testing decisions beyond the "Angelina Jolie effect." A study published in the July issue of *Prevention Science* demonstrates the "Charlie Sheen effect," which found that the actor's public disclosure of his positive HIV status drove record sales of rapid in-home HIV test kits. Furthermore, the researchers found that increased sales can be predicted by Web searches, which may provide a future means of planning for public health screening responses to real-time events.

The U.S. Centers for Disease Control and Prevention says that untested individuals are responsible for most new HIV infections and that seizing on opportunities to increase testing awareness is the most cost-effective HIV prevention strategy. This study can inform how to capitalize on future opportunities to increase screening.

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Consortium Releases New Interoperability Standard for Lab IT Systems, *from page 1*

The standard was released by the IVD Industry Connectivity Consortium in collaboration with Integrating the Healthcare Enterprise's (IHE's) Pathology and Laboratory Medicine domain, Regenstrief Center for Biomedical Informatics, the U.S. Centers for Disease Control and Prevention, and the U.S. Food and Drug Administration and was based on efforts resulting from the National Institutes of Health's (NIH's) 2016 workshops on Promoting Semantic Interoperability of Laboratory Data. The LIVD specification adopts interoperability, as defined by the Office of the National Coordinator for Health IT's Interoperability Roadmap.

"The LIVD specification addresses a major pain point for today's clinical laboratory."

— Serge Jonnaert, president, IVD Industry Connectivity Consortium

The LIVD specification outlines an IVD industry-defined format to facilitate the publication and exchange of LOINC codes for vendor IVD test results.

"This effort will accelerate the inclusion of universal LOINC codes in laboratory reports to clinicians and health care systems because it will eliminate the additional laboratory effort now needed to figure out the right LOINC code for each laboratory test," said Clem J. McDonald, M.D., director of the Lister Hill National Center for Biomedical Communications at the NIH, in a statement. "The increasing use of universal LOINC codes in laboratory reports will unleash the same wave of efficiency and quality improvements as bar codes did for grocers and retailers."

LIVD complements IHE's Laboratory Analytical Workflow (LAW) profile, which contains rules for exchanging orders and results between IVD devices and health IT systems. Together, LIVD and LAW offer a "plug-and-play" solution.

While some vendor systems began documenting PDF instructions on how to associate LOINC codes with laboratory information systems, it was a manual process and a potential source of errors. The new standard allows automatic sending of lab values to the electronic health records and enables units of measure standardization to normalize laboratory result values.

"The LIVD specification addresses a major pain point for today's clinical laboratory," said Serge Jonnaert, president of the IVD Industry Connectivity Consortium, in a statement. "We finally have a true plug-and-play solution to interface IVD instruments to middleware and LIS systems. Clinical laboratories will no longer be subjected to outrageously high fees for custom connectivity implementations."

It has been reported that Abbott Laboratories, Roche, and BioMérieux are among the companies that committed LIVD will available on product websites for labs to download. It is hoped that in the future there may be a central web-based portal to act as a repository of files, but for now downloadable versions of the LIVD specifications are available voluntarily by manufacturers.

Takeaway: Adoption of the LIVD standard will improve results standardization, plus transmission efficiency and quality by automatically linking IVD test results with lab IT systems.

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Curetis to Launch Multiplex MDx for Hospital Infections in U.S.

Molecular diagnostics firm Curetis (Germany) specializes in solutions to rapidly diagnose and profile antibiotic resistance for severe infections in hospitalized patients. The company currently has its Unyvero platform and four cartridge-based tests—for pneumonia, implant and tissue infection, blood stream-related infections, and intra-abdominal infections—commercially available in Europe.

Oliver Schacht, Ph.D.
CEO, Curetis

DTET recently spoke to Curetis' CEO Oliver Schacht, Ph.D., about the company's plans in the United States, as well as the company's comprehensive approach to defining test value.

Will the U.S. commercialization strategy be similar to that taken in Europe?

When we started the Unyvero endeavors in Europe, we started out one cartridge at a time with the pneumonia panel, the implant and tissue infections, eventually the bloodstream infections, and the intra-abdominal infections earlier this year. In the United States we do expect the clearance of the Unyvero system to coincide with clearance of the lower respiratory tract infection panel, which is basically very similar to European hospital pneumonia panel. The FDA has requested the label to say lower respiratory tract and we are subject to pending agreements with the FDA on label claim and clearance. We have guided towards up to 36 analytes in the U.S. version versus the 40 we have in Europe. The reality is that in the multicenter trial with more than 2,200 patients there are a few analytes with not enough cases to sufficiently validate them in a prospective trial. But, it does tell you that they are very rare and all of the important ones—the gram positive and gram negative bacteria and all of the key antibiotic resistance markers, the hospital superbugs—will be on there.

Similar to the European approach, the second U.S. product that we are planning is the invasive joint infection panel. It is a variant from the European implant and tissue infections panel. Basically, in the United States we are looking at a particular sample type, synovial fluid, both from prosthetic joints and from acute joint infections. It is not covering all of the sample types in Europe, which also covers diabetic foot ulcers, burns, and soft tissue infections.

The strategy here has been first-in-class products. Today there is no pneumonia or lower respiratory infection multiplex, polymerase chain reaction (PCR), sample-to-answer panel in the United States. Similarly on the invasive joint infection, there is currently not a multiplex PCR panel straight from synovial fluid.

It becomes a question of priorities, funding, and resources. We have not yet made a determination of what products three, four, and five will be, but it is safe to assume we will proceed with applications or assays we already developed and have some data from European trials. But, over time we can also have U.S.-specific offerings.

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What is the timeline for commercialization in the United States?

For the first cartridge we are offering guidance that we currently expect an FDA clearance decision later in 2017. We have been in very close interaction with the FDA since submitting in January. It has been an interactive review and our goal is to deliver all answers to their questions in the coming weeks. For the invasive joint infection our goal is to complete trial enrollment and run the trial in 2018 with FDA-approval and launch more like 2019. Beyond that the question is how many trials can we run in a staggered fashion and that is about funding and resources.

"Just because a diagnostic is technically feasible, at the end of the day, that doesn't mean it should be developed as a product."

— Oliver Schacht, Ph.D.
CEO, Curetis

Will Curetis branch out from hospital infection testing?

There is so much more that these multiplex platforms can do—oncology, genetic testing, companion diagnostics, but as a small company you have to focus. From a clinical development and commercial standpoint strategically we have focused on hospital infections. There is a big enough problem in clinical hospital infections to keep us busy for years.

Aside from the technological feasibility what other considerations go into building out the company's test pipeline?

Just because a diagnostic is technically feasible, at the end of the day, that doesn't mean it should be developed as a product. We are looking at unmet medical need and unanswered diagnostic questions that require testing for dozens and dozens of putative pathogens, whether bacteria, fungi, and down the road viruses, as well as the pattern of antibiotic resistance markers.

We are looking at things that suffer from the standard of care being microbiology culture that takes several days or sometimes weeks to complete. Of course, the markets need to be sizable enough and it has to answer a question that not only delivers medical benefit to patients and doctors, but it also has to deliver health economic benefit to the hospital customers to be a commercially viable product.

Curetis has been publishing comprehensive studies that assess tests' impact from an economic point of view and recognize importance of sound antibiotic stewardship. Why is this strategy important?

From a European perspective, a hospital laboratory is often viewed as a cost center and not a profit center. Therefore, if we add any novel molecular diagnostic (MDx), especially tests that come at premium prices, they will be viewed initially as incremental costs into the system. However, you have to factor in extended length of stay or extra time in intensive care while taking broad-spectrum antibiotics.

From all of the data we have seen in Europe there is every reason to believe that modern MDx can contribute in a cost-effective way towards improving antibi-

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otic stewardship and optimizing health economic outcomes for individual hospitals, while simultaneously delivering medical benefit to patients. One of our distribution partners ran a study in Europe showing that for the implant joint infection cartridge in prosthetic joint infections was able to achieve net savings, after the additional cost of the test, of more than €2,000 per patient.

Will you reexamine the economics case in the United States?

U.S. hospitals are aware of the publications, but we will be doing some of the same types of projects in leading U.S. health systems as well to make sure we generate U.S. data. But frankly, a day in a U.S. hospital or intensive care costs twice of that in Europe. I would anticipate the net health economic benefit would be even greater in the United States.

Why do other diagnostics companies not approach the value question with the same comprehensiveness?

These studies are not easy to do. These studies are complex, and take time and a lot of resources. Historically, diagnostics have been viewed as "cost plus" from a pricing and reimbursement perspective, while therapeutics are very often value-priced. By and large diagnostics are supposed to be cheap. With for example a sub-$100 screening test it is extremely hard to run these multiyear, multicenter million dollar clinical outcomes studies, that would be standard in the therapeutics world. It is not for lack of wanting to do it. The question is from a commercial standpoint can you justify the expense? I think ultimately, there is no avoiding it and we will see more and more of this type of data required.

How do you see MDx for infectious disease testing in hospitals evolving?

If you look at where we are today with infectious disease diagnostics in hospitals in the United States and in Western Europe, the gold standard, which is not so golden, is microbiology culture. We have been doing this for 130 years and it is still the de facto clinical standard of care. We are only beginning to see the advent of molecular tests in infectious disease. In many ways the MDx arena of infectious disease, is where oncology pathology was 15 years ago. Fast forward to today, every pathologist is still looking in a microscope, but they are all doing companion molecular diagnostic testing, too. We are going to see the same thing, hopefully in five years.

By the Numbers

- **4** types of Unyvero application cartridges currently marketed in Europe.
- **4 - 5** hours = time to result for pathogens and resistance results
- **130** diagnostic analytes covered from a single patient sample with the Unyvero intra-abdominal infection cartridge, including 92 bacteria, 13 fungi, 3 toxins, and 22 antibiotic resistance markers.
- **€132** million raised by Curetis to date
- **161** Unyvero analyzers installed globally at the end of Q2 2017.
- **350,000** clinical datapoints from Unyvero lower respiratory tract infection FDA trial.

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Whether BioMérieux, Luminex, GenMark, Accelerate, ourselves, we are all singing the same song—bringing infectious disease microbiology labs into the 21st century by adding molecular diagnostic weapons to the arsenal to combat the threat. Unlike climate change, there seem to be very few, if any, deniers that we have a massive antibiotic stewardship problem if we continue on the path we are on. There is no doubt we will run out of therapeutic options, whether that is in 10 years or 50 years. It will happen and it is broadly acknowledged.

We are not trying to replace culture. There is every reason to believe culture will still be around in the next decade because there are some things you can only do with microbiology culture, but the first line of defense will be much broader, rapid molecular diagnostic assays that give clinicians the answers they need to drive therapeutic decision making in 80 to 90 percent of cases.

Celebrity Power to Drive Testing Extends Beyond 'Angelina Jolie Effect', *from page 3*

OraQuick (OraSure Technologies; Bethlehem, Penn.) is the only Food and Drug Administration-approved rapid in-home HIV test kit available in the United States. U.S. sales of OraQuick were evaluated weekly from April 12, 2014, to April 16, 2016, along with Web searches for the terms "test," "tests," or "testing" and "HIV" using Google Trends. Changes in OraQuick sales around Sheen's disclosure based upon expected sales and prediction models using Web searches were assessed.

"The public's health decisions are heavily influenced by public figures and reveal an opportunity for the prevention community to target health behaviors when related issues are widely publicized in the media."

— Jon-Patrick Allem, Ph.D.

The researchers found that OraQuick sales rose significantly, 95 percent, the week of Sheen's disclosure and remained significantly elevated for four more weeks. In total, there were 8,225 more sales than expected following Sheen's disclosure, surpassing orders around the World AIDS Day campaign by a factor of seven. For comparison, OraQuick sales the week of World Aids Day increased significantly, but by only 31 percent. Following World Aids Day sales returned to expected levels the next week.

Web searches mirrored OraQuick sales trends, demonstrating their ability to foretell increases in testing. The researchers found that knowing search volumes alone produced sales predictions with an average relative error rate within 7 percent.

"The public's health decisions are heavily influenced by public figures and reveal an opportunity for the prevention community to target health behaviors when related issues are widely publicized in the media," write the authors led by Jon-Patrick Allem, Ph.D., from University of Southern California in Los Angeles.

Takeaway: Web searches immediately following celebrity health-related announcements can be used to capitalize on opportunities to drive screening and predict volume increases.

Defense Dept. Extends Lab-Developed Test Demonstration for TRICARE

The Department of Defense announced June 20 that it approved a three-year extension of the Defense Health Agency Evaluation of Non-United States Food and Drug Administration (FDA) Approved Laboratory Developed Tests (LDTs) Demonstration Project. The extension permits TRICARE to continue to LDTs for safety and value and approve their use for beneficiaries.

TRICARE, the health care program for active duty and retired uniformed service members and their families, and is managed by the Defense Health Agency (DHA). However, not all care is provided in military treatment facilities and TRICARE requires that all covered tests have FDA approval. This requirement eliminates LDTs for care consideration for its 9.4 million beneficiaries, limiting application of technological advancements, particularly in the area of genomic medicine.

The Laboratory Joint Working Group, consisting of clinical and laboratory experts from across military services, prioritizes tests for review based on published evidence of medical effectiveness. The group forwards its recommendation to the director of the Defense Health Agency for final approval for use. So far, the Military Health System says 100 tests have been given the green light, including those for cancer risk, diagnosis and treatment; pharmacogenetic testing; and diagnosis of genetic syndromes and inherited cardiovascular conditions.

Even with approval for use by TRICARE beneficiaries, pre-authorization is required and providers must submit a letter of attestation, with the test name, CPT code, and indication that the beneficiary meets the coverage criteria requirements.

"During the next three years, the DHA will continue to evaluate the LDT examination and recommendation process to assess feasibility, resource requirements, and the cost-effectiveness of establishing an internal safety and efficacy review process to permit TRICARE cost-sharing for an ever-expanding pool of non-FDA approved LDTs," said Aaron Siegel, a spokesperson for the Department of Defense, in a statement. "The results of the evaluation will… support future regulatory revisions which will enhance the flexibility of the Military Health System in responding to emerging technologies."

Takeaway: The extension of the DHA's LDT demonstration project has the potential to further expand LDT test coverage among TRICARE beneficiaries.

Protein Patterns Investigated for Markers of Early Ovarian Cancer

The combination of liquid chromatography and tandem mass spectrometry enabled the discovery of four biomarkers holding promise to become "useful" in the development of a multipanel test for the early detection of ovarian cancer, according to a study published July 6 in *BMC Cancer*.

Diagnostic methods are notoriously lacking for early detection of ovarian cancer, with single cancer biomarkers, including cancer antigen 125 (CA125) and human epididymis protein 4 (HE4), having proven insufficient to detect early tumors.

While two multimarker tests have been U.S. Food and Drug Administration-approved for evaluation of pelvic masses (Fujirebio Diagnostics's ROMA test and Vermillion's OVA1), no such tests exist for screening.

Identification of distinctive protein expression patterns is being held out as a promising strategy for understanding molecular alterations associated with ovarian cancer. In the BMC Cancer study serum samples (44 ovarian cancer and 45 healthy controls based on histopathological analysis) were pretreated using micropipette tips ZipTips, a solid-phase extraction method, was used as a depletion method with the goal of enabling low-molecular protein-peptide profiles. Using the combination of ZipTips technology and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF) analysis generated a total of 170 spectral components (m/z unique peaks), with 98 peaks significantly different between the two groups.

Next, a classification model identified the most discriminative factors using three mathematical algorithms (SNN, GA, and QC). Finally, the results were verified on an independent test set of samples of (11 ovarian cancer patients and 12 healthy controls). The SNN model yielded the best differentiating capabilities and satisfactory values of sensitivity (71.0 percent) and specificity (68.6 percent).

"The novel approach, which enabled protein-peptide profiling as well as identification of four potential ovarian cancer biomarkers (complement C3, kininogen-1, inter-alpha-trypsin inhibitor heavy chain H4 and transthyretin) using MALDI-TOF MS, may contribute to the creation of new effective multicomponent diagnostic tools," write the authors led by Agata Swiatly, from Poznan University of Medical Sciences in Poland.

Takeaway: Given the lack of available screening tools for detection of early ovarian cancer, protein profiling using MALDI-TOF MS may have identified four markers that will be useful components of a future multimarker diagnostic tool.

Researchers Identify Potential Markers for Chronic Fatigue Test

Stanford University researchers have identified a cytokine signature associated with severity of chronic fatigue syndrome (CFS), according to a study published July 31 in *Proceedings of the National Academy of Sciences*. The findings, the authors say, provides further evidence that CFS involves a systemic inflammatory process and may lead to a test for the controversial disease.

CFS, also known as myalgic encephalomyelitis (ME) is debilitating and affects more than one million patients in the United States. However, CFS remains a mystery, with a heterogeneous clinical presentation, little understanding about its biological cause, and no known reliable treatment.

"There's been a great deal of controversy and confusion surrounding ME/CFS—even whether it is an actual disease," said Mark Davis, Ph.D., the study's senior researcher in a statement. "Our findings show clearly that it's an inflammatory disease and provide a solid basis for a diagnostic blood test."

The researchers used high-throughput analysis to evaluate 51 cytokines, cell signaling molecules produced by immune cells, in 192 ME/CFS patients and 392 healthy controls (average age, 50 years; average symptom duration for cases, 10 years). A 51-multiplex Luminex array was used for analysis.

The researchers found that only two cytokines significantly differentiated patients from controls (TGF-β was higher and resistin was lower in patients).

"The two cytokines that did distinguish cases from controls, TGF-β and resistin, did not exhibit a linear relationship with disease severity," wrote Davis and colleagues. "It may be that TGF-β and resistin contribute to ME/CFS pathogenesis independent of disease severity."

There were, however, 17 cytokines correlated with ME/CFS severity—CCL11 (Eotaxin-1), CXCL1 (GROα), CXCL10 (IP-10), IFN-γ, IL-4, IL-5, IL-7, IL-12p70, IL-13, IL-17F, leptin, G-CSF, GM-CSF, LIF, NGF, SCF, and TGF-α. Thirteen of these cytokines are proinflammatory, likely contributing to many of the symptoms and establishing a strong immune system component of the disease, the authors say. Only CXCL9 (MIG) was inversely correlated with fatigue duration.

Takeaway: Identification of these cytokine markers may be a first step towards developing a test capable of definitively diagnosing CFS.

Testing Guidelines *at a Glance*

The American Society of Clinical Oncology (ASCO) published updated practice guidelines Aug. 14 in the *Journal of Clinical Oncology* regarding the use of targeted immunotherapy for patients with stage IV non–small-cell lung cancer. The recommendations, an update from those published in 2015, are based on a systematic review of 14 randomized controlled trials conducted from February 2014 to December 2016, and focus on EGFR, ALK, and ROS1 alterations, as well as PD-L1 expression.

- The immunotherapy drug pembrolizumab is recommended as a first-line treatment in patients who don't have sensitizing EGFR mutations, ALK rearrangements, or ROS1 rearrangements, but who have high PD-L1 expression. For patients with low PD-L1 expression, clinicians should use standard chemotherapy.
- Despite recommending different treatments based on PD-L1 status, the guideline update does not direct physicians to use a specific PD-L1 assay or test, nor does it delineate a cutoff point for what it considers high or low PD-L1 expression.
- The guidelines maintain the 2015 recommended use of first-line targeted treatment with EGFR mutation-positive, ALK rearrangement-positive, or ROS1 rearrangement-positive tumors.

In July, ASCO also provided a focused update recommending the use of the MammaPrint (Agendia; Irvine, Calif.) multigene panel to help guide decisions on the use of adjuvant systemic therapy for women with early-stage breast cancer. The recommendations update ASCO's 2016 clinical practice guideline on the use of biomarkers in these patients. The focused update was the result of the 2016 study from a randomized phase III clinical trial of the MammaPrint gene test. Specifically, ASCO recommends the use of the test in patients with hormone receptor–positive, human epidermal growth factor receptor 2 (HER2)–negative, node-negative breast cancer to inform decisions on withholding adjuvant systemic chemotherapy. ASCO says MammaPrint is able to to identify a good-prognosis population with potentially limited chemotherapy benefit.

American Association for Cancer Research

The American Association for Cancer Research (AACR) published its first set of consensus screening recommendations for children with common cancer predisposition syndromes. The CCR Pediatric Oncology Series, published in June and July in *Clinical Cancer Research*, sought to develop recommendations for primary and specialty pediatric clinicians for the management of children at significant hereditary risk for cancer, but who have not yet developed their first cancer.

Pediatric Cancer Working Group of the AACR convened a workshop that included 65 professionals. The group reviewed existing data and practices, and established recommendations for cancer surveillance for the 50 most common syndromes that predispose children to cancer. These syndromes were clustered into nine major groups based on the major cancer types (Li-Fraumeni

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syndrome, neurofibromatoses, overgrowth syndromes and Wilms tumor, neural tumors, GI cancer predisposition, neuroendocrine syndromes, leukemia predisposition, DNA instability syndromes, and miscellaneous syndromes).

The group developed 18 position papers that provide recommendations for surveillance, focusing on when to initiate or discontinue specific screening measures, which modalities to use, and how frequent to screen patients. The group established a 5 percent prevalence (or higher) as a "reasonable" threshold to recommend screening. It should be noted that the strength of screening recommendations vary as many of these diseases are rare and no existing protocols exist.

American Academy of Pediatrics recently released several guidelines.

- The 2017 guidelines on preventive health care for children were approved by the American Academy of Pediatrics (AAP) and the Bright Futures Periodicity Schedule Workgroup and published in the April issue of *Pediatrics*.
  - Recommendations for screening for dyslipidemia have been updated to occur once between 9 and 11 years of age and once between 17 and 21 years of age to be consistent with guidelines of the National Heart, Lung, and Blood Institute.
  - Universal screening for HIV has been updated to occur once between 15 and 18 years of age to be consistent with recommendations of the U.S. Preventive Service Task Force.
- The AAP's Committee on Nutrition, Section on Endocrinology and Section on Obesity published a clinical report on screening for components of metabolic syndrome (MetS) in children in the August issue of *Pediatrics*. While MetS is defined in adults as the presence of any three of five cardiovascular disease risks: hyperglycemia, hypertriglyceridemia, central adiposity, elevated blood pressure, and low high-density lipoprotein cholesterol, diagnosis remains controversial in pediatric populations. The AAP urges pediatricians to follow current recommendations to screen for and treat obesity, glucose abnormalities, hypertension, and dyslipidemia to address the major MetS-associated cardiometabolic risks in pediatric populations. This includes
- Lipid screening (nonfasting or fasting) in all children between the ages of 9 and 11 years.
- Fasting glucose testing every two years for children 10 years or older (or pubertal) with a body mass index at the 85th percentile or greater and two additional risk factors.