Diagnostics, access, therapies on minds ahead of ASCO

Charna Albert

April 2025—Rebecca Previs, MD, MS, gynecologic oncologist and director of medical affairs at Labcorp, captures the vibe ahead of the ASCO conference next month in Chicago in just a few words.

“It’s exciting,” she says. “This is unprecedented territory.”

With the field undergoing “a major shift toward biology-driven rather than tissue-of-origin-driven oncology treatment,” Dr. Previs is far from the only industry representative who is optimistic about the future—though the many challenges ahead temper that excitement.

At AbbVie, antibody-drug conjugates are at the forefront, says Shilpen Patel, MD, global development leader in oncology. The company is building a pipeline in both solid and hematologic tumors, Dr. Patel says, “leveraging biomarkers like c-Met and SEZ6.” In the pipeline now is Teliso-V, which is under regulatory review for the treatment of previously treated nonsquamous non-small cell lung cancer; Temab-A (ABBV-400), a c-Met targeted antibody-drug conjugate; ABBV-706, which targets SEZ6; PVEK, which targets CD123; and ABBV-969, which targets PSMA/STEAP1. “It’s worth noting that both ABBV-400 and ABBV-706 use a proprietary AbbVie payload, the topoisomerase 1 inhibitor,” he says.

Dr. Patel

Dr. Patel is confident that antibody-drug conjugates will continue to gain ground not only in solid tumors but also in hematologic malignancies. “At AbbVie, we view ADCs as a potential replacement for chemotherapy in colorectal, lung, and ovarian cancer,” he says. “New combination strategies with ADCs are also being explored, highlighted by the recent approval of ADC-IO combinations.” Antibody-drug conjugate research, too, is undergoing a “fundamental shift,” he says, driven by industrywide efforts to craft novel trial designs and regulatory strategies.

One thing Dr. Previs of Labcorp would like to see from clinical trial design in this space is an end to the requirement that participants who have had biomarker testing be retested, which can cause delay. In addition, eliminating “overly exclusive inclusion criteria,” she says, would allow for various testing methods. The focus should be nailing down the preclinical work before the trial takes off, she says, “specifically, what is the biomarker and what is the threshold we’re going after. That’s best practice for making sure we’re getting the right patients on the therapies but avoiding untoward toxicities.”

Sophia Yohe, MD, a hematopathologist and molecular genetic pathologist, notes that although antibody-drug conjugates work well in hematologic malignancies, they can also make disease monitoring more difficult. “Flow [cytometry] assays that worked fine before the era of targeted therapies don’t work as well for patients who are on those targeted therapies. It just means we have to change what we’re doing and change how we practice and evolve,” says Dr. Yohe, director of the molecular diagnostics laboratory at the University of Minnesota Medical Center.

Pantumor drugs are a focus for AbbVie. At ASCO and ESMO last year, Dr. Patel says, AbbVie presented data on antibody-drug conjugate Temab-A in both non-small cell lung cancer and colorectal cancer. In addition, he says, “our investigational drug ABBV-706 is currently being studied in neuroendocrine tumors, and Elahere, approved for

platinum-resistant ovarian cancer, is also being evaluated for platinum-sensitive ovarian cancer."

Dr. Previs acknowledges that not all molecular alterations confer the same benefit across tumor types. "We have to understand the nuances of disease-specific response and focus on that as a priority," she says. It's true, too, that not every patient will respond. "Tumors evolve," she says. "They develop other mutations. And eventually they're going to progress, following the natural history of that tumor." The goal is to prolong the time the patient can benefit from therapy, she says. "Eventually, resistance is going to come about, and so we need to fully investigate the resistance mechanisms and how we can overcome them."

Jodi Bass, senior director of precision medicine in oncology at Johnson & Johnson, says Johnson & Johnson will present data from across its portfolio, with a focus on lung, prostate, and bladder cancer. "We're particularly focused on breakthrough treatment modalities and expanding access to biomarker-driven therapies," she says. Improving antibody-drug conjugate delivery is another objective. "Part of that is strengthening the linkers that hold those two things together, and then targeting new antigens to enhance treatment."

Bass

From Bass' vantage point, "The challenges in implementing pantumor therapies lie in diagnostic standardization across tumor types, access to comprehensive biomarker testing, and physician education. While tissue-agnostic approvals offer exciting treatment options," she says, "the variability in testing, availability, and interpretation across health care settings can limit their real-world impact."

At Johnson & Johnson, "We're going to focus on validated biomarkers that can guide therapies across multiple cancers, rather than a broad one-size-fits-all approach," she adds. "Our approach is targeted biomarker delivery."

Dr. Yohe notes that testing cost can be a limitation when the indication for the tissue-agnostic therapy is rare, as is the case with *NTRK*. In most tumors, *NTRK* fusions are rare, she says. "They're a small percentage." Then, too, reimbursement for testing in the pantumor setting isn't assured. "It's easier to get reimbursed for testing that is more tumor-specific, based on guidelines," she says.

The diagnostic difficulty of pantumor therapy isn't lost on John Longshore, PhD, head of scientific affairs for global oncology diagnostics at AstraZeneca. "Depending on the type of tumor you are working with, a different immunohistochemistry assay could be required. When you're looking at a gastric sample, for instance, versus a breast sample, it may be a different scoring algorithm that's involved in determining if patients are eligible for treatment, and the cut point of expression that is used may be different," he says. "But this is a small issue compared to the exciting opportunities these new pantumor diagnostics bring to patients."

Dr. Longshore has seen diagnostics assume a more central role at ASCO over the years.

"It's always interesting to see the increased number of therapeutics, posters, and platform presentations that have a diagnostic component," he says. "We used to think of diagnostics as an afterthought to targeted oncology therapeutics. Now virtually every drug that comes to market has some type of associated diagnostic."

Dr. Longshore

Moving from digital to computational pathology for diagnostic assistance and patient stratification for biomarker selection is one of the major trends Dr. Longshore sees on the meeting circuit. Another frequent topic, of increasing importance to AstraZeneca, is liquid biopsy. “Genotyping with liquid biopsy to supplement what we can get from genotyping with a tissue-based test is only the tip of the iceberg,” he says. “When we get into monitoring minimal residual disease and early detection, that’s going to require liquid-based solutions.”

AstraZeneca late last year partnered with three companies to expand access to liquid biopsy testing in Europe. “Our data shows us that only one in 10 labs in Europe that perform next-generation-sequencing-based tissue testing perform liquid biopsy testing,” Dr. Longshore says. AstraZeneca is working with academic institutions in Europe to train laboratory directors and technologists in the techniques so they can bring the testing to their own laboratories. The company also works with oncologists to establish liquid biopsy ordering patterns. “We see this as a supply-demand continuum,” he says. “It’s preparing for the future.”

Next-generation sequencing company Pillar Biosciences is one of AstraZeneca’s partners in the education initiative. The goal is to enable local laboratories worldwide to validate liquid biopsy testing, says Dan Harma, chief commercial officer at Pillar Biosciences. “This will allow for identification of patients who have the gene specific to a new AstraZeneca drug for breast cancer, due late this year or early next year.”

For Pillar Biosciences, ASCO is an opportunity to get its kitted, rapid NGS solutions in front of oncologists. “While targeted, first-line NGS panels aren’t necessarily as thorough as comprehensive genomic profiling, they enable a sample-to-answer turnaround time in approximately two to three days,” says chief marketing officer Brian Wright. “And they’re broad enough to find an actionable target in 80 to 90 percent of patients, requiring just a tenth of the DNA input from a patient sample. There are typically only so many key driver biomarkers for the majority of solid and heme tumors.” As for the need for faster results: “It’s not just a laboratory or biopharma play,” he says. “It’s an oncologist requesting information to help improve patient care. If the rapid front-line NGS panel comes back positive for a druggable targeted alteration, it enables improved patient care at a reduced laboratory cost.” If no alteration is found, he adds, the remaining sample input can be “easily reflexed, internally or externally,” for a more expansive comprehensive genomic profiling assay.

Wright

“If you are an oncologist sending out to a large reference laboratory, between patient tissue acquisition, shipping, accessioning, processing, and analysis, your team is probably going to wait around two to three weeks for the NGS results and report to come in,” Wright says. As such, the treating oncologists often put their patients on toxic chemotherapy before they receive the NGS results. In addition, in the case of send-out testing, he says, the local laboratory does not retain its patient’s raw genomic data, nor is it able “to derive any sort of revenue or value creation from the testing that could be performed in-house.”

Says Dr. Previs of Labcorp: “Every second, hour, day, counts when you’re a patient with cancer waiting to start treatment. And one of the risks is a patient is too sick to wait for their results and they miss the option for targeted

therapy."

AstraZeneca's Dr. Longshore agrees with the push to get patients on targeted therapies more quickly. "It's important for us to realize that just because we have an approved drug and an approved therapeutic, the problems do not stop there," he says.

One such problem: As more therapeutics indicated for low levels of expression come to market, "diagnostics may need something beyond what the human eye can deliver," Dr. Longshore says. "As we continue to see diagnostics move into these lower levels of expression and lower levels of mutation, the ability of artificial intelligence and computational pathology—not to replace what a pathologist does, but to supplement it—is going to be increasingly important."

HER2-low and HER2-ultralow come to mind for Dr. Previs. "HER2 testing historically was designed to be positive or negative, not to define or discriminate low expression levels, and variability is going to impact treatment decisions. This is where solutions like digital pathology and AI scoring algorithms may improve standardization," she says.

"If the algorithms are done right," Dr. Yohe agrees, "that's something that could potentially be performed." Certainly, the use case has been studied. "But you still run into the issues you have with humans, which is that you can have bright staining, which is easy to pick up, and you can have partial staining. Instead of a visual cutoff, it's going to be a numerical cutoff. And where that numerical cutoff is—is that going to be the exact same at my lab where I'm running this IHC as it is at your lab, running that IHC? There are issues that come up with validating AI for that purpose," she says.

For Dr. Previs, the major hurdle of the moment is to bridge the gap between science and clinical practice, and the barriers are access, awareness, and infrastructure.

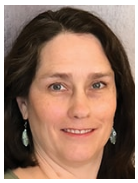
"Many oncologists, especially in the community setting, are managing incredibly complex patients, often with limited bandwidth, resources, and time," she says. "We're starting to see this ongoing conversation in the literature, in social media, in all different outlets, about how we bridge the science, innovation, and invention with real-world clinical adoption."

Dr. Previs

Dr. Previs and her colleagues at Labcorp are exploring ways to better integrate biomarker testing into existing clinical workflows. "That means providing clear testing guidelines," she says, and ensuring that physicians need not go through an excessive number of steps to order it. They're also making patient education a priority. When patients are invested in their treatment options, she says, "they're more likely to ask about testing, and that can also help drive uptake."

In follow-up assessments after a Labcorp educational event for patients with metastatic breast cancer, Dr. Previs and her colleagues found that 60 percent of attendees were unaware of their HER2 status, "but this type of education had prompted them to talk to their doctor to learn more." That event, she says, was part of a larger initiative to educate patients about HER2-low—and more than half of those who responded to an online survey to assess baseline knowledge had never heard of it. "I was surprised by that," she says. "It is a new biomarker, but we launched the campaign several months after the approval."

Even in the metastatic setting, says Bass of Johnson & Johnson, “we know that disparities in access to comprehensive genomic profiling exist.” Is receiving care in the community setting a factor? She’s skeptical. “The community oncology space is becoming more and more advanced in its ability to provide precision medicine at the same level as many other centers,” she says. Rather, she points to coverage-related access, or even lack of physician awareness of coverage. “Often that’s part of the issue—providers assuming there’s a problem with access.”



Dr. Yohe

Even when it comes to the laboratory, there is an understanding-related gap. The time and expense required to bring up a new test in the laboratory “isn’t on the radar” for those outside pathology, Dr. Yohe says.

Her institution, the University of Minnesota Medical Center, is attempting to drive up the number of patients who get tested by enabling pathology-initiated workflows and testing, with biomarker testing ordered concurrently when a pathologist makes a diagnosis of cancer. “It gets the testing done quicker,” Dr. Yohe says, “because it doesn’t wait for the result to go back to the clinician and for them to order it and call pathology about which block they should order it on. It’s just more efficient.”

It can be more challenging to get preauthorization and insurance coverage for the testing, she concedes, given that payers are accustomed to the physician doing the ordering. But the problems with reimbursement haven’t detracted from its overall success.

“We did a before and after and saw a much higher proportion of patients getting tested,” she says.

Charna Albert is CAP TODAY *associate contributing editor.*