EXACT SCIENCES

City of Hope

Building & Scaling a Precision Oncology Program: Lessons From City of Hope

BECKER'S HEALTHCARE

When it comes to cancer diagnostics and patient care, clinical adoption of molecular testing is on the rise, yet the rate of adoption is often outpaced by the rate of innovation in the space. To fully realize the benefits of this advancing field and provide patient care at scale, however, hospitals and health systems must create a comprehensive precision oncology program.

City of Hope in Duarte, Calif., has successfully built a precision oncology program which has improved patient care and clinical outcomes, delivering benefits to patients and healthcare professionals.

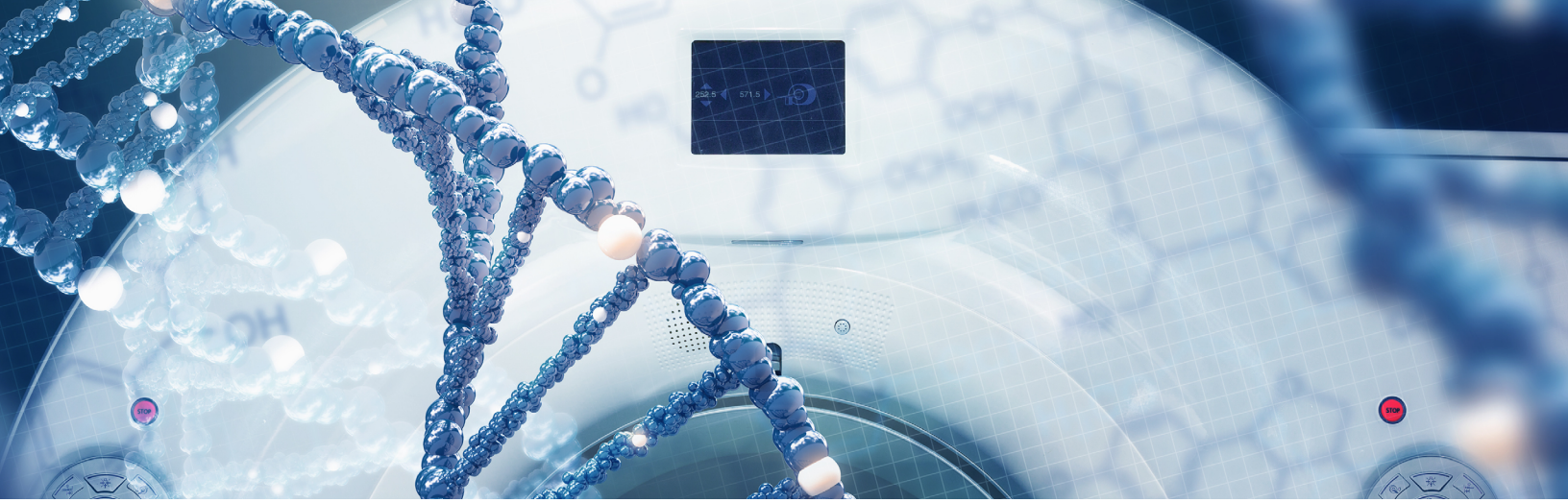
To learn more, *Becker's Healthcare* spoke with four experts on precision oncology programs, including three members of the City of Hope team:

- Rick Baehner, MD, chief medical officer, Exact Sciences Corporation Precision Oncology
- Stephen Gruber, M.D., Ph.D., M.P.H. Vice President, City of Hope National Medical Center; Eva and Ming Hsieh Family Director's Chair of the Center for Precision Medicine
- Stacy W. Gray, M.D., A.M. Chief, Division of Clinical Cancer Genomics; Deputy Director, Center for Precision Medicine, City of Hope
- Sumanta "Monty" Pal, M.D., FASCO Co-Director, Kidney Cancer Program; Professor, Department of Medical Oncology & Therapeutics Research, City of Hope

The evolution of precision oncology: From "genetic snapshot" to "genetic panorama"

In recent years, the focus of precision oncology has shifted. Historically, clinicians sought very specific, individual genetic alterations that would answer pointed questions about a patient's disease. Today, physicians and researchers are taking a more comprehensive look at patients' genomes.

"In the beginning, we shined a spotlight on specific areas of the genome — kind of a 'genetic snapshot' approach," Dr. Gruber said. "We focused on areas of the genome that we knew or suspected had major relevance based on research. As time has passed and the practice has advanced, City of Hope has turned its attention to the entire genome, taking a more panoramic approach."



This has given the team greater insights into the types of alterations that drive cancer behaviors and the potential for different types of cancers to respond to treatments. Now clinicians are in a better position to choose the right treatments for the right patient.

"In both hereditary and tumor testing, we started with individual biomarker tests, then we used smaller DNA-based gene panels, and this evolved into larger gene panels," Dr. Baehner said. "Now in tumor testing, we interrogate DNA plus RNA, with whole exome and whole transcriptome testing available through Exact Sciences' OncoExTra™ test". According to one estimate, 20% of cancer morbidity occurs in tumors driven by translocations and gene fusions identifiable through RNA sequencing.[1] Many of these variants are actionable and may be missed by DNA panel-based testing.[2,3] In fact ASCO recommends fusion testing when there are FDA-approved fusion-targeted therapies for that specific disease, as well as testing for other fusions if no other variants are identified on panel-based DNA sequencing.[5] OncoExTra, a Medicare covered test, interrogates nearly 20,000 genes and covers all DNA protein-coding sequences as well as all RNA transcripts.[4] The highly accurate test has 98.8% sensitivity and >99.9% specificity.[4] Additional detail is provided with optional immunohistochemical (IHC) panels, single stains and available consultations.

To deliver the greatest benefit, precision oncology requires standardization of care

Traditionally, genomics has been implemented in a way where decisions are made on a provider-by-provider and patient-by-patient basis. "Providers sit down and assess what's indicated for each patient, what tests should be ordered, what company should be used for testing and whether the patient needs testing of both the tumor and their inherited DNA," Dr. Gray said.

This creates two issues. The first is considerable variation in care. Some providers are more likely to order testing than others and some providers are more likely to put patients on targeted therapies.

"The second problem is that an approach driven by individual patients and providers misses about half the people who could benefit from precision medicine," Dr. Gray said. "This leads to complex and variable processes, as well as and very importantly, inequities in cancer care."

To address these challenges, City of Hope created an enterprise-wide system that enables all patients to benefit from precision medicine by participating in a research study that includes testing of tumors and inherited DNA.

"We extend this offer to everyone, so precision medicine is no longer a patient-by-patient decision," Dr. Gray said. "It's a decision that's made for everyone across the health system. This approach drives standardization of practice and processes. It lets us focus on what really matters most, which is the best possible care for our patients."

Furthermore cancer care equity can be aided by the technology itself. OncoExTra provides a more equitable option for therapy selection through its patient-matched tumor-normal sequencing technology. Filtering benign variants through germline subtraction uses each patient's normal sample as reference, as opposed to a reference database.

Precision oncology delivers benefits to patients, families and the community

Clinicians at City of Hope are using precision medicine to extend the lives of cancer patients. A 30-year-old woman, for example, with a rare form of kidney cancer wasn't responding to conventional therapies, so Dr. Pal ordered gene profiling.

"What we found was an alteration that is quite rare in lung cancer and even more rare in her type of papillary kidney cancer," Dr. Pal said. "We identified a treatment that aligned to that and the patient did quite well for a period of time. It's exquisitely rare to see some of these mutations in some cancer types like the ones I treat, but when you have wins like this, it's tremendously valuable."

With precision medicine, not only are physicians able to identify the right treatments for patients, but they can also treat and prevent illness in family members. "We identified a person whose cancer was clearly related to an inherited predisposition to cancer," Dr. Gruber said. "Within a matter of months, we'd identified six family members who also carried that same susceptibility gene. That gave us an extraordinary opportunity to intervene and reduce the risk of cancer in those family members."

By engaging patients in precision medicine, City of Hope has succeeded in delivering a holistic care experience to both patients and families. All patients are educated about how genomic information can guide their treatment.

"This helps providers make decisions in a collaborative way with patients and their families," Dr. Gray said. "We can give patients insight into what we know about their disease and why they got their disease. It relieves some of the stress for patients and families and enables them to make the best possible decisions during a very difficult time."

City of Hope's precision medicine program has yielded positive results and has been widely embraced by the community the hospital serves. Thanks to an enterprise-wide approach to inviting patients to provide consent into the precision medicine research protocol, City of Hope can offer genetic testing and genomic profiling at scale.

"More than 93 percent of patients opt in for genetic testing and we've provided results to over 13,500 patients," Dr. Gruber said. "We've been incredibly impressed with the positive reception this information has had among our patients and physicians."

To scale a precision oncology program, organizations must deploy the right infrastructure and processes

One of the challenges that City of Hope faced when building its precision oncology program was systematically integrating test results and finding matching clinical trials. In response, the organization established an institutional precision oncology tumor board to consolidate and process information.

"Genomic testing generates a massive amount of information," Dr. Pal said. "The precision oncology tumor board reviews all the data and distributes it in a digestible format to physicians and caregivers who might be less comfortable with some of the newly emerging technologies."

One way in which Exact Sciences enables the interpretation of results is through an easy-to-interpret report. The OncoExTra report focuses on the most clinically relevant information first, and all the details second. Thoughtfully organized, the report caters to your workflow by summarizing personalized insights upfront for quick, shared decision making. In addition, medical and clinical experts are made available to customers through multiple means to provide insights and aid in interpretation of reports.

In this way, treating clinicians receive in-depth guidance. Looking ahead, City of Hope plans to augment information from the precision oncology tumor board with bite-sized precision education modules that are delivered to providers at the point of care.

A second challenge is making workflow changes in conjunction with the lab. When City of Hope moved to a paired tumor-germline testing protocol, it had to overcome infrastructure-related hurdles. "Systems need the ability to order the test," Dr. Gruber said. "At the same time, you must ensure that the companion blood sample is available to accompany the tumor tissue. Most importantly, results need to be delivered to patients and physicians in real time."

Despite the aforementioned clinical and equity advantages of paired tumor-germline testing, the shift from tumor-only testing to paired tumor-germline testing creates a learning curve for both clinicians and pathology laboratories. "It's imperative for the reference or testing laboratory to be integrally involved in establishing those workflows with two goals in mind: educating around best practices and building trusting relationships with the pathology teams," Dr. Baehner said.

A third obstacle is genetic counseling and patient consent. City of Hope moved consent for germline testing upfront in the patient processes. In addition, the organization changed its approach to genetic counseling. "We transitioned from pre-test counseling with every patient before ordering testing to a model where expert genetic counselors deliver clinically relevant information to patients after tests are complete," Dr. Gray said. "We also provide patient education materials so they can understand the implications of testing for family members."

Five lessons learned about precision oncology

Based on their precision oncology program, the City of Hope team shared these lessons:

1. *Precision medicine improves clinical trial enrollment.* The information gathered from genomic testing shows whether patients are eligible for targeted therapies and can participate in clinical trials. "It's been a tremendous advantage to our patients and clinical trialists," Dr. Gruber said. "They can accrue patients faster and in a more targeted manner."
2. *Discipline-to-discipline engagement is enhanced.* City of Hope has focused on integrating all of the specialties that touch a cancer patient, so they process and interpret genomic data in the same way.
3. *Patient outcomes improve.* Genomic information can open up new therapeutic paths for patients. A City of Hope ovarian cancer patient, for example, had run out of treatment options. After genomic testing illustrated a specific signature, the team had the opportunity to include the patient in the category of cancers that have a very high likelihood of responding to new therapies. With the aid of these new therapies, she entered complete remission.
4. *More extensive profiling yields significant rewards.* Genomic data contains an enormous amount of information that can be harnessed in advanced disease clinics and medical oncology. "I would love to see a future state where every patient who can benefit from targeted therapies has access to them," Dr. Gray said. "Many targeted therapies are oral and have fewer side effects and they are often highly effective."

5. *Early testing means better therapies and earlier disease detection.* With early screening and germline information, the rates of cancer in families with genetic susceptibility can be dramatically reduced. "One of our main goals is to prevent cancer in high-risk families," Dr. Gray said. "If we do that, we could save hundreds of thousands of lives every year. I'm extraordinarily excited."

Conclusion

The depth and breadth of information provided by genomic testing has opened the door to comprehensive precision oncology programs. The data alone, however, doesn't guarantee success. New teams, processes, workflows and partnerships are needed to ensure that standardized care is provided to all patients and a collaborative relationship between the health system and the molecular diagnostic laboratory provider can aid along the process

The future looks bright. "We are now able to treat cancer as a disease of the DNA, not just a particular organ," Dr. Pal said. "That gives us a lot more latitude."

1. Mitelman F, Johansson B, Mertens F. The impact of translocations and gene fusions on cancer causation. Nat Rev Cancer. 2007;7(4):233-245.

2. Drenner K, Basu GD, Goodman LJ, et al. The value of comprehensive genomic sequencing to maximize the identification of clinically actionable alterations in advanced cancer patients: a case series. Oncotarget. 2021;12(18):1836-1847.

3. Nikanjam M, Okamura R, Barkauskas DA, Kurzrock R. Targeting fusions for improved outcomes in oncology treatment.

4. White T, Szelinger S, LoBello J, et al. Analytic validation and clinical utilization of the comprehensive genomic profiling test, GEM ExTra®. Oncotarget. 2021;12:726- 739.

5. Chakravarty D, Johnson A, Sklar J, et al. Somatic genomic testing in patients with metastatic or advanced cancer: ASCO provisional clinical opinion. J Clin Oncol. 2022;40(11):1231-1258.