Advancing Immuno-Oncology in the Community Setting

BY STEVEN POWELL, MD

As cancer treatment evolves with the emergence of genomics, personalized therapies, and immunotherapies, care delivery must also transform. Sanford Health's integrated, multidisciplinary cancer care team provides care for more than 4,500 cases each year. Sanford's four major cancer centers, located in Sioux Falls, S.D., Fargo, N.D., Bismarck, N.D. and Bemidji, Minn., serve as regional hubs to deliver immunotherapy and other novel treatments. An innovative, multidisciplinary approach has propelled Sanford Health to the forefront of providing the next generation of cancer treatments.

As the largest rural healthcare provider in the nation, Sanford faces challenges familiar to other rural providers in trying to offer advanced technologies and services in areas with low population densities—for example, patients having to travel long distances to receive treatment. Sanford has embraced the challenge of serving its communities and patients with the most cutting-edge care in the nation.

Through innovative approaches to care delivery, including integrating telemedicine across the health system; implementing genomic tumor boards, as well as virtual tumor boards; and increasing access to clinical trials, Sanford cancer care has expanded its services and specialties to bring access to innovative technologies and procedures in targeted therapy, genomics, and immunotherapy to provide individualized treatment options for patients.

By taking advantage of technology and blending innovation with a Midwestern, rural compassion, Sanford Health is able to show that unsurpassed cancer care can be provided at centers of any size, anywhere.

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Sanford Health Cancer Care

The Sanford Health cancer program's mission is aimed at:

- Developing cancer therapies that will help transform cancer care
- Expanding access to promising new cancer therapies through clinical trials
- Improving the precision of novel therapies through genomic and molecular testing
- Leading the provision of innovative cancer care in the community.

Sanford's cancer care program brings together a team of experts who collaborate with one another and cultivate an atmosphere of straightforward communication.

More successful cancer treatment often means increasingly complicated treatments. To meet this challenge, Sanford has developed a unique approach to care where each provider contributes to the discussion and decision-making process of developing a personalized care plan that is tailored to each patient. Generally, it is not going to be one therapy alone, but rather a strategic combination of therapies that requires collaboration between a multidisciplinary team.

Leveraging Telemedicine

As stated previously, many of Sanford's patients travel great distances to receive treatment. To simplify the process for patients, Sanford made concerted efforts to provide clinical trials that use telemedicine. For example, through a rural virtual infusion grant, Sanford has been able to leverage telemedicine to improve clinical trial access for its patients. The grant first enabled Sanford to establish dedicated telemedicine equipment at two sites, followed by implementation at two additional sites. These initial sites included both Sanford Health and non-Sanford Health sites that are located one to three hours away from a medical oncology clinic. Using the rural infusion grant as a foundation for continued expansion, Sanford will continue to bring advanced treatments safely to additional rural locations. Today Sanford experts oversee state-of-the-art infusion therapies at these sites. Strategic use of telemedicine is making previously unavailable patient therapies options in small, rural areas that did not have the capacity to provide complex chemotherapy or immunotherapy on a regular basis.

Another example of how Sanford is expanding access to clinical trials through telemedicine is the work of gynecologic oncologist Maria Bell, MD, who successfully petitioned GOG (now NRG) to permit the option of telemedicine visits in many clinical trials, opening these trials as treatment options for patients who were previously excluded due to the travel burden.

The Role of Tumor Boards

Sanford cancer program's approach to multidisciplinary care has evolved through its tumor boards. In 2014 Sanford developed a unique genomic tumor board that evaluated use of molecular testing. Through live videoconferencing Sanford made this genomic tumor board available at all of its clinical sites. The large geographic area Sanford covers includes urban areas, such as Sioux Falls, where there may be as many as 10 oncologists, as well as smaller communities, where there may be only a sole practitioner. Sanford's virtual tumor boards are a valuable resource to help solo oncologists feel they are part of a larger practice—that they have colleagues to collaborate with and talk through cases. Furthermore, virtual tumor boards serve as a vehicle to deliver up-to-date medical education to all of the participants and to increase clinical trial matching.

It is important to note that operationalizing the virtual genomic tumor board required a great deal of perseverance given Sanford's large geographic footprint, which crosses state lines, involves several different practice types, and includes consultants and researchers.

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Today, the genomic tumor board meets twice weekly (in person and via video conference), allowing experts across Sanford Health to weigh in on all of the cases presented. Sanford has also had the good fortune of expanding the breadth and depth of clinicians and providers participating in the patient care discussions. Experts and focused clinicians weigh in on very rare tumors that a community cancer center may see infrequently. Consulting together, clinicians see unique cases more often, and if an expert has the necessary experience, he or she has the opportunity to share. Genomic tumor board participants include:

- Clinical geneticists
- Genetic counselors
- Medical oncologists
- Oncology subspecialists (surgeons, radiation oncologists, palliative care specialists)
- Pathologists
- Pharmacists
- Research scientists
- Clinical research coordinators.

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Sanford Investigator-Initiated Immunotherapy Research

Phase IB Study: Pembrolizumab with Chemoradiotherapy

Due to Sanford's surgical and multidisciplinary expertise, head and neck cancer patients comprise a disproportionately high percentage of patients at its clinical sites. As Sanford grew its immunotherapy program, collaboration between researchers and clinicians led to a clinical trial to serve these patients.

Utilizing its multidisciplinary team, Sanford developed a clinical trial using the investigational drug pembrolizumab in combination with chemotherapy and radiation therapy for patients with advanced head and neck cancer. The study explores the drug's ability to activate the body's immune system to fight head and neck cancer during this curative intent approach. As an immune checkpoint inhibitor, pembrolizumab allows the body's immune system to recognize and attack the cancer. The study is evaluating the benefit and safety of adding this immunotherapy to standard therapy to improve long-term outcomes. It is supported through the Merck Investigator Studies Program.

GEMMA/COMPASS Studies

In 2014 Sanford launched the GEMMA study. GEMMA (the Genetic Exploration of the Molecular Basis of Malignancy in Adult) was critical to advancing Sanford's ability to use targeted chemotherapy and genomic information to treat its patients. In 2016 the GEMMA program expanded into the COMPASS (Community Oncology use of Molecular Profiling to Personalize the Approach to Specialized Cancer Treatment at Sanford) study following extremely successful uptake of the operational workflows and outcomes achieved through the GEMMA trial.

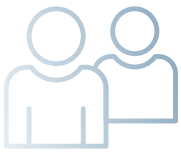
GEMMA concentrated on targeted chemotherapy and next-generation sequencing (NGS), using the technology to analyze tumor samples and providing real-time clinical information for each patient's care team. The study enrolled 120 patients with refractory, incurable cancers. It demonstrated that molecular profiling increases awareness of clinical trial and off-label treatment options for patients with incurable cancer. As part of the study, 39 percent of patients who had genomic testing completed were treated with matched targeted therapies.

Sixteen percent of the patients were treated on genomic-matched clinical trials. In the end, this study highlighted the importance of delivering molecular profiling to patients in the community and allowed for more treatment options for patients in this setting.

The COMPASS study examines the latest genetic sequencing tools to personalize cancer treatments based on each patient's genomic information. The study expands eligibility of patients and allows for more comprehensive genomic analysis. Tumors are analyzed sooner, providing information and targeted treatment plans earlier on in the treatment course. It seeks to collaborate with other efforts, such as the NCI MATCH study, ASCO TAPUR, and other industry-sponsored precision medicine trials. As part of this effort, Sanford has been able to bring in more than 60 different personalized therapy options for patients through clinical trials.

The goal of the COMPASS study is to better understand the impact of genomic testing on patient outcomes and the overall cost of care. These programs have unintentionally shown the importance of immunotherapy in precision medicine. With Sanford's tumor profiling, providers also receive information on the mutational burden and DNA mismatch repair. Depending on the mutational burden and other signatures suggestive of immune response, clinicians can identify patients who may have a higher chance of benefit from immunotherapy. As PD-L1 testing becomes part of standard practice, Sanford has integrated this testing into its program. As newer technologies become available, they will also be rapidly integrated.

A cancer's genetic code holds information vital to understanding how cancer affects each person differently. By better understanding cancer genomics, clinicians can identify treatment options that may have not been previously available. COMPASS seeks to help us understand how this testing can be most effectively used for our patients.



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Commitment to Clinical Trials

Sanford physicians and administrators work with the executive team on the vision for the organization: what we want to be and the care we want to provide to our patients. Realizing this vision requires an understanding that proper staffing ratios are essential to providing new and innovative therapies. Sanford's executive team has been receptive to staffing needs as we commit to increasing accruals into clinical trials for the cancer program. The executive team shares in the desire to provide advanced care for patients across the enterprise, along with a commitment to develop state-of-the-art, advanced treatments in all organizational hubs—as without this effort Sanford cannot reach out to the smaller, rural areas.

Sanford firmly believes that clinical trials are not only the way to deliver the most advanced care to its patients, they are also the critical vehicle to gather the data and evidence to form and direct the cancer treatments of tomorrow. Collecting data in a rigorous manner facilitates innovation as cancer treatments accelerate, and clinical trials are the best way to innovate. Thus, Sanford continues to prioritize increasing accruals to clinical trials. New industry immunotherapy trials at Sanford have increased from 3 in 2014 to 4 in 2015 to 15 in 2016 with enrollments over that period increasing from 7 to 28 to 59, respectively.

Sanford takes every opportunity to present to patients the potential benefits to clinical trial participation should they be eligible—both to themselves and to future patients. From Sanford's navigators, who meet patients the first time they come into the center, to the nursing staff and the physicians, Sanford advocates and educates regarding the importance of clinical research.

This message is carried over into every multidisciplinary conference. When cases are presented, clinicians devote a screen to pathology, a screen to radiology, a screen to nuclear medicine, and a screen to clinical trials for which the patient may be eligible. For every patient, Sanford seeks an answer, evaluating available trials as well as assessing where Sanford may be missing trials that might fit a group of patients.

Sanford works hard to open clinical trials appropriate for its specific patient population and by maintaining this focus, Sanford has made strides in gaining access to trials for more of its patients. Designing trials for the patient base through investigator-initiated trials is one part of a multi-pronged approach to advance care, add to the number of clinical trials, and increase accrual rates. Sanford's investigator-initiated trials facilitate recognition of and service to the needs of its populations. For more on these investigator-initiated trials, see the sidebar at right.

Sanford also works with government entities and industry to bring immunotherapy options to patients, including the National Cancer Institute (NCI), the National Clinical Trials Network (NCTN), Merck, Bristol-Myers Squibb, Pfizer, and AstraZeneca.

Driving Change in Care toward Precision Medicine

Over the last several years, treatment options for cancer patients have expanded greatly, including the addition of new chemotherapy agents and the tests to identify patients likely to respond to these agents. Likewise, immunotherapy agents and biomarker tests now reveal who is likely to benefit most from immunotherapy agents. For example, PD-L1 testing is now hitting the clinic and helping clinicians identify patients who may benefit from immunotherapy over chemotherapy. Because of this technology, lung cancer is seeing a huge treatment paradigm shift after the results of KEYNOTE-024 were released. This study showed that patients whose tumors had high PD-L1 expression benefitted more from up-front pembrolizumab compared to standard chemotherapy. When the results of this study were released, Sanford moved PD-L1 testing into its lung cancer diagnostic panel, which already included genomic testing for EGFR, ALK, and ROS aberrations. As other similar companion biomarkers are developed, it will be very important to integrate these into routine clinical care. These changes can be challenging for many reasons. First, these biomarkers are coming out at rapid pace and may change for each companion drug. Additionally, these tests may require different techniques for testing (immunohistochemistry, next-generation sequencing, FISH, etc). Some of these tests can be done in-house, while others must be sent to an outside laboratory. Further complicating matters is the limit on the amount of tumor tissue that may be available, which makes it very important to stratify the tests clinicians want to perform for each individual patient. In the end, Sanford understood that these tests are integral to patient management so the cancer program built an infrastructure to support them, integrating these tests into routine clinical care as rapidly as possible. This infrastructure consists of physicians (pathologists, interventional radiologists, oncologists) and support staff (nurses, nurse navigators, technicians, social workers) who are continually eager to learn about companion biomarkers and motivated to move them into practice. With this adaptable team, Sanford is able to bring innovative tests from the experimental phase into the clinic as soon as they are available, improving patient access to precision treatments.

Immunotherapy—Changing the Landscape of Cancer Care

Immunotherapy and treatments targeting cancer genomics are moving cancer care beyond standard chemotherapy, offering the hope that cancer can be transformed into a chronic—rather than acute—disease. Immunotherapy deploys the patients' own immune

system in fighting the cancer in their bodies. At the same time, lower toxicity and late effects profiles that immunotherapy may offer make these therapies extremely attractive to patients. While immunotherapy alone is not the answer, it is an important part of the cancer-fighting armamentarium—along with surgery, radiation therapy, and chemotherapy.

In April 2012, Sanford provided its first PD-1 inhibitor treatment. Through July 2016, 349 unique patients have been treated with 1,326 doses, 18 percent of which were administered as part of a clinical trial. (Note: these doses include both pembrolizumab and nivolumab.)

Delivery of immunotherapy treatment at Sanford is a multifaceted operation, requiring a focused team to provide advanced, innovative care to our patients, including:

- Pharmacy to provide medication therapy management as well as patient advocacy and pre-authorization.
- Nursing support to provide training and education as well as triage protocols to assist the investigator in managing adverse events for study subjects.
- Psychosocial support to treat the "whole patient" via social work and palliative care.

Sanford has passionate physician champions who work with supportive staff to innovate and subsequently implement the innovations into daily practice. For example, Sanford has reworked the way its research-focused physicians practice within the clinic, pairing them with a dedicated nurse practitioner and nursing staff. In addition, the operation's research-focused workflow has been adjusted to enable clinicians to see as many research patients as possible on a designated "study day." To be on the leading edge of advanced treatment plans requires a willingness to deliver care in innovative ways, integrating chemotherapy, radiation therapy, and immunotherapy. OI

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Sanford Health At-a-Glance

Sanford Health, an integrated health system headquartered in the Dakotas, is one of the largest health systems in the nation with 45 hospitals and nearly 289 clinics in 9 states and 4 countries. Sanford medical services reach 2.74 million people across over 250,000 square miles, providing healthcare close to home in more than 300 communities. Sanford Health's 2,251 providers and 6,100 registered nurses deliver care in more than 80 specialty areas of medicine. Sanford Health's 28,000 employees make it the largest employer in the Dakotas.

Nearly $1 billion in gifts from philanthropist Denny Sanford have allowed for several initiatives, including global children's clinics, genomic medicine, and specialized centers researching cures for type 1 diabetes, breast cancer, and other diseases. With a team of more than 200 researchers, Sanford Research is comprised of several centers that bridge translational and clinical research including Children's Health Research Center, Edith Sanford Breast Center, Cancer Biology Research Center, Center for Health Outcomes and Population Research and Sanford Sports Science Institute.