Precision Medicine in the Community – Physician Perspective

James L. Wade III, MD, FACP, FASCO
Associate Professor of Clinical Medicine
Feinberg School of Medicine, Northwestern University
Principal Investigator, Heartland NCORP
President, Cancer Care Specialists of Illinois

Dr. Wade placed precision medicine in the context of many different promising cancer treatments over the past few decades and described the participation of Heartland CORP in precision medicine trials.

Precision medicine is an exciting development in cancer, but it must be placed in a historical context. Over the past few decades, many waves of promising cancer treatments have waxed and waned. Each wave has come with great hope and enthusiasm, but has left us with some disappointment. This is not because people have failed, but because it is hard.

One such wave was interferon, which many experts thought would cure everything from small cell lung cancer to ovarian cancer. Interferon is still used, but its role is limited. Other waves have included multi-agent chemotherapy, non-cross resistant chemotherapy, bone marrow transplant for solid tumors, biotherapeutics such as IL-2, and antibodies such as bevacizumab for multiple cancers. Each wave has brought progress, but has not proven to be the final solution. For this reason, we need to rein in our enthusiasm for precision medicine. Some successful results have been reported, but these are often heavily influenced by patient variation (ethnicity, background, age, pharmacogenomics, immune response, metabolism, etc.).

Heartland NCORP is an Illinois-based alliance that serves 6 million people and treats 16,000 new cancer cases annually. We are currently involved in 6 molecular target driven studies: SWOG Lung-MAP, ECOG/ACRIN MATCH, NCI Exceptional Responders, SWOG 1403 (A Randomized Phase II/III Trial of Afatinib Plus Cetuximab versus Afatinib Alone in Treatment-Naïve Patients with Advanced, EGFR Mutation Positive Non Small Lung Cancer, and Alliance (Combination Chemotherapy With or Without Atezolizumab in Treating Patients With Stage III Colon Cancer and Deficient DNA Mismatch Repair).

My overall experience is that molecular trials hold promise, but for a few. Over the last 3 years, sequencing and identification of molecular subtypes has grown at a staggering rate. At the same time, payers such as Medicare have begun focusing on cost of care. Medicare is now evaluating cost of care (eg, sequencing, drug expenses, etc.) in their determinations of reimbursement.

Progress in cancer treatment will require many different solutions. One avenue for exploration is to search closed phase 3 trials of patients with metastatic disease to look for unexpected survivors (expanded, validated data set). Often cancerous tissue and germ line DNA were collected as part of the parent trials and they may produce important clues. Another avenue is to search prevention trials for

those who subsequently developed cancer. Would we find early circulating DNA clues? The blood is already stored and the analytic technologies are far superior today than they were in the past.

Audience Questions and Answers

- *What happened to the 90% plus patients who didn't get into the MATCH trial? Did you learn anything from their biopsies?* Their tissue has been sequenced and they may have had mutations for which there was not a target. They went on standard of care, and having had advanced disease, most have passed away.
- *How does the American Affordable Care Act impact your work presently and what do you anticipate its effect to be in the future?* Losing it hurts, having it helped. There were a number of exchanges that opened in our area, but have now closed. People who had never had insurance before got screened and their cancers were detected and treated early; that was exciting to see. It's sad now that it's gone.
- *NCI has formed a committee called Core Correlative Science Committee and they field requests for research with biospecimens that have been previously collected, and it's interesting that they aren't getting more applications to study those tissues.* Yes, there's gold out there we haven't mined.
- *You described a patient with squamous cell cancer whose disease progressed with targeted therapy. What do you think went wrong; do you think the dose was off? How do you think about dosing with targeted therapies when you aren't looking for maximum tolerated doses?* There are many parallel signaling pathways and sometimes we accelerate signaling in another pathway when we block one. The drug might have done exactly what it was supposed to do, but we might have turned something else on as an unintended consequence.