Andrea Wang-Gillam, MD, PhD

Andrea Wang-Gillam received an MD and PhD from the University of Arkansas for Medical Science (UAMS). She completed her internship at Cleveland Clinic Foundation in Ohio. After completing her internal medicine residency and hematology/oncology fellowship training in UAMS, she joined the Division of Oncology at Washington University in St. Louis. She is an assistant professor specializing in gastrointestinal malignancies. Her research interest is the area of preclinical evaluation and early phase clinical trial of novel therapies in pancreatic cancer. She is a principal investigator for multiple pancreatic cancer clinical trials.

Kristina Williams

Kristina Williams is the Manager of Oncology Clinical Research at Washington University School of Medicine. She joined the Division of Oncology in 2006.

The ideas and viewpoints expressed in this commentary are those of the author and do not necessarily represent any policy, position, or program of NCCN.

Paving the Road to Clinical Trial Participation: Removing Road Blocks and Directing Patients Toward Novel Therapies

Andrea Wang-Gillam, MD, PhD, and Kristina Williams

Clinical trials are the key to the development of safe and effective therapy. Within the sphere of oncology, where patients are in desperate need of therapies that effectively control disease, clinical trials play a uniquely significant role in patient care compared with other therapeutic areas.

Early in my career, I determined that I should understand the mechanics of clinical trial operations at my institution so that I would be prepared to conduct my own clinical studies. After a while, I realized that my senior colleagues' complaints about the lengthy and tedious regulatory process required to open a trial is unfortunately a common phenomenon. The laborious and exhausting process of opening US oncology trials has been well described and clearly dissected by Dilts et al.¹⁻³

Although my area of clinical focus is gastrointestinal malignancies, my research has gravitated toward novel therapeutic development in pancreatic cancer. Patients with pancreatic cancer have a poor prognosis, with a 5-year survival rate less than 5%.⁴ My opinion is that everyone with pancreatic cancer should be presented with the opportunity to participate in a clinical trial, because currently available standard therapy is simply not good enough. To improve patient access and awareness of clinical studies in pancreatic cancer at Washington University in St Louis (WUSTL), I set 2 goals: to decrease the time required to open a pancreatic cancer trial and to improve the clinical trial participation rate.

To fully understand the challenges at our institution and to get some ideas from other institutions, including those outside the United States, I worked with Kristina Williams, one of our research managers. We compared the processes involved to open oncology trials at WUSTL with those at the University of Torino (UT) in Italy, a comparable institution. Based on retrospective reviews of recently conducted thoracic oncology trials, the median time from submission to the opening of a trial was significantly longer at WUSTL than at UT (163.0 vs 112.5 days; $P=.048$). Additionally, the median number of patients accrued per trial was lower at WUSTL (7.4 vs 37.5). Unfortunately, our results are fairly consistent with those reported in the literature.³ Although our study only included thoracic oncology trials, the result of the study reflected more generalized phenomena experienced across therapeutic areas. I did not need additional studies to believe that the oncology clinical trial system in the United States is broken. The key is how to identify ways to improve it.

WUSTL and the Siteman Cancer Center have made conscience efforts to shorten the length of oncology trial activation since 2010. A careful process review was used to identify opportunities for improvement, and the institution began reaching out to various stakeholders to identify ways to increase efficiency. For example, in 2010, a single scientific review committee (SRC) met once per month to review all research protocols conducted in the oncology patient population. This meeting was identified as a bottleneck, because protocols received too near the submission deadline were required to wait 4 weeks for the next available meeting. After this concern was identified, research administration worked with the Siteman Cancer Center to add a second SRC meeting 2 weeks after the traditional meeting date. Having 2 meetings per month, as opposed to 1, helps reduce the amount of time between protocol receipt and submission while simultaneously enabling review of a larger volume of studies. Research leadership has also developed relationships with our local Institutional Review

Clinical Trial Participation

Board (IRB) to brainstorm ways the groups can work together to improve efficiency. A fast-track program has been developed to allow the concurrent submission of select protocols to our SRC and IRB if the protocol meets specific criteria. The studies that met these criteria in 2014 obtained approval in an average of 37 days—a marked improvement over the 163 days noted in 2010.⁵ In addition, research leadership now tracks all pending trials as they are actively moving through the approval process to identify and address barriers in real time, heightening awareness and improving collaboration among financial, contractual, and regulatory teams. The shortening and simplification of the regulatory and administrative procedures has ignited the interest of not only clinical researchers but also pharmaceutical companies.

Given the regulatory process improvements, my focus shifted to the second objective of improving the trial accrual rate. Researchers have estimated that only 5% of patients with pancreatic cancer participate in a clinical trial⁶ and that most are not even referred for studies. This begs the question of what factors play major roles in trial accrual.

I personally think that the quality of the clinical study carries the most weight; therefore, carefully selecting trials for each stage of pancreatic cancer has been a priority for our program. With the increased access to and use of the Internet, many patients are sophisticated at navigating cancer Web sites to look for novel treatment options and research opportunities. “Innovation” is the buzzword for most of my patients. For example, we found that many patients are willing to travel considerable distances specifically to participate in a trial at our institution using a *Listeria* vaccine, because they want the opportunity to receive the most innovative therapies available.

Social media and the Internet play an increasingly important role in engaging patient perspectives on cancer therapy. I have noticed that more than half of my patients have visited the Pancreatic Cancer Action Network (PanCAN) Web site, and some have regular communication with PanCAN personnel specifically about clinical trials. I find it refreshing when patients come to the clinic with a stack of clinical trial printouts courtesy of the organization. In addition, patients, family, and friends collect information from TV programs, Facebook, Twitter, and cancer-related Web sites.

Several years ago, patients asked me for drugs that could potentially target a “cocoon.” They understood the concept that pancreas tumor cells reside in stroma, the cocoon, based on discussion boards and resources that they had found on the Internet. Now, patients are starting similar conversations regarding immunotherapy approaches. Media exerts a powerful influence on patients seeking specific clinical studies, and it certainly has the potential to improve patient participation rates.

Our multidisciplinary clinic has been a tremendous help in terms of screening patients for clinical studies. If patients with borderline resectable and locally advanced pancreatic cancer are seen by surgeons, radiation oncologists, and medical oncologists at the same time and the recommendation for treatment is consistent, then the patient is more likely to consider the clinical study. Many of our patients are enthusiastic about trials when they are consistently discussed and recommended by all providers.

Prescreening and frequent communication with patients are other important factors in patient enrollment. Patients with pancreatic cancer have a narrow window of participation in clinical studies, because protocol criteria limit when and in what circumstances patients are eligible. Manual screening for new consults every week has helped identify potentially eligible patients for trial, which has been shown to be an effective way to improve clinical trial accrual.⁷

Historically, insurance has also been a barrier to clinical trial participation,⁸ particularly for patients seeking to enroll on early phase trials. To address this, our institution has designated personnel to assist in the clinical trial appeal process.

Wang-Gillam and Williams

By employing individuals knowledgeable in this area and training staff in how to most effectively interact with insurance providers, we have been able to increase the number of approvals. Implementation of the Affordable Care Act, which supports patient enrollment to clinical trials, has also helped increase our approval rate. We expect this trend to continue as grandfathered plans become less common.

With these new processes, social media penetration into daily life, innovations in technology, and novel drug developments, accruing patients to clinical studies within the pancreatic cancer program at our institution has become easier. Patients inquire about clinical trials and are committed to the trials that appeal to them. As a result, in 2012, the pancreatic cancer therapeutic trial rate at WUSTL exceeded 35%.

This progress is pleasing, but developing a successful clinical research program is an ongoing endeavor. Investigators must continually seek novel clinical trials that help meet the needs of their patients. Centers must be intentional about engaging available social media outlets and patient advocacy groups in order to understand patient interests. In addition, investigators and administrators must continually evaluate for potential opportunities to improve the administrative aspects of the process.

Acknowledgments

This publication was supported by the Washington University Institute of Clinical and Translational Sciences grants UL1 TR000448 and KL2 TR000450 from the National Center for Advancing Translational Sciences. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

References

1. Dilts DM, Sandler A, Cheng S, et al. Development of clinical trials in a cooperative group setting: the Eastern Cooperative Oncology Group. *Clin Cancer Res* 2008;14:3427–3433.
2. Dilts DM, Sandler AB. Invisible barriers to clinical trials: the impact of structural, infrastructural, and procedural barriers to opening oncology clinical trials. *J Clin Oncol* 2006;24:4545–4552.
3. Dilts DM, Sandler AB, Baker M, et al. Processes to activate phase III clinical trials in a Cooperative Oncology Group: the case of Cancer and Leukemia Group B. *J Clin Oncol* 2006;24:4553–4557.
4. Wolfgang CL, Herman JM, Laheru DA, et al. Recent progress in pancreatic cancer. *CA Cancer J Clin* 2013;63:318–348.
5. Wang-Gillam A, Williams K, Novello S, et al. Time to activate lung cancer clinical trials and patient enrollment: a representative comparison study between two academic centers across the Atlantic. *J Clin Oncol* 2010;28:3803–3807.
6. Hoos WA, James PM, Rahib L, et al. Pancreatic cancer clinical trials and accrual in the United States. *J Clin Oncol* 2013;31:3432–3438.
7. Chen L, Grant J, Cheung WY, et al. Screening intervention to identify eligible patients and improve accrual to phase II-IV oncology clinical trials. *J Oncol Pract* 2013;9:e174–181.
8. Klamerus JF, Bruinooge SS, Ye X, et al. The impact of insurance on access to cancer clinical trials at a comprehensive cancer center. *Clin Cancer Res* 2010;16:5997–6003.