Reflections on a Generation of GI Oncology Research

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Having had the privilege to lead the Gastrointestinal (GI) Committee for more than two decades under three Group Chairs, I witnessed a generation of clinical trials that evolved from a more empirical design of A vs. B to complex designs based on preclinical observations aimed at linking tumor biology with targeted drug selection. Innumerable profound changes permeated the entire oncology domain, driving the field forward to the as-yet unrealized goals of creating patient-centered care in clinical practice and a research agenda that is decidedly focused on personalized medicine.

More than the concept of delivering the right treatment to the right individual at the right time, cancer care delivery models emphasized comprehensiveness and access. This trend generated a vast network of clinical practices and cancer centers across the country, offering unparalleled opportunities to provide state-of-the-art care where people live. Given that comprehensive care now embraces a multitude of disciplines, there is a growing recognition that the breadth of essential cancer care services and the scope of oncology research must integrate the entire spectrum of the oncology sphere from screening to end of life.

It is imperative that this thinking heralds the transformation of oncology since proclamation of the “War on Cancer” in 1971 during the Nixon administration. The oncology landscape altered in ways scarcely imagined in 1971 due to stunning advances in medical oncology, radiation, surgery, diagnostics, and symptom management; along with powerful contributions from nurses, social workers, pharmacists, psychologists, other allied health professionals, and patient advocates.

For example, the National Cancer Institute-sponsored cooperative groups have been the public face, at least in part, of US efforts over the years to promote clinical research through their nationwide infrastructure for multidisciplinary clinical trial accrual of hundreds of thousands of individuals across the country in both community and academic settings.

This national infrastructure was realized in a sparse funding environment and made possible by the volunteer efforts of thousands of healthcare professionals supported by their institutions and community practices that were members of cooperative groups. It was also made possible by innumerable collaborations among the groups, investigators, industry, and the government. Today, the groups continue to foster a spirit of camaraderie among institutions and investigators, including members of community practices, and provide a fertile field to train and mentor the next generation of researchers.

When I declared myself a GI oncologist 30 years ago, it was certainly a lonely professional choice. Only a few of us practiced at the time. Outside of surgery and radiation, the few available treatment options centered on the only drug we had, fluorouracil (5-FU), which we relentlessly pursued across the spectrum of GI cancers in a host of different doses and schedules. What a difference three decades can make! Representing nearly 20 percent of all cancers, our GI cancer patients benefited from the development of many new systemic treatments and advances in radiation, surgery, and symptom management, all resulting in improved survivorship and quality of life. It is gratifying that so many of our fellows and junior colleagues are now pursuing a career in GI oncology.

The ECOG-ACRIN GI Committee certainly felt the impact of a growing enthusiasm for our field, as we now have talented new and young investigators spearheading many of our clinical trials. These new trials include not only novel targeted therapies and laboratory correlates, but also take full advantage of the ECOG-ACRIN merger by integrating imaging techniques, which enhance the ability to determine drug efficacy. Indeed, the most significant challenge facing the GI and other ECOG-ACRIN disease-oriented committees is how best to identify and integrate
genomic technology and advanced imaging to optimize patient treatment selection strategies in this era of constraints in funding and availability of investigator time and resources.

**Challenges in the Competitive Enterprise**

As members of the oncology community, we collectively face complex challenges that are enveloped in uncertainty. The current trend of consolidation and efficiency is very clearly evidenced by the recent merging of the cooperative groups serving adults with cancer, as well as the many mergers that have occurred among individual and community-based practices that are now part of networks and/or hospital-based systems. Great care must be taken to avoid the disengagement of investigators who may feel that it is too difficult to find a role or research opportunity in a streamlined cooperative group system or an institution that might not be so willing to offer the volunteer time of its investigators and institutional resources to supplement the unfunded and unreimbursed costs of cooperative group clinical trials in an economic-driven model of care.

The complexity of translational research, including the incorporation of genomic platforms, will mandate that the cooperative groups engage in an array of partnerships that are much more nimble and efficient than currently available. They will need to more quickly execute contracts with companies whose drugs are of interest and laboratories that have the necessary correlative science capabilities—including partnerships along both imaging and biologic parameters. They will need to more rapidly develop the protocols associated with these partnerships, open the trials more quickly, and accrue patients with greater speed. Their trial timelines must compress considerably to produce trial results much more quickly than has been done traditionally. The groups must do this to remain attractive to industry, which controls the vast majority of drugs in development. Furthermore, these new partnerships will need to be inclusive of government, institutions, a variety of industries, and insurance carriers.

With these complexities, the entire oncology community, including but not limited to the cooperative groups, will need to be much more competitive in the global clinical research enterprise so that patients will have optimal opportunities to take advantage of new treatments and innovative clinical trials. It will also be important for the cooperative groups to be well-positioned to take full advantage of their extensive databases and tumor banks as a means of expanding research opportunities such as the area of comparative-effectiveness research. We must be proactive in seeking new resources to pay for our ambitious endeavors.

**In Closing**

As I reflect on my tenure with the GI Committee, I am aware that I am truly blessed. I am so grateful to my patients, mentors, and wonderful colleagues. In particular, I want to thank my colleagues at Northwestern University, ECOG-ACRIN, and the GI Intergroup who have offered support, friendship, and collaboration through the years. To my family, who has somehow endured the long hours and endless travel, I am deeply grateful. I look forward to the future as an enthusiastic participant in the GI Committee and other ECOG-ACRIN activities.

Dr. Benson was appointed Co-Chair of the Gastrointestinal (GI) Committee in 1989 and named its Chair in 1991. During Dr. Benson’s 24-year tenure, the GI Committee became a major national force in GI cancer research. The GI Committee led E5202 and E4203, two of the first biomarker-driven trials ever to be performed in the cooperative group system in colorectal cancer.

E5202, the first national trial to include stratification to observation vs. randomization, used a real-time assay of microsatellite instability/18q loss of heterozygosity status for treatment selection in 3000 patients with stage II colon cancer. The trial established the cooperative groups’ ability to perform large-scale trials on a national level, wherein risk stratification was accomplished through rapid, clinically acceptable laboratory turnaround times. E4203, a trial for patients with advanced colorectal cancer, assigned patients to treatment on the basis of thymidylate synthase expression. Notably, these two trials demonstrated the feasibility of the cooperative groups to conduct biomarker-driven studies.

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