Commentary: Timing Is Everything

By Robin Zon, MD, FACP

For more than a decade, many experienced research sites have recognized that per-case reimbursement for National Cancer Institute (NCI)–sponsored trials is insufficient and have developed strategies in an attempt to run cost-neutral, cost-efficient research programs. There have been many venues in which spirited discussions have been held regarding how to utilize clinical trial mix, in-kind contributions, and local institutional support to achieve the goal of cost neutrality without sacrificing research quality.

The recent online poll conducted by ASCO and published in this issue of *Journal of Oncology Practice* documents that inadequate NCI per-case reimbursement negatively affects cooperative group trial participation, despite the fact that investigators prefer government-sponsored trials.¹ If research programs have been directing their participants—their most valuable resource for clinical trials—away from cooperative group studies, is the ASCO survey relevant today? Is the information embodied in the survey timely and important?

Baer et al¹ remind us that the cooperative group per-case reimbursement of \$2,000 has not increased in 10 years. Published data from the 2005 ASCO and C-Change (Washington, DC) studies indicate that during this same time period, the average cost per enrollee was \$5,000 to \$6,000.^{2,3} These discrepancies are difficult to ignore. An examination of the past-year budgets of our local research site validates a net loss for government-sponsored participant enrollment. Similar to survey respondents' intent to increase participation in industry-sponsored trials, we use a diversification of clinical trial mix, including NCI-sponsored trials, pharmaceutical trials, and other noncooperative group trials, to broaden our portfolio and balance our budget while maintaining an impressive array of clinical trials for the community we serve. Additionally, we continuously monitor the study mix of enrollment to assure the financial sustainability of our program.

Two additional corollary considerations are revealed by the survey. First, some sites limit NCI-funded trial participation to maintain staffing for research and regulatory functions. Second, one might imagine that community-based research programs would be most sensitive to the financial constraints associated with participating in federally funded trials. This proved not to be the case. In fact, all responding sites, including academic hospitals, nonacademic hospitals, and private practices, reported needing to make adjustments because of insufficient reimbursement from participating in NCI-sponsored trials.

The article¹ highlights the important and invaluable contributions that NCI-funded clinical trials have made to the practice of oncology, but it also suggests that the NCI may underestimate the importance of adequate funding as a means of sustaining enrollment and participation in NCI cooperative group trials. To further examine this claim, I direct the reader to

“Restructuring the National Cancer Clinical Trials Enterprise,” released in June 2005.⁴ In this report, the Clinical Trial Working Group, established by the NCI, advises whether, and in what ways, the NCI-supported clinical trials enterprise should be restructured to realize the promise of molecular medicine for advancing the future of oncology practice. This document details a blueprint of strategies, proposed restructuring, and an implementation timeline. Major initiatives, including improvement of operational efficiency, are described. Specifically, the operational efficiency initiative addressed financial considerations, including the restructuring of the funding model for phase III trials to incentivize more rapid rates of accrual. To the credit of the NCI, a recently implemented program to better align per-case reimbursement with trial complexity establishes a tiered reimbursement schedule to match more closely the actual cost of accrual for select highly complex trials. However, the initiatives do not specifically include a global increase of reimbursement to compensate for actual costs for all NCI-funded trials.

Furthermore, the importance of adequate reimbursement for the implementation of a successful clinical research enterprise has been documented and published in several studies. The Summit Series on Cancer Clinical Trials, which included ASCO, the Cancer Leadership Council, the Cancer Research and Prevention Foundation, the Coalition of National Cooperative Groups, and the Oncology Nursing Society, in “Cancer Clinical Trials: Elements of Success,” identifies “adequate financial resources” as one of the six essential elements of a successful, high-quality cancer clinical trial site.⁵ Similarly, the guidance document by C-Change on implementing effective cancer clinical trials, also published in June 2005,³ identifies operational and cost benchmarks for sites conducting cancer clinical trials. This report was primarily based on data gathered from a survey administered to a sample of 14 clinical trial sites. The respondents noted three financial keys to success, including obtaining adequate compensation for clinical trials, controlling expenses, and performing efficiently. On the basis of the respondents' observation that government-sponsored studies were generally underfunded, the guidance document highlights the importance of developing trial selection and mix as appropriate for the patient population of a site and references this as a strategy “to improve payment relative to costs.” This strategy continues to be supported and publicized, as indicated by its inclusion in various workshops and meetings directed toward clinical research sites and most recently in this issue of *JOP* in the Attributes of Exemplary Research Sites series.⁶

Is the ASCO survey relevant today? Is the warning by Baer et al¹ that the cooperative group trial system may be in jeopardy timely and important? If so, why? First, an unpublished survey conducted approximately a decade ago indicated less than a

quarter of oncologists had actually calculated the cost of participating in clinical research and therefore did not fully appreciate whether an enrollee on a government trial resulted in a net gain or loss.² I speculate that as information regarding reimbursement and cost has become repeatedly publicized and critical to the discussion of budgets, more oncologists and administrators are aware of this financial variance. Second, the current economic climate is much different than that of the previous decade. Insurance reimbursement challenges, lack of sufficient insurance coverage by patients, and cuts in revenue for daily practice operations may also support the inclination to avoid high-risk, financially costly activities. Furthermore, many oncologists no longer donate personal income to support research. Third, integrating industry-sponsored trials into the clinical trial menu may not be as viable to supplement funding for local research operations because of potential decreases in industry sponsored trials. Fourth, reports document that on average, 29% of revenue for support of the clinical research program originates from nontrial sources.³ This suggests that institutional commitment, and even community charitable giving, may provide alternate funding. However, many institutions are currently faced with financial challenges resulting in decreased resources to allocate for clinical trial programs. Charitable giving has declined for many organizations as a reflection of economic times and does not appear to be a reliable resource for many programs. Lastly, the legacy of dedication and in-kind labor of the more seasoned investigator is being threatened as young oncologists face competing issues such as practice concerns, lack of education in regulatory issues, and an underappreciation of the long-term value of clinical trials. The additional challenge of loss of income for NCI trial enrollees will not incentivize these inexperienced and uncommitted investigators to participate in the clinical trial system.

The comments by Baer et al¹ regarding the sequelae of insufficient per-case reimbursement as jeopardizing the infrastructure supporting the cooperative group trial system should be taken seriously and serve as a call to action. Compensation for the actual cost of conducting these important studies appears necessary to enable continued conduct of NCI-sponsored trials. However, as the authors imply, this is only part of the

solution. The NCI, research-committed organizations such as ASCO, investigators, and administrators need to collaboratively develop models of excellence to address the many barriers to clinical trial development and accrual, including the structure of a cost-efficient clinical trial program.

The NCI-sponsored clinical trial system conducts the highest quality and least biased work we do in cancer research. These trials have significant impact by providing evidence that translates into practice-changing algorithms of care. Our patients depend on the NCI clinical trial system to be functional, effective, and efficient in bringing forth new personalized therapies to prevent, control, and cure cancer. Among many oncologists, there is continued loyalty and belief that clinical trials, especially NCI trials, represent the best oncologic care available for our patients.

On the basis of past and recent activities of the NCI, one can see a clear commitment to address the many factors influencing the decision to participate in government-funded trials. The ASCO survey documents insufficient reimbursement as a significant deterrent to cooperative group trial participation. Increasing NCI funding to better cover actual research costs represents an additional solution to advancing cancer trial accrual. Timing is everything, both for actions to preserve the invaluable NCI clinical trial system and for clinical research to continue to influence patient care.

Accepted for publication on March 10, 2010.

Author's Disclosures of Potential Conflicts of Interest

The author indicated no potential conflicts of interest.

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DOI: 10.1200/JOP.091093; posted online ahead of print at <http://jop.ascopubs.org> on April 15, 2010.

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