Discussions About Clinical Trials Among Patients With Newly Diagnosed Lung and Colorectal Cancer

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Clinical trial enrollment among adult cancer patients in the United States is low and presents a major impediment to the advancement of cancer care and prevention. Fewer than 5% of adult cancer patients in the United States are estimated to participate in National Cancer Institute (NCI)-sponsored clinical research trials, a statistic that has been stagnant for decades (1–4). Furthermore, certain subsets of the US population, including the elderly, racial or ethnic minorities, and women, have historically been underrepresented in clinical trials (3). Underrepresentation by these groups does not reflect the heterogeneity of the US population or of cancer biology. This shortcoming of the clinical trial enterprise implies inequitable access to clinical trials, threatens the generalizability of trial results, and hinders meaningful subgroup analyses. Concomitantly, many clinical trials close with accrual insufficient to answer their scientific questions. Among phase III trials sponsored by NCI-sponsored clinical trial cooperative groups, 34% closed with insufficient accrual to address the trials’ primary endpoint (5). Furthermore, the Institute of Medicine (IOM) report “A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program” stated that 40% of oncology trials of all phases approved by the NCI close without meeting target accrual (1). Trial closure because of insufficient patient accrual represents missed opportunities to advance cancer treatment and ineffective allocation of limited funding and patient resources.

Barriers to accrual are multifactorial and involve factors related to patients, physicians, and the trials themselves. Commonly cited physician barriers include lack of resources and time, inadequate reimbursement or other reward for participation, and lack of an interesting research question, among others. For patients, barriers include lack of awareness of trials, unavailability of an applicable trial, preferences for certain treatments or fear of randomization, and possibly additional expenses or lack of insurance coverage (6–9). A comprehensive review of evidence on barriers and promoters of trial participation among underrepresented populations categorized barriers into three groups: (1) awareness of trials, (2) opportunity to participate in trials, and (3) acceptance of trial participation (10). The most common group of barriers, however, relates to the opportunity to participate (10).

In this issue of the Journal, Kehl and colleagues (11) present survey results from patients diagnosed with lung or colorectal cancer about their discussions regarding clinical trial enrollment with physicians and about participation in therapeutic trials. The 7887 patients comprising this multiregional cohort received care in various settings, including large integrated healthcare systems. This study finds that only 14% of patients recall having discussed clinical trial enrollment as a treatment option and that fewer than 4% participated in a treatment trial. These rates were slightly higher when limited to patients with late-stage disease who were treated with chemotherapy (26% discussed trials, less than 8% enrolled in a trial), likely reflecting that more trials are available for late-stage disease. These disappointing rates are consistent with recruitment fractions reported in large population-based studies, with recruitment fractions of roughly 14% reported in select institutions with highly organized clinical trial infrastructures (3,9).

The authors also find that trial participation is discussed less often with patients over 65 years of age, nonwhite race, lower attained education levels, and lower income. Notably, trial enrollment rates among discussants are not associated with age, race, education level, or income. Additionally, trial participation is less commonly discussed with patients having earlier stage disease; yet, trial enrollment does not vary statistically significantly by stage among discussants. The results demonstrate that the key obstacle to clinical trial accrual is lack of opportunity to participate in trials, as opposed to acceptance of trial participation. This study cannot differentiate whether this lack of opportunity to participate is because of a paucity of trials relevant to the study population or to lack of physician engagement in the process of trial recruitment. The overarching finding reinforces what is already known about barriers in the trial recruitment process. However, the size and design of this study, in particular the depth of patient factors collected, make this study a valuable and compelling contribution to the medical literature. The authors also collected information on patient perspectives on fatalism, preference on quality of life vs quantity of life, and preference on cost vs quantity of life. In the end, however, these patient factors were not consistently statistically significant in an adjusted model, while the usual factors of race, age, education level, and income remained statistically significantly associated with the opportunity to enroll in a trial as reflected through discussions with physicians regarding trial participation.

Limitations of this study include not knowing if applicable trials were available for individual patients or if physicians had documented discussions about trials differently than patients recalled them. Despite this, the authors have reaffirmed in a large population of patients suffering from common, frequently lethal malignancies and receiving treatment in different geographic regions and healthcare systems that the primary barrier to trial participation is the opportunity to participate. Importantly, the opportunity...
to benefit from treatment in a clinical trial is not offered equally to patients, affecting equitable access to promising new therapies and generalizability of trial results. Physicians function as the key catalyst in upholding or overcoming this particular barrier. Incentives and strategies to promote offering trial participation equitably deserve renewed attention. This report by Kehl et al. (11) reveals an opportunity both to rectify health disparities in cancer and to improve clinical trial enrollments. To take advantage of these opportunities, there is a need for a collective will of clinical investigators, hospital systems, and funding agencies to facilitate and to support making more trials available to patients and to provide patients with ready access to information about clinical trials for which they may qualify.

References

Note
The authors have no conflicts of interest to declare.

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