Editorial

Local Clinical Trials: The Need of the Hour to Improve Global Cancer Care

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Advances in the care of cancer patients are almost always due to clinical trials that demonstrate improved patient outcomes in terms of better survival or improved quality of life. Pharmaceutical companies invest a large amount of time, effort, and money in developing novel agents, but only a few of these end up actually changing patient care. Agents such as imatinib, osimertinib, trastuzumab, rituximab, and pembrolizumab, among others, are prime examples of this approach. A recent analysis found that the median cost of development of an anticancer drug was $648.0 million.[1]

Research is key to the long-term improvement of cancer control. In fact, the National Comprehensive Cancer Network states that the best treatment of any cancer patient is administered in the context of a clinical trial (www.nccn.org). Unfortunately, even in advanced countries, the proportion of cancer patients enrolled on to clinical trials is very low (<10%).[2] Global studies tend to accrue patients from countries that have robust clinical trial infrastructure that allow for increased efficiency. Another possible reason for this could be the regulatory atmosphere in countries where pharmaceutical companies are interested in selling their product. On the other hand, patients in countries that did not participate in these trials may be treated based on data that may not necessarily be applicable to them.

Recently the U.S. Food and Drug Administration (FDA) refused approval to an immune checkpoint inhibitor, sintilimab, which was studied in China.[3] The ORIENT-11 trial was a randomized, double-blind, phase 2 study of 397 patients administered a platinum-pemetrexed doublet with or without sintilimab as first-line treatment of metastatic nonsquamous nonsmall cell lung cancer.[4] The addition of sintilimab was associated with a significant improvement in progression-free survival (8.9 vs. 5.0 months; $p < 0.00001$). Despite the clinical efficacy, there was concern regarding the applicability of the results of a trial conducted in subjects who are ethnically different from the U.S. population.

This concern is not unwarranted, as there are significant differences in the tolerability and efficacy of anticancer drugs between different populations. For example, irinotecan was shown to be significantly superior to etoposide, when combined with cisplatin in patients with extensive stage small cell lung cancer in a Japanese population.[5] However, a similar study in the United States failed to show difference between the two drugs, and the pharmacogenetic differences between the two populations were thought to be the cause of the differential results between the two trials[6]

While cancer is often thought to be a disease of the affluent, there has been an increased incidence of cancer in lower- and middle-income countries (LMICs). Currently, although LMICs have a lower incidence of most malignancies than developed countries, almost two-thirds of cancer cases and >70% of cancer deaths worldwide in 2020 occurred in LMICs.[7] While cancer death rates seem to be declining in the United States and other developed countries, this is not the case elsewhere.[8] Another aspect that needs to be remembered is that the incidence of individual malignancies is different in different parts of the world. For example, invasive cervical cancer is a major problem worldwide, but over 75% of the cases occur in Asia and Africa, probably due to a robust implementation of cancer screening in Europe and North America.[9] Similarly, the common causes of cancer morbidity and mortality are not the same worldwide. Lung, colorectal, pancreatic, and central nervous system cancers have a higher mortality in high and middle sociodemographic regions, while the most common causes of high morbidity and mortality in the lower sociodemographic regions were cervical and oral cancer.[10] Hence, studies to improve outcomes need to be done in the countries where these cancers are more prevalent and aggressive, as tumor biology may not be the same worldwide.

It is obvious that the benefits of research in the developed world are not reaching the countries with the highest burden of cancer. A major reason for this may be the limited

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ability of individual countries to deliver optimal cancer care to their population based on research conducted elsewhere. Hence to ensure that patients are treated with treatments that are most likely to be relevant to them, local research is mandatory.

This is, however, not without its own challenges. Conducting clinical trials requires formal training in the research methodologies and unfortunately a lot of clinicians in LMICs lack the necessary training to conduct research.[11] Another aspect that needs to be considered is the lack of time available to devote to research activity given the overwhelming clinical volume for oncologists practicing in these settings.[12] The clinical burden often lead to a deprioritization of research and consequently a lack of adequate research infrastructure. Educating the population regarding the benefits of participating in the research is another aspect that needs to be considered. Studies have shown that among certain ethnic groups, individuals with a less than high school education were less likely to participate in research studies.[13]

Given the novel challenges with logistics and resources in each part of the world, individual governments should consider facilitation of clinical trials. This should include, among others, establishment of adequate infrastructure staffed by trained research personnel, development of training programs geared toward busy clinicians and decreasing the barriers that currently exist while conducting research. This will not only allow the conduct of trials pertinent to the local population but also facilitate increased efficiency and quality of care. The development of research infrastructure can foster regional collaborations and thereby enable individual centers to incorporate best practices from partnering institutions, thereby improving the quality of care overall. This is an important factor that can potentially reduce disparities in cancer care and alleviate the cancer burden worldwide.

Conflict of Interest
No relevant conflicts of interest related to this work. Other unrelated conflicts include Consultant: AstraZeneca, Jazz Pharmaceuticals, Flagship Biosciences, Sanofi, Regeneron Pharmaceuticals, Cardinal Health DSMC chair: Y-mAbs Therapeutics, outside the submitted work.

References

1 Prasad V, Mailankody S. Research and development spending to bring a single cancer drug to market and revenues after approval. JAMA Intern Med 2017;177(11):1569–1575
2 Unger JM, Vaidya R, Hershman DL, Minasian LM, Fleury ME. Systematic review and meta-analysis of the magnitude of structural, clinical, and physician and patient barriers to cancer clinical trial participation. J Natl Cancer Inst 2019;111(03):245–255
3 Oncologic Drugs Advisory Committee (ODAC) Meeting. FDA website. Accessed February 10, 2022 at: https://www.fda.gov/media/157576/download
4 Yang Y, Wang Z, Fang J, et al. Efficacy and safety of sintilimab plus pemetrexed and platinum as first-line treatment for locally advanced or metastatic nonsquamous NSCLC: a randomized, double-blind, phase 3 study (Oncology pRogram by InnovENT anti-PD-1–11). J Thorac Oncol 2020;15(10):1636–1646
5 Noda K, Nishiwaki Y, Kawahara M, et al; Japan Clinical Oncology Group. Irinotecan plus cisplatin compared with etoposide plus cisplatin for extensive small-cell lung cancer. N Engl J Med 2002;346(02):85–91
6 Lara PN Jr, Natale R, Crowley J, et al. Phase III trial of irinotecan/cisplatin compared with etoposide/cisplatin in extensive-stage small-cell lung cancer: clinical and pharmacogenomic results from SWOG S0124. J Clin Oncol 2009;27(15):2530–2535
7 Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin 2023;73(01):17–48
8 National Cancer Institute.Global Cancer Research. Accessed April 10, 2023 at: https://www.cancer.gov/research/areas/global-health
9 International Agency for Research on Cancer.Estimated number of new cases in 2020, World, both sexes, all ages (excl. NMSC). Accessed April 10, 2023 at: https://gco.iarc.fr/today/online-analysis-table?v=2020&mode=cancer&mode_population=continents&population=900&populations=900&key=asr&sex=0&cancer=39&type=0&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&group_cancer=1&include_nmsc=0&include_nmsc_other=1
10 Lin L, Li Z, Yan L, Liu Y, Yang H, Li H. Global, regional, and national cancer incidence and death for 29 cancer groups in 2019 and trends analysis of the global cancer burden, 1990-2019. J Hematol Oncol 2021;14(01):197
11 Pramesh CS, Badwe RA, Bhoo-Pathy N, et al. Priorities for cancer research in low- and middle-income countries: a global perspective. Nat Med 2022;28(04):649–657
12 Rubagumya F, Hopman WM, Gyawali B, et al. Participation of lower and upper middle–income countries in oncology clinical trials led by high-income countries. JAMA Netw Open 2022;5(08):e2227252
13 Palmer NR, Borno HT, Gregorich SE, Livaudais-Toman J, Kaplan CP. Prostate cancer patients' self-reported participation in research: an examination of racial/ethnic disparities. Cancer Causes Control 2021;32(10):1161–1172