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COMMENTS AND CONTROVERSIES

Hispanic Accrual on Randomized Cancer Clinical Trials: A Call to Arms

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The Hispanic population is the fastest growing demographic group in the United States and is expected to triple from 46.7 million to 132.8 million by 2050.[1] Hispanics suffer from major health disparities, and they have low participation in cancer screening and prevention programs and higher incidence rates for cancers of the cervix, stomach, liver, and gall bladder compared with non-Hispanic whites.[1,2] Despite the compelling impact of cancer on Hispanics as evident from the death of 17,400 Hispanic men and 15,800 Hispanic women as a result of a malignancy in 2012 alone, the data on Hispanic enrollment onto practice-changing cancer clinical trials are negligible.

South Texas is the largest geographic region in Texas, about the size of Pennsylvania, and the population in this region is predominantly of Hispanic ethnicity. Of note, 58% of the population of San Antonio—the largest city in South Texas—is Hispanic, although the upward trend (approaching 90%) of Hispanic population is evident in the region referred to as the Lower Rio Grande Valley, which is adjacent to United States–Mexican border. The South Texas region has an area of 45,926 square miles, and the 2010 census report on demographic distribution indicates that 67% of the region's inhabitants are Hispanic compared with 28% non-Hispanic white in a total population of 4.49 million.[3]

To reduce the health care disparities of Hispanics, the National Cancer Institute–designated Cancer Center for South Texas, the Cancer Therapy and Research Center (CTRC), has a strategic focus on improving the health care in the region by increasing participation of Hispanics in cancer clinical trials. The CTRC catchment area consists of 38 counties, 25 in rural areas and 13 in metropolitan areas of South Texas.

In 2012 alone, CTRC evaluated and treated 3,096 patients (41% were Hispanic and 42% were non-Hispanic whites) with a newly diagnosed cancer. Our accrual efforts in 2012 were successful in enrolling 822 patients onto a wide array of therapeutic clinical trials available at CTRC. Of note, a large percentage (45%) of the 822 patients enrolled onto the clinical trials offered at CTRC were Hispanic. Thus, our remarkable success in enrolling these bona fide minority patients onto clinical trials prompted us to examine the national experience in the United States for enrolling this minority group onto large-scale clinical trials. Our major objective was to assess the adequacy of national efforts to determine the optimal management of cancer in the fastest-growing racial/ethnic group in the United States.

With a view toward comprehending the rates of participation of Hispanic patients in major cancer clinical trials, we analyzed the accrual data of all phase II or phase III cancer clinical trials published in the year of 2012 by exclusively selecting the trials conducted by clinical investigators in the United States. We focused on studies that we deemed were most likely to be standard-of-care changing and were published in one of the following journals: *The New England Journal of Medicine*, *Journal of Clinical Oncology*, *Journal of the National Cancer Institute*, *Lancet*, and *Blood*. From these studies, we sought data on several aspects relevant to total accrual, any reports on the accrual of Hispanics, and the details of accrual of Hispanics. We were able to identify 159 clinical trials that met our specific search criteria to be qualified for detailed review. Categorically, of these 159 clinical trials, 68 were phase II and 91 were phase III studies. Initially, our analysis revealed that only 33 of the total of 159 reports (about 20.75%) presented data regarding accrual of minorities. Further scrutiny revealed that only 13 of these 33 minority accrual reporting studies contained data on the rates of accrual of Hispanics. More precisely, our investigation indicates that merely 8.18% (13 of 159 total trials) provided information on the accrual of Hispanics (Table 1).[4-16] Moreover, it is noteworthy that accrual of Hispanics ranged from the low of one patient (0.5%) enrolled onto a phase II lung cancer trial to a high of 17 patients (26%) accrued in a phase II study of acute lymphoblastic

Table 1. Cancer Clinical Trials With Reports of Minority Accrual in 2012

Reference	Trial Phase	Total Accrual	Hispanic Accrual	
			No.	%
O'Brien et al[4]	II	65	17	26
Levine et al[5]	II	40	10	25
Kindler et al[6]	II	115	6	5.22
Lynch et al[7]	II	204	1	0.5
Tap et al[8]	II	38	6	16
Uldrick et al[9]	II	17	3	17.64
Sosman et al[10]	II	132	2	2
Karlan et al[11]	II	161	5	3.10
Cruciani et al[12]	III	376	5	1.32
Paz-Ares et al[13]	III	772	16	2.07
Scagliotti et al[14]	III	1,090	66	6.05
Levenback et al[15]	III	452	9	2
Socinski et al[16]	III	1,052	16	2
Total		4,154	162	3.9

leukemia. Overall, the Hispanic accrual rate was 3.9%, as estimated from the accrual of 162 Hispanics of a total 4,154 patients reported in 13 trials.

Our observation, which implicates a profoundly lower rate of Hispanic accrual in nationwide cancer clinical trials, is in conformity with a recent review that also describes enrollment of only 2.2% Hispanic patients of 104,337 participants in an array of cancer clinical trials conducted between 2001 and 2010.[17] Given the rapid growth of this ethnic group, one might have expected a significant increase in the accrual rate of Hispanics in clinical trials. In fact, at the CTRC in San Antonio, the accrual rate of this minority group (45%) is significantly higher than that for any trial reported in Table 1. In general, the major challenges of accruing Hispanics in clinical trials are a lack of understanding of the consent forms and poor communication with counseling physicians and research coordinators because of the language barrier and missing recurrent clinic visits because of economic constraints.[18] Keeping these issues in mind, at our Cancer Therapy and Research Center, we have ensured that all consent forms and study brochures are available in Spanish and that bilingual study team members are available for counseling patients. Before approval by the Protocol Review Committee for submission to the Institutional Review Board, the investigator must provide a Minority Accrual Plan (MAP).[19] The MAP requires the investigators to proactively outline their plans for overcoming enrollment barriers and achieving optimal participation by minorities, specifically Hispanics. In fact, the MAPs of individual investigators are monitored semiannually to assess our accrual goals and to monitor minority enrollment. To help investigators, a minority recruitment toolbox was developed that includes media contacts and forms to ensure the widespread dissemination of bilingual information about the study and to reduce, to the extent possible, any accrual barriers that may be unique or specific to Hispanics. A coordinator of minority programs who is bilingual helps each investigator develop and monitor the MAP. Thus, the deliberate actions resulting from standalone performance on the minority accrual at CTRC in San Antonio definitely invokes the necessity for a change in the processes to improve Hispanic recruitment in cancer clinical trials nationwide, particularly in the areas that are heavily populated by this minority group.

We are aware that our analysis has some limitations because we arbitrarily chose data published in a limited set of high-impact journals. Because these are not the only journals that publish major clinical trials, it is possible that other journals that were not included in our review reported results of clinical trials that accrued greater numbers of Hispanics. A second limitation is related to lower rates of cancer because of the younger population of Hispanics in the United States.[20] Enrollment rates on Southwest Oncology Group trials from 1997 to 2000 showed enrollments of self-identified Hispanics to be 4.1% compared with 3.8% in the US population.[21] Nonetheless, with such low rates of accrual for this increasingly important ethnic group, it is not possible to draw conclusions about ethnicity-related treatment efficacy, toxicity, and treatment adherence.

There are lessons to be learned from the crisis of underrepresentation of women in cardiovascular randomized clinical trials (CV RCTs) in the United States before the 1980s.[22] In 1986, the National Institutes of Health (NIH) established a policy for including women in clinical research as a result of their under-representation in CV RCTs. The NIH policy was subsequently enacted into public law when Congress approved the NIH Revitalization Act of 1993. The stated goal of the Act is to "ensure that the trial is designed and carried out in a manner sufficient to provide for valid analysis of whether the variables being studied in the trial affect women or members of minority groups, as the case may be, differently than other patients in the trial."[23] Despite a federal mandate for significant inclusion of women in federally sponsored clinical trials, women remain underrepresented in NIH-supported CV RCTs.[24]

Despite Hispanics being a growing proportion of the US population, most recently reported cancer clinical trials either do not report the proportion of accrued Hispanic patients or they report rates that are far lower than the proportion of this ethnic group in the US population. Steps must be taken at this time to improve the accrual and reporting of Hispanics in clinical trials to be able to best monitor and treat neoplastic disease in this ethnic group.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

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