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Clinical trial enrollment in patients with endocrine neoplasm: Parity achievable, but cancer type-specific

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ABSTRACT

Background: We sought to assess participation of underrepresented minorities with endocrine neoplasms in clinical trials conducted in the National Cancer Institute's (NCI) Intramural Research Program.
Methods: We performed a retrospective analysis of patients enrolled in Endocrine Oncology Branch (EOB) clinical trials, comparing demographics to regional and national demographics. We compared specific endocrine cancer patient data to data from NCI's Surveillance, Epidemiology, and End Results (SEER) program.
Results: Comparing EOB patients to national demographics, we found more white (77% vs 74%, $P < 0.001$) and black patients (14% vs 12%, $P < 0.001$). For thyroid cancer, there were more black (16% vs 7%, $P < 0.0001$) and other minority patients (17% vs 11%, $P < 0.0001$) compared to SEER. For gastroenteropancreatic neuroendocrine tumors (GEPNETs), there were fewer black (6% vs 19%, $P < 0.0001$) and other minority patients (6% vs 8%, $P < 0.0001$).
Conclusion: Enrollment parity of underrepresented minorities into clinical trials is achievable, although possibly cancer type-specific.

Introduction

Many breakthroughs are being made in the diagnosis and treatment of a variety of cancers. Over the last two decades, mortality has declined for many cancer types, such as breast and colorectal cancers.[1,2] Yet, these gains are not equally distributed across all patient populations. Patients from minority populations often experience greater morbidity and mortality than their white counterparts or have fewer gains in these same areas.[3] For example, non-Hispanic black patients have a mortality rate from colorectal cancer that is 40% greater than non-Hispanic white patients and double that of Asian/Pacific Islander patients.[4] Long-term breast cancer mortality is 42% higher in black women as compared to white women. Black men have higher incidence and death rates compared to white men for all tumor sites, with the exception of renal cell carcinoma, despite comprising a smaller proportion of the population.[5]

It has been well-documented in the literature that racial and ethnic minorities and low socioeconomic status are associated with lower rates of participation in clinical investigative studies and trials than expected.[6] This results in clinical study findings that lack generalizability to all patient populations, patients from minority populations and economically disadvantaged backgrounds not having access to potentially beneficial experimental therapies, and lack of access to comprehensive care received as part of treatment protocols. Although proportional representation of black and Hispanic patients in NCI-supported cooperative trials has been described,[7] disparity in outcomes and enrollment into clinical trials still persist.

Barriers to enrollment of racial and ethnic minorities and individuals with low socioeconomic status into clinical trials have been described as: structural, clinical, attitudinal, and demographic and socioeconomic.[8] The design of the Intramural Research Program of the National Cancer Institute (NCI) is such that many of these barriers are not realized. The structure of the Intramural Research Program provides access to any qualified patient, including transportation, regardless of insurance status once they have enrolled into a study. Trials have been designed to be inclusive across patient populations, while maintaining a profile of safety, where many community trials are limited by narrow eligibility

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criteria. Principle investigators of the NCI Intramural Research Program are devoted to the conduct of research, with protected time and resources, which is often not the case with clinical trials conducted in the community. Once enrolled into a clinical trial, patients receive all study related care at no cost, potentially relieving a significant financial burden for those of low socioeconomic status.

The aim of this study is to assess the enrollment of minority patients with endocrine neoplasms in clinical trials conducted in the EOB (Endocrine Oncology Branch), Center for Cancer Research (CCR), NCI Intramural Research Program. The clinical protocols and trials conducted in this environment control for many of the barriers previously identified for minority population participation in clinical trials, thus allowing a unique opportunity to determine if parity can be achieved.

Patients and methods

We performed a retrospective analysis of patients enrolled in clinical trials at the EOB, CCR, NCI. A total of 1,978 patient consent events (1,715 unique patients) were identified for patients who were enrolled in 11 clinical protocols approved by the Office of Human Subject Research at the National Institutes of Health (NIH). There were 162 patients excluded from the analysis due to incomplete demographic data being available. The proportions of patients enrolled in EOB protocols based on self-reported race (American Indian or Alaska Native, Asian, black, multiracial, Native Hawaiian or other Pacific Islander, white, and unknown) were compared to the racial distribution in the United States population[9] (Table 1). Additionally, the demographic data of patients enrolled in the clinical protocols in the NCI Intramural Research Program at-large were compared to national population data to ascertain whether the observed proportions for EOB were specific to the branch. Also, we analyzed the demographics of EOB patients at the regional level. Patients enrolled in EOB protocols were from 30 countries and 49 states in the United States plus the District of Columbia. The most commonly reported home state for patients enrolled in EOB protocols was the state of Maryland (27%). Those patients from Maryland were compared to the overall population of the state. National and regional population demographic data were obtained from the U.S. Census Bureau's 2006–2010 American Community Survey.[9]

We compared disease-specific enrollment demographic data to national population frequency data from the NCI's Surveillance, Epidemiology, and End Results (SEER) database. We analyzed the proportion of EOB patients with thyroid cancer and gastroenteropancreatic neuroendocrine tumors (GEPNETs), two common endocrine cancers with an increasing incidence, to national frequency in the SEER database.[10,11] These disease entities comprise the majority of diagnoses for patients enrolled into EOB protocols. Patients with neoplasms of the adrenal and parathyroid glands were not included due to low enrollment numbers.

Statistical analyses

Statistical analysis was conducted using GraphPad Prism (GraphPad Software, La Jolla, CA, USA). For group comparisons, the chi-square test was used to analyze the difference in categorical variables. For non-parametric variables, Fisher's exact test was used for categorical variables.

Results

Patients enrolled in EOB clinical protocols had higher proportions of white (77% vs 74%, $P < 0.001$), black (14% vs 12%, $P < 0.001$), and Asian patients (6% vs 5%, $P < 0.001$) as compared to the United States population. However, the proportion of patients that self-identified as American Indian/Alaska Native or Native Hawaiian/other Pacific Islander was lower than the United States population rate, 0% vs 1% ($P = 0.0006$) and 0% vs 0% ($P = 0.008$), respectively (Table 1).

In comparison to state demographics (Maryland), there was a smaller percentage of white (51% vs 60%, $P < 0.001$) and patients of other races (including American Indian or Alaska Native, multiracial, and Native Hawaiian or other Pacific Islander) (3% vs 6%, $P < 0.001$) and greater percentages of black (36% vs 29%, $P < 0.001$) and Asian patients (10% vs 5%, $P < 0.001$) that were enrolled in EOB clinical protocols.

Across all protocol types for the NCI Intramural Research Program, there was a larger proportion of white patients compared to the United States population (83% vs 74%, $P < 0.001$), an equal proportion of black patients (12% vs 12%, $P < 0.001$), and a smaller proportion of Asian patients (4% vs 5%, $P < 0.001$) and other races (3% vs 6%, $P < 0.001$) (Table 2).

For patients with thyroid cancer enrolled in EOB clinical protocols as compared to national SEER data, we found the proportion of white patients (66% vs 81%, $P < 0.001$) was lower, and the proportion of black patients (16% vs 7%, $P < 0.001$) and other minority patients (17% vs 11%, $P < 0.001$) was higher (Table 3). In patients with GEPNETs, a higher proportion of patients enrolled were white (88% vs. 73%, $P < 0.001$) and a lower proportion were black (6% vs 19%, $P < 0.001$) and of other races (6% vs 8%, $P < 0.001$) compared to the SEER database (Table 4).

Table 1

Comparison of patient demographic data to the United States population data.

Self-Identified Race/Ethnicity	EOB[a]		United States[a]	
American Indian or Alaska Native, Hispanic or Latino	0	(0%)	431681	(0%)
American Indian or Alaska Native, Not Hispanic or Latino	1	(0%)	2048784	(1%)
Asian, Hispanic or Latino	0	(0%)	163519	(0%)
Asian, Not Hispanic or Latino	96	(6%)	14021974	(5%)
Black or African American, Hispanic or Latino	6	(0%)	856327	(0%)
Black or African American, Not Hispanic or Latino	221	(14%)	37122425	(12%)
Multiracial, Hispanic or Latino	18	(1%)	2002041	(1%)
Multiracial, Not Hispanic or Latino	17	(1%)	5327340	(2%)
Native Hawaiian or Other Pacific Islander, Hispanic or Latino	3	(0%)	32898	(0%)
Native Hawaiian or Other Pacific Islander, Not Hispanic or Latino	1	(0%)	458775	(0%)
White, Hispanic or Latino	77	(5%)	28322928	(9%)
White, Not Hispanic or Latino	1113	(72%)	196572772	(65%)
Some Other Race alone, Hispanic or Latino	0	(0%)	15918139	(5%)
Some other race alone, not Hispanic or Latino	0	(0%)	685669	(0%)

[a] Data from the United States Census Bureau's 2006–2010 American Community Survey, EOB = Endocrine Oncology Branch.

Table 2
Comparison of patients enrolled in EOB and NCI clinical protocols to the United States population data.

Self-Identified Race	EOB	NCI	US
White	1388 (77%)	51696 (83%)	224895700 (74%)
Black	262 (14%)	7226 (12%)	37978752 (12%)
Asian	106 (6%)	2388 (4%)	14185493 (5%)
Other	49 (3%)	1057 (2%)	26905327 (9%)

EOB = Endocrine Oncology Branch.
*Includes American Indian and Alaska Native, Native Hawaiian and Other Pacific Islander, Some other race alone, Two or more races.

Table 4
Comparison of EOB patients with GEPNETs to national frequency data from NCI SEER database.

Self-Identified Race	EOB	SEER
White	213 (88%)	15702 (73%)
Black	15 (6%)	3998 (19%)
Other[a]	14 (6%)	1795 (8%)

EOB = Endocrine Oncology Branch, GEPNET = gastroenteropancreatic neuroendocrine tumor, SEER = Surveillance, Epidemiology, and End Results Database.
[a] Includes Asian, American Indian and Alaska Native, Native Hawaiian and Other Pacific Islander, Some other race alone, Two or more races.

Discussion

In this study, we assessed the enrollment of minority patients in clinical trials in the EOB, CCR, NCI Intramural Research Program, as well as in other clinical protocols of the NCI Intramural Research Program. When looking at the overall demographic data for EOB and NCI, patients were enrolled in proportions that were similar to those of the United States population. This includes all protocol types (treatment, diagnostic, natural history, and genetic studies). However, there were significant differences observed when looking at disease-specific enrollment for thyroid cancer and GEPNETs. This suggests that enrollment may be dependent on factors that are disease-specific.

Despite increasing awareness and efforts to improve the participation of minority populations in clinical studies and trials, these populations remain underrepresented in both prevention and treatment trials.[5] The study findings demonstrate that improved representation of underrepresented minority populations in clinical research is possible in the unique environment of the Intramural Research Program. This parity, however, is not distributed equally among patients and varied by cancer type. We found improved representation of minority patients with thyroid cancer in comparison to patients with GEPNETs, in which these same patients were underrepresented. The reasons for this disparity are likely multifactorial. One significant difference between the two cancers is their manifestations. GEPNETs tend to be more chronic and can have significant symptomatology secondary to carcinoid syndrome or functional tumors, better lending themselves to longitudinal study. Whereas thyroid cancer does not tend to be symptomatic and any symptoms usually resolve after definitive therapy. As such, chronicity of the cancer type may play a role in the differences observed in the rates of patient enrollment.

The management of thyroid cancer is well-established and can be readily performed in the community. It is common enough to where community providers feel confident in providing standard care, with less patients looking to quaternary referral centers or clinical trials for optimal management. On the other hand, patients with GEPNETs often find that community providers are not knowledgeable about their diseases and often seek care at specialty centers. Therefore, it is likely that the referral patterns vary based on the specific cancer type.

Table 3
Comparison of EOB patients with thyroid cancer to the NCI SEER database.

Self-Identified Race	EOB	SEER
White	122 (66%)	60433 (81%)
Black	28 (16%)	5233 (7%)
Other[a]	29 (17%)	8180 (11%)

EOB = Endocrine Oncology Branch, SEER = Surveillance, Epidemiology, and End Results Database.
[a] Includes Asian alone, American Indian and Alaska Native, Native Hawaiian and Other Pacific Islander, Some other race alone, Two or more races.

Patients treated in clinical protocols of the NCI Intramural Research Program are not charged for their medical care and receive financial support such as travel reimbursement for treatment, standard of care management, and experimental medications, such that out-of-pocket expenses are minimal or nil. Economic barriers to care have been well-documented, but such barriers are virtually non-existent for patients enrolled in the NCI Intramural Research Program clinical protocols. Yet, differences for enrollment are still evident, suggesting that we can still expect differences in rates of participation based on cancer type, as we have demonstrated, even when accounting for traditional financial barriers to participation.

The stark difference observed between the two cancer types suggests that there may be issues that we are not recognizing, barriers that we cannot effectively target, or lack of traditionally regarded barriers. Such disparities may be inherent to the nature of the disease itself. As such, it may be better to target specific cancer types with the understanding that differences in enrollment may persist despite our best efforts.

The study conducted is limited by the data used for regional and national comparisons. We chose to use general population data, rather than compare our cohort to the segment of the population with cancer diagnoses, though this was mitigated by including all protocol types in aggregate, which would also include healthy volunteers. This study did not examine patient specific factors, such as motivation for participation in clinical trials and referral patterns, which may contribute to the significant differences observed between cancer types. This study did not look at other confounding factors known to contribute to cancer disparity, such as health literacy and socioeconomic status. Additionally, inconsistent classification of ethnicity between clinical trial enrollment data and United States population demographic data did not allow for comparisons based on ethnicity, limiting the analysis to comparisons by race.

Conclusions

Parity in the enrollment of underrepresented patient populations can be achieved at a research hospital where traditional economic barriers do not exist. Differences may persist based on the patient's cancer type. As such, we recommend targeting specific cancer diagnoses for ensuring parity in clinical study and trial involvement across all races in the population.

Disclosure summary

I certify that neither I nor my co-authors have a conflict of interest as described above that is relevant to the subject matter or materials included in this Work.

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