Recruiting for diversity in immunotherapy trials for breast and gynecologic cancers: moving beyond under-representation

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The evolving treatment for patients with advanced/recurrent breast and gynecologic malignancies increasingly includes targeted and immune modulating agents. This creates an essential need for understanding how racial and ethnic differences are associated with clinical and biological outcomes. Furthermore, even when immunotherapy trials are considered a success, the response rates are typically well below 50%. It is therefore imperative to refine our understanding of the interplay between the host's immune system, cancer biology, and the tumor microenvironment. For example, the higher rates of high risk and microsatellite stable histological subtypes of endometrial cancer in black women[1] may translate into greater benefit from the combination of pembrolizumab and lenvatinib. However, this potential benefit must be weighed against the higher prevalence of cardiovascular disease in this population, that may lead to an increase in the risk of potentially serious adverse events. This illustrates how an accurate assessment of the risk–benefit ratio requires adequate representation of minority populations, especially in registration-enabling clinical trials, to ensure that novel immunotherapies/combinations, are indeed effective and safe for all patients.

To determine the representation of black or African American women in clinical trials using immunologic agents, Grette and colleagues retrospectively reviewed 53 completed clinical trials involving immunotherapy for breast and gynecologic cancers that included 8820 patients.[2] The authors found that minority women are poorly represented in immunotherapy clinical trials for breast and gynecologic cancers. Furthermore, the enrollment of black or African American women in these trials was especially low, accounting for only 5% of participants. The authors' accompanying discussion entails a very thoughtful analysis of the data, while acknowledging its potential shortcomings.[2]

The reasons for the especially low rates of enrollment in clinical trials by minorities, particularly black or African American women, are complex and include, but are not limited to, issues related to socioeconomic status, dependable transportation, health literacy, misinformed understanding about the nature of medical research, and a historical, although understandable, fear of abuse, exploitation, and experimentation.[3 4] So how can we overcome these obstacles to achieve equity and reach more valid clinical and translational conclusions?

First, increasing representation will demand innovative strategies for recruiting patients from under-represented populations.[5] Such strategies include focusing on needs assessments and education, infrastructure. and transportation support, and better alignment between specific clinical trial eligibility criteria and the 'real world' clinical characteristics of the patient populations most likely to receive those treatments when approved.[5 6] Second, we must educate current and future generations of investigators, research staff, and sponsors, on the racial and ethnic makeup of gynecologic cancers and how inequalities in clinical outcomes are intertwined with the disparities seen in clinical trial patient enrollment. Third, we need to incorporate considerations of ethnic and racial composition in the early stages of clinical trial design. This allows time and opportunity for community engagement, and the strategic inclusion of study sites that serve under-represented minorities. Early planning will also allow for the inclusion of prospective translational and disparities research aimed at improving our understanding of potential population-based biological differences in tumor, its environment, and response to investigational therapies. Last, with the growing costs associated with novel drug development, health systems and insurers are likely to mandate further robust confirmation of efficacy within specific populations of patients according to their disease site.

In summary, for clinical investigators, especially those who participate in designing clinical trials, improving enrollment of under-represented

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minorities in immunotherapy and other clinical trials should be an important priority that makes both scientific and ethical, sense.

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