Inclusion of Adolescents and Young Adults in Cancer Clinical Trials

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Objectives: *To discuss recent and current initiatives to increase enrollment of adolescents and young adult (AYA) cancer patients onto National Cancer Institute-funded clinical trials to improve outcomes.*

Data Sources: *Peer-reviewed publications, websites of professional organizations.*

Conclusion: *Despite many challenges facing AYAs, recent studies illustrate that AYA-focused cancer clinical trials can be successfully developed and conducted. Development of the National Cancer Institute National Clinical Trials Network and related AYA-focused initiatives create new opportunities to expand clinical trials that serve AYAs.*

Implications for Nursing Practice: *Nurses can influence AYA outcomes by leveraging their roles as educators and collaborators to increase participation in cancer clinical trials.*

Key Words: *Adolescent and young adult, AYA, cancer, clinical trials*

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Cancer occurring in adolescents and young adults (AYA; defined by the United States National Cancer Institute [NCI] as 15 to 39 years of age),[1] is most often lymphoma, leukemia, central nervous system tumor, melanoma, thyroid cancer, germ cell tumor, or bone or soft tissue sarcoma.[2] However, this age group is also remarkable for its susceptibility to malignancies more commonly seen in younger or older patients, such as neuroblastoma[3] and breast cancer.[4] This spectrum of diseases, spanning as it does the age limits delineating the disciplines of pediatric and medical oncology, as well as age-specific differences in tumor biology observed for some common AYA cancers,[5] poses unique challenges for the treatment and study of cancer and cancer-related issues in this population.

Over a period of nearly 30 years, consistently lower average annual improvement in 5-year survival has been documented for AYAs compared with younger and older age groups.[6] The explanation for these disparities is thought to be multifactorial. In addition to poorer tolerance of intensive therapy,[7] lower levels of treatment adherence,[8] difficult geographical access to optimal therapy,[9] and lack of insurance,[9] the markedly inferior participation of AYAs in clinical oncology trials is suspected to be one of the most important factors contributing to the lower survival improvement.[10,11] Although a causal relationship between low clinical enrollment and poorer survival improvement in AYAs is difficult to prove, their correlation is strong.[11] Further, survival improvements have been demonstrated when AYA patients with common pediatric malignancies are treated through clinical trials or regimens based on recent clinical trials.[12-16] In addition to improving population-level survival over time, other probable benefits of consistent enrollment of AYAs into therapeutic clinical oncology trials include having access to novel therapies, accessioning tumor and host biospecimens, and gaining access to studies of supportive care, quality of life, and other non-survival endpoints. The importance of large-scale clinical trials as a mechanism for advancing cancer treatment has recently been affirmed.[17]

For all these reasons, improving accrual of AYA cancer patients into clinical trials has emerged as a priority within the NCI-sponsored clinical trials enterprise.[18,19] The purpose of this article is to describe new mechanisms, recent initiatives, and continuing challenges in an effort to increase participation in NCI-funded clinical trials and improve outcomes for AYAs with cancer. Table 1 provides a list of acronyms used in this article.

The AYA Population in Cooperative Group Trials: Historical Perspective

The Children's Oncology Group (COG) is the world's largest pediatric cancer consortium and was formed in 2000 through merging four separate, smaller cooperative groups (Pediatric Oncology Group, Children's Cancer Group, National Wilms Tumor Study Group, and Intergroup Rhabdomyosarcoma Study Group). As many as 90% of the approximately 13,500 children and adolescents newly diagnosed with cancer in the United States each year are treated at COG member institutions.[11,20] It is estimated that up to 70% of newly diagnosed children with cancer are enrolled onto clinical trials when available.[21] Over the past 50 years, the successful conduct of sequential studies by the COG and its legacy groups, made possible in part by this consistently high level of enrollment, is considered the most important factor in achieving the current combined survival of over 80% for childhood cancer.[20]

However, differences in enrollment exist by age. In a population-based study of data from the Surveillance, Epidemiology, and End Results (SEER) Program and COG over the time interval 1992 to 1997, registration of newly diagnosed patients with COG was highest for children <5 years of age, between 5 and 9 years, and between 10 and 14 years (74%, 73%, and 63%, respectively).[21] In contrast, registration was only 24% for patients 15 to 19 years of age. In a more recent analysis of patients diagnosed with cancer in the United States from 1997 to 2003, enrollment onto clinical trials was estimated to have occurred for only 10% to 15% and <2% for patients 15 to 19 and 20 to 30 years of age, respectively.[11] To understand these differences and develop corrective strategies, it is important to consider contributing factors.

Clinical trial design is largely dependent on the sponsoring cooperative oncology group. Protocols developed through the COG and its legacy groups historically restricted age eligibility to ≤21 years of age. More recent COG protocols have increased the upper age limit to 30, 40, or even 50 years in an