# The Globalization of Cooperative Groups

Manuel Valdivieso,[a] Benjamin W. Corn,[b] Janet E. Dancey,[c] D. Lawrence Wickerham,[d] L. Elise Horvath,[e] Edith A. Perez,[f] Alison Urton,[g] Walter M. Cronin,[h] Erica Field,[i] Evonne Lackey,[j] and Charles D. Blanke[k]

The National Cancer Institute (NCI)-supported adult cooperative oncology research groups (now officially Network groups) have a longstanding history of participating in international collaborations throughout the world. Most frequently, the US-based cooperative groups work reciprocally with the Canadian national adult cancer clinical trial group, NCIC CTG (previously the National Cancer Institute of Canada Clinical Trials Group). Thus, Canada is the largest contributor to cooperative groups based in the United States, and vice versa. Although international collaborations have many benefits, they are most frequently utilized to enhance patient accrual to large phase III trials originating in the United States or Canada. Within the cooperative group setting, adequate attention has not been given to the study of cancers that are unique to countries outside the United States and Canada, such as those frequently associated with infections in Latin America, Asia, and Africa. Global collaborations are limited by a number of barriers, some of which are unique to the countries involved, while others are related to financial support and to US policies that restrict drug distribution outside the United States. This article serves to detail the cooperative group experience in international research and describe how international collaboration in cancer clinical trials is a promising and important area that requires greater consideration in the future.
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Cancer is one of the most common worldwide causes of morbidity and mortality. It is estimated that in 2012, there were 14.1 million adults diagnosed with cancer and 8.2 million deaths attributable to this disease. It is also estimated that the number of cancer cases will increase from 14.1 million in 2012 to 22 million in the next two decades.[1] The most common cancers in adults are breast, prostate, lung and gastric cancers. From the standpoint of mortality, lung and gastric cancers are, respectively, the first and second most common causes of cancer death in the world.[2] Globally, more

[a]Division of Hematology/Oncology, University of Michigan; and SWOG, Executive Officer, Quality Assurance and International Initiatives, Ann Arbor, MI.
[b]Institute of Radiotherapy, Tel Aviv Medical Center, Tel Aviv, Israel; and Department of Radiation Oncology, Jefferson Medical College, Philadelphia, PA.
[c]Director, NCIC Clinical Trials Group; Scientific Director Canadian Cancer Clinical Trials Network; Program Leader, High Impact Clinical Trials, Ontario Institute for Cancer Research; Professor of Oncology, Queen's University, Kingston, Ontario, Canada.
[d]Deputy Chairman, NRG Oncology, Pittsburgh, PA; Department of Human Oncology, Pittsburgh Campus, Drexel University School of Medicine; Allegheny Cancer Center at Allegheny General Hospital, Pittsburgh, PA.
[e]Executive Officer, Alliance for Clinical Trials in Oncology, Chicago, IL.
[f]Deputy Director at Large, Mayo Clinic Cancer Center; Group Vice Chair, Alliance for Clinical Trials in Oncology; Hematology/Oncology and Cancer Biology Mayo Clinic, Jacksonville, FL.
[g]Group Administrator, NCIC Clinical Trials Group, Queen's University, Kingston, Ontario, Canada.
[h]Associate Director, NRG Oncology Statistics and Data Management Center (SDMC); Associate Director, Biostatistics, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA.
[i]Project Specialist III, RTOG, Philadelphia, PA.
[j]Coordinating Center Manager, SWOG Statistical Center, Seattle, WA.
[k]Chair, SWOG; Department of Medicine, Division of Hematology and Medical Oncology, Oregon Health & Science University and Knight Cancer Institute, Portland, OR.
From the Alliance for Clinical Trials in Oncology, NCIC CTG, NRG Oncology, RTOG and SWOG adult NCTN research groups.
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Address correspondence to: Manuel Valdivieso, MD, MS, CPE, University of Michigan Comprehensive Cancer Center, Division of Hematology/Oncology, C335 Med Inn Bldg, 1500 E Medical Dr, SPC 5848, Ann Arbor, MI 48109. E-mail: manuelva@med.umich.edu
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than 60% of the total number of new cases diagnosed annually occur in Africa, Asia, and Central and South America. These regions account for 70% of the world's cancer deaths.[1] This is particularly important to the United States and other developed countries because of immigration from these regions and its subsequent effect on the makeup of their populations. For example, Hispanics are the largest minority in the United States, comprising 16.3% of the total population in 2010, and having grown by 43% since 2000. At this rate, it is estimated that by 2050, one of every four Americans will be Hispanic.[3] It is not fully known what the impacts of immigration will be on cancer epidemiology in the United States, but it behooves the US medical community to be prepared for change.

Cancer-related risk factors also vary geographically. Tobacco use is the most important cancer risk factor responsible for 20% of global cancer deaths and approximately 70% of global lung cancer deaths. Infections represent a risk factor that starkly differs among regions, and they are related to 8% of cancers in developed nations and up to 23% in countries under development. Cancer-causing viral infections such as hepatitis B and C viruses (HBV/HCV) and human papilloma virus (HPV) are responsible for up to 20% of cancer deaths in low- and middle-income countries.[2] Cervical cancer, a consequence of HPV along with lack of access to appropriate screening, is a leading cause of death in low-income countries.

With the increasing improvements in our understanding of the molecular biology of cancer and the subsequent development of improved methods of cancer prevention, detection, and therapy, there is increasing interest in applying these methods to improve cancer control throughout the world. In the United States, these efforts are led by the National Cancer Institute (NCI) through its Center of Global Health and other institutes at the National Institute of Health (NIH). Trimble et al have described these efforts and those of other centers around the world, efforts that have led to improved standardization of cancer staging, increased awareness of the importance of securing patient's informed consent, better understanding of developing, applying, monitoring, and publishing cancer clinical trials, as well as the limitations of applying these efforts due to economics, politics, regulatory, tissue procurement and distribution, drug distribution, and other issues.[4] Additionally, and in response to the increasing interest of US Cooperative Groups in international trials participation, the NCI-Cancer Therapy Evaluation Program (CTEP) is working collaboratively with both the Food and Drug Administration (FDA) and with the Office for Human Research Protections (OHRP) on the clarification of regulatory and logistical aspects regarding the entire clinical trials process, including design, implementation, monitoring, analysis and publication of trial results that include NCI-sponsored Cancer Cooperative Groups (http://ctep.cancer.gov/branches/ctmb/clinicalTrials/docs/nci_clin_intl_guidelines.pdf).

As an extension of the interest of the US Government to improve the infrastructure of Europe after the Second World War, resources were provided for the establishment of the European Organization for Research and Treatment of Cancer (EORTC) in 1962. Subsequently, funding assistance was provided to the former National Cancer Institute of Canada Clinical Trials Group (now known as "NCIC Clinical Trials Group" or NCIC CTG) in 1997. All involved countries have significantly now contributed to the sustainability of these efforts.

The NCI-sponsored US Network groups have extended their trial network to include many countries around the world. These efforts have been primarily focused on Canada, where a strong clinical research partnership has been developed with the NCI CTG. Other efforts principally involve Europe and Australia and, to a lesser extent, Asia and Latin America. This article provides an overview of international collaborations coordinated by the NCI-sponsored adult cooperative oncology research groups.

## SEEKING INFORMATION ON GLOBALIZATION FROM ADULT COOPERATIVE GROUPS

The leadership of the National Clinical Trials Network (NCTN) was invited to participate in this review and asked to provide their experience on international collaborations, including information on countries, sites, investigators, and clinical trials and associated publications.

This article includes summary tables of the groups' involvement in international collaborations, although data on patient accrual and publications are available for only those groups providing this information. Overall activity is summarized in Table 1.

## NCIC CTG EXPERIENCE

### Overview and the NCIC CTG Perspective

Established in 1980, the NCIC CTG has 273 phase III ongoing or completed studies, as well as 197 Investigational New Drug trials, enrolling a total of over 75,000 patients. NCIC CTG has collaborated with sites in 41 countries, across 54 trials, with 26,189 patients accrued. It is important to note the significance of the partnership with US cooperative groups and sites that contributed 18,624 of the 26,189 patients accrued through