CLINICAL INVESTIGATION

The Big Ten Cancer Research Consortium: teaming up to fight cancer

The Institute of Medicine report in 2010 highlighted the need for changes in the framework for clinical cancer research in USA. The newly formed Big Ten Cancer Research Consortium was developed with attention to the challenges of clinical trial development, with special focus on collaborative science, the approval process and efficiencies in development and completion of clinical trials. The consortium provides for the development of team research with established leaders from academic institutions with an additional emphasis on mentoring junior investigators within and across institutions.

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Background

Significant changes have occurred to the framework of clinical cancer research in USA since the initial report in 2010 by the Institute of Medicine and subsequent Operational Efficiency Working Groups [1–3]. These changes have reinvigorated the publicly funded clinical trial system with the restructuring and consolidation of the cooperative system. The creation of the National Clinical Trials Network, which consolidated the 11 cooperative groups to 5 network operation groups, has the goal to enhance the science of clinical trials while decreasing the time required for their development [4]. While greater collaboration should be achieved with this consolidation, a potential challenge may be diminished opportunities for junior investigators to participate in and lead national clinical trials.

Given the longstanding relationships in both athletics and science, through the Committee on Institutional Cooperation, synergy exists among the member universities of the Big Ten athletic conference. Additionally, the cancer centers at these institutions are historically charged with mentoring and developing young investigators. Therefore, the Big Ten cancer centers have united to conduct cancer research through collaborative translational oncology trials that leverage the scientific and clinical expertise of the Big Ten universities. Launched during the American Society of Clinical Oncology annual meeting in 2013, the Big Ten Cancer Research Consortium (BTCRC) allows the development of team research with established leaders from academic institutions collaborating with and mentoring junior investigators within and across institutions. Given the inherent scientific strengths of these institutions, this collaborative effort can leverage the expertise and science of multiple centers. Additionally, drawing from a large patient population at these institutions, trial accrual will be completed with more efficiency. The purpose of this article is to describe the structure, administrative support, progress to date and future direction of the BTCRC.

Structure

The clinical trials of the consortium are translational, Phase II or earlier, with a focus on a precision medicine or genomic-based approach. Additionally, each trial must include a senior and a junior faculty member, preferably from different institutions, as the leaders of these multi-institutional trials. To accomplish these goals, the structure of the BTCRC (Figure 1) was designed to allow the coordination and cooperation of multiple participants. The functions and respon-

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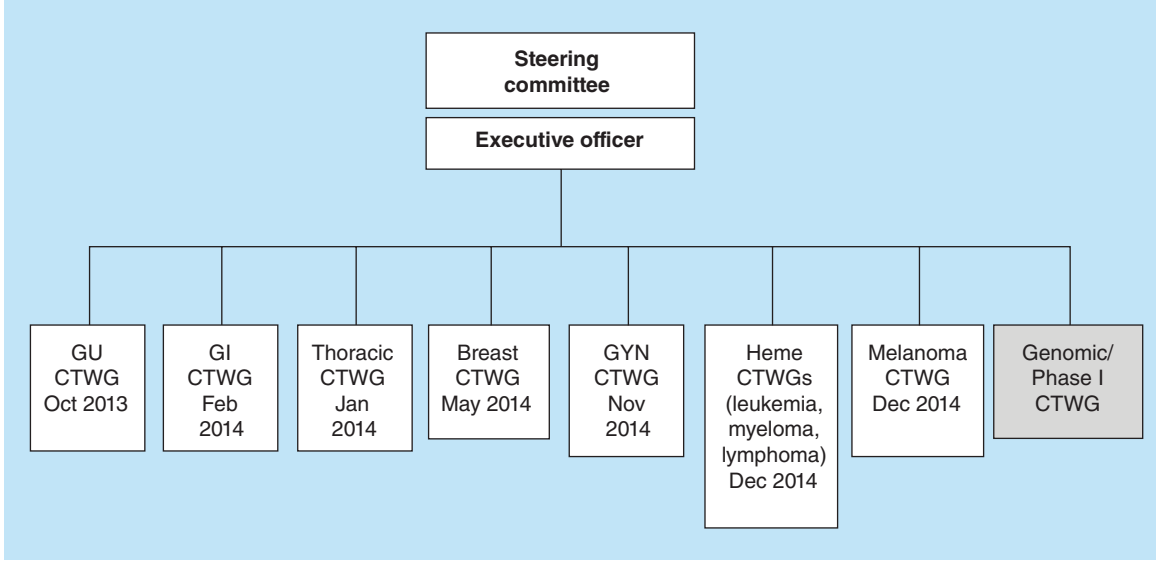

Figure 1: Structure of the Big Ten Cancer Research Consortium. The dates indicate the formation of the CTWG and the gray box represents a CTWG to be formed in the next 6 months.
CTWG: Clinical Trial Working Group; GI: Gastrointestinal; GU: Genitourinary; GYN: Gynecologic; HEME: Hematologic.

sibilities of each of the structural components of the BTCRC are outlined below.

Steering committee

The Steering Committee is responsible for defining and overseeing the strategic plan of the consortium, the oversight of the activities of the BTCRC and making decisions on matters of policy. The committee is composed of representatives from each member institution (Box 1). The cancer center director of each member institution appointments its representative to the Steering Committee. They meet by teleconference on a monthly basis to primarily review the activities of the BTCRC. A component of strategic planning includes the development of new Clinical Trial Working Groups (CTWGs) for the BTCRC, which must be approved by the Steering Committee.

Executive officer

The executive officer of the BTCRC is responsible for overseeing the daily activities of the consortium. This includes working with consortium staff regarding communications with consortium members, cancer center directors, CTWGs and study sponsors. Additionally, the executive officer has the authority to speak on behalf of the consortium and with the assistance of consortium staff, to negotiate and review budgets, contracts, site agreements and institutional review board processes. The executive officer is a faculty member from a member institution and is appointed by the cancer center directors to a 3-year term.

Clinical trial working groups

CTWGs are responsible for the design, development, prioritization and approval of research protocols to be conducted by the BTCRC. Member institution leaders, junior faculty and basic science researchers are included in the CTWG membership. Optimally, CTWGs have a basic science member to provide direct input regarding correlatives and translational science possibilities for proposed concepts. Members of CTWGs also are able to leverage additional cores, resources and expertise from their respective centers. Each CTWG is led by two co-chairs who facilitate the meeting agenda and approval of concepts. Co-chairs are appointed by the Steering Committee and serve a 2-year term. Similar to the Steering Committee, the CTWGs meet by teleconference monthly or sooner if a concept has been submitted. In addition to the monthly teleconferences, each CTWG has a live meeting at least annually at a national disease specific meeting or at the American Society of Clinical Oncology annual meeting.

The current CTWGs of the consortium are shown in Figure 1, with their corresponding date of initiation. Critical to the development process of clinical trials are the steps and approvals required [5,6]. To minimize the number of steps required to approve a letter of intent (LOI) or concept and ultimately a full clinical trial within the consortium, approval is only required by the CTWG. Once a CTWG approves an LOI, trial development and budget negotiations with sponsors are initiated. Additionally, when an investigator submits an LOI to the consortium, it is immediately disseminated to the CTWG members and a teleconference is sched-

Box 1. Member Institutions of the Big Ten Cancer Research Consortium.

- University of Illinois Cancer Center
- Indiana University Melvin and Bren Simon Cancer Center
- University of Iowa Holden Comprehensive Cancer Center
- University of Michigan Comprehensive Cancer Center
- Michigan State University Breslin Cancer Center
- Masonic Cancer Center, University of Minnesota
- Fred & Pamela Buffett Cancer Center (University of Nebraska)
- Robert H Lurie Comprehensive Cancer Center of Northwestern University
- Penn State Hershey Cancer Institute
- Purdue University Center for Cancer Research
- Rutgers Cancer Institute of New Jersey
- University of Wisconsin Carbone Cancer Center

uled if it is longer than 2 weeks before the next scheduled meeting. Each of these processes, along with support of an administrative group, are meant to enhance the efficiency in the process of developing, activating, opening and accruing to consortium clinical trials.

Administrative support & processes

The Institute of Medicine report outlined the need for collaboration around clinical trials [1]. Collaboration includes support of the functions to facilitate the development of trials, specifically to improve the time from an idea of a concept to the institutional review board (IRB) submission of a full protocol [5,6]. This also includes the need for standard licensing language, contracting, management of intellectual property issues and IND management. To facilitate these activities, the consortium has an administrative headquarters that coordinates the work of the CTWGs and brings expertise to the development and conduct of multicenter trials.

Upon approval of an LOI by a CTWG, a feasibility survey is distributed to all institutions to determine the accrual capabilities within the consortium. In parallel, the research development director for the consortium begins the development of the clinical trial with the senior and junior investigator. This is facilitated by the use of an approved BTCRC protocol template and consent. Additionally, investigational new drug (IND) submission and management occurs through the administrative headquarters of the BTCRC. All BTCRC trials are required to have a correlative component. Accordingly, the manager of the biospecimen repository at the consortium administrative headquarters develops a procedure manual for specimen collection as a part of the protocol. Each of these administrative support functions is designed to enhance the efficiency in the protocol development process.

The administrative headquarters of the BTCRC also centrally manage budget development, negotiation and contracting with sponsors. Multicenter study budgets can be complex, with study initiation and IRB fees, per-patient costs and nonstandard of care costs. Utilizing a central administrative group with experience working with each of the member institutions results in rapid development of budgets and approval by sponsors. Similarly, central contracting is utilized to speed the approval and opening of a clinical trial. To facilitate the contracting process for these multicenter studies, all member institutions have signed an agreement for participating in BTCRC trials. For each clinical trial, contracting with a sponsor involves a three-way contract with a scope of work agreement with the BTCRC and the principal investigators institution. Once approved, the administrative headquarters of the BTCRC execute a work order with each participating site and no additional contracting is necessary.

Progress

Since its launch in 2013, the consortium has seen significant activity. Nine CTWGs are established and we will be launching our Genomics/. I CTWG by the end of 2015. Every member institution is represented on each of the CTWGs and each institution has submitted at least one concept through a CTWG. The BTCRC activated its first clinical trial in March 2015, NCT02348008, a Phase Ib/II trial in renal cell carcinoma. The time from LOI approval to protocol approval was 138 days. Two additional trials will launch by the fourth quarter of 2015 and there are 20 concepts in development.

The clinical trials and concepts thus far have involved engagement with industry. Recognizing the opportunities for the translation of science from the member institution cancer centers, funding of trials without industry support is imperative. In May of 2015, the BTCRC Foundation was formed as a nonprofit 501c3 to raise funds to support translational trials, banking of specimens and basic science research.

Future perspective

Significant progress has been made by the consortium in the last 2 years to establish the processes and procedures for the BTCRC. The launch of the BTCRC's first trial reinforced the procedures established for central contracting and budgeting, but highlighted the need for efficiency in the IRB process. The consortium is working toward a reliance review mechanism for IRB approval within the BTCRC. Under this mechanism, the principal investigators institution will be the IRB of record for the BTCRC and all participating sites will cede IRB approval to this site. The consortium is currently working with the IRBs from our member institutions to create policy and procedures around this process with the goal to have the reliance review process in place by the end of 2015.

Currently, BTCRC's the clinical trial portfolio is focused on interventional therapeutic clinical trials. Targeted therapy and precision medicine are of great interest to patients and researchers and the consortium is currently forming its genomics/. Phase I group to conduct trials with integrated and/or integral genomic biomarkers. Recognizing the strengths of population science within the BTCRC member institutions, discussions are underway to form a CTWG for population studies. Similarly, with cancer survivors numbering more than 13 million, the consortium will be developing trials in this population. Finally, quality of life components will be assessed in the majority of clinical trials.

The BTCRC was formed out of the opportunity to build on the strong scientific achievements of the Big Ten universities and the need to provide opportunities to junior investigators to lead multicenter national trials. In its first 2 years, the consortium has established the infrastructure and procedures to facilitate the development of translational clinical trials. The future is focused on expanding the types of trials and enhancing the processes to expedite the development and accrual to high-priority clinical trials.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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