Multicenter Trials

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Why do multicenter trials?

Pros:

- Faster accruals
- More robust results
- Less biased populations
- Leveraged expertise
  - Clinical expertise
  - Scientific expertise
- Builds collaborative relationships

Cons

- Significant regulatory responsibility
  - Preservation of safety across sites
    - IRB
    - PI and staff training
    - Drug supply
  - Data collection and protection
  - Site monitoring and auditing
  - Increased variability and risk out of your control

Most clinical trials, from phase I to III, are now multicenter studies

Multicenter – Choose your model

Academic

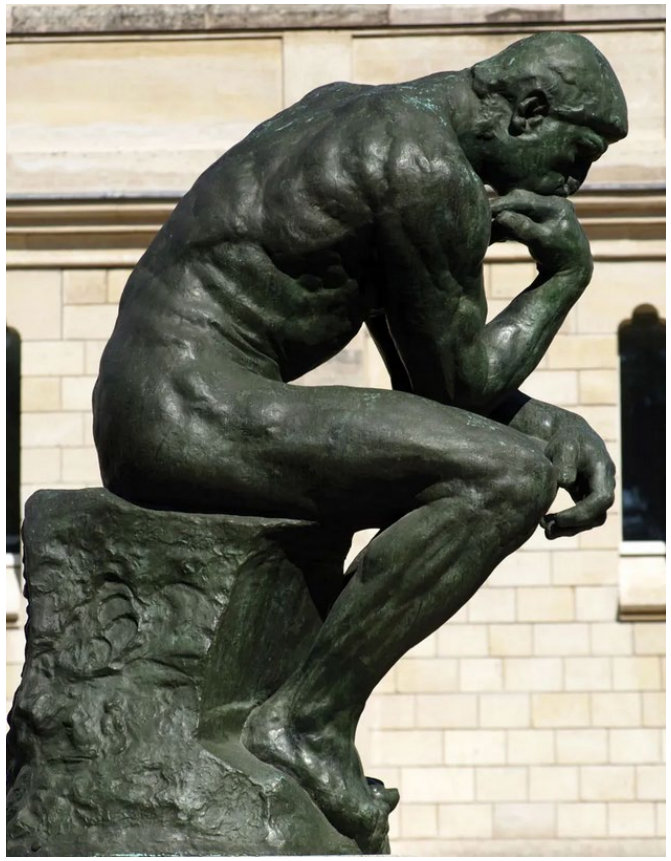
NCI

Industry

Consortium

pcdtc The Prostate Cancer Clinical Trials Consortium

PI perspective of choosing a multicenter trial model:



Who's trial is it, anyway?

Who will do all of the work?

- Answer investigator phone calls about the protocol
    - Eligibility
    - Management questions
- Sign off on all SAE's that occur
- Circulate safety information
- Ensure training of study staff
- Oversee all centers' drug dispensation and pharmacy
- Meet regulatory requirements and perform filings

Who will pay for the study?

Who will pay for the science?

Who will receive credit for the trial?

Industry

- Does trials that benefit industry
- Distinguish between big pharma and small biotech – these are different experiences
- Small biotech has major advantages
  - Small group of leaders
  - Rapid decision-making
  - True close collaborations with academia
  - You can be involved with drug development every step of the way, from soup to nuts
  - Expect major changes in structure and ownership
  - Example:

ENDOCYTE

PSMA ADC

ABX

PSMA Radioligand

Advanced Accelerator Applications

NOVARTIS

Pluvicto

Big Pharma

- Ample resources for virtually all aspects of trial design and execution
- Able to perform large international trials with intent of regulatory registration
- Complex and opaque decision-making structures
- Limited influence by the investigator on design
- Can be limited expertise and disease-knowledge (depending on the company and disease)

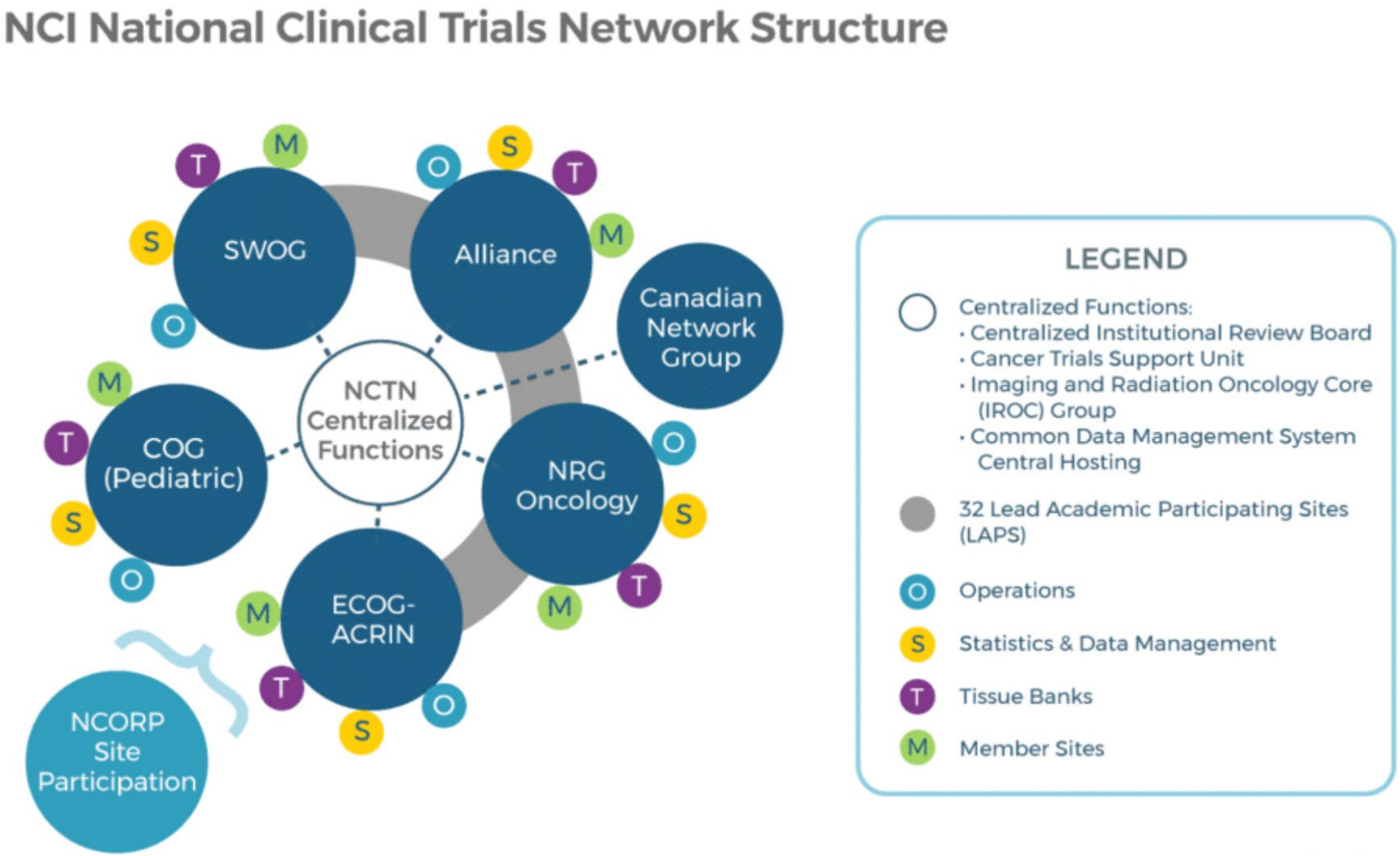
IIT vs. Industry Sponsored

- Industry sponsored:
  - Amply resourced
  - Trial is generally paid for, soup-to-nuts
  - Trial is written by the company
  - Back-end activities such as amendments, safety reporting, and others regulatory issues are the company's responsibility
  - Site communication is done by the company
  - It is THEIR study

IIT:

- Company resources may be variable
  - Some are drug only
  - Some are drug and the study itself
- You write the trial
- You are responsible for the regulatory issues
  - Includes site communication, monitoring, data protection, etc.
- Quite possible you will hold the IND
- It is YOUR study

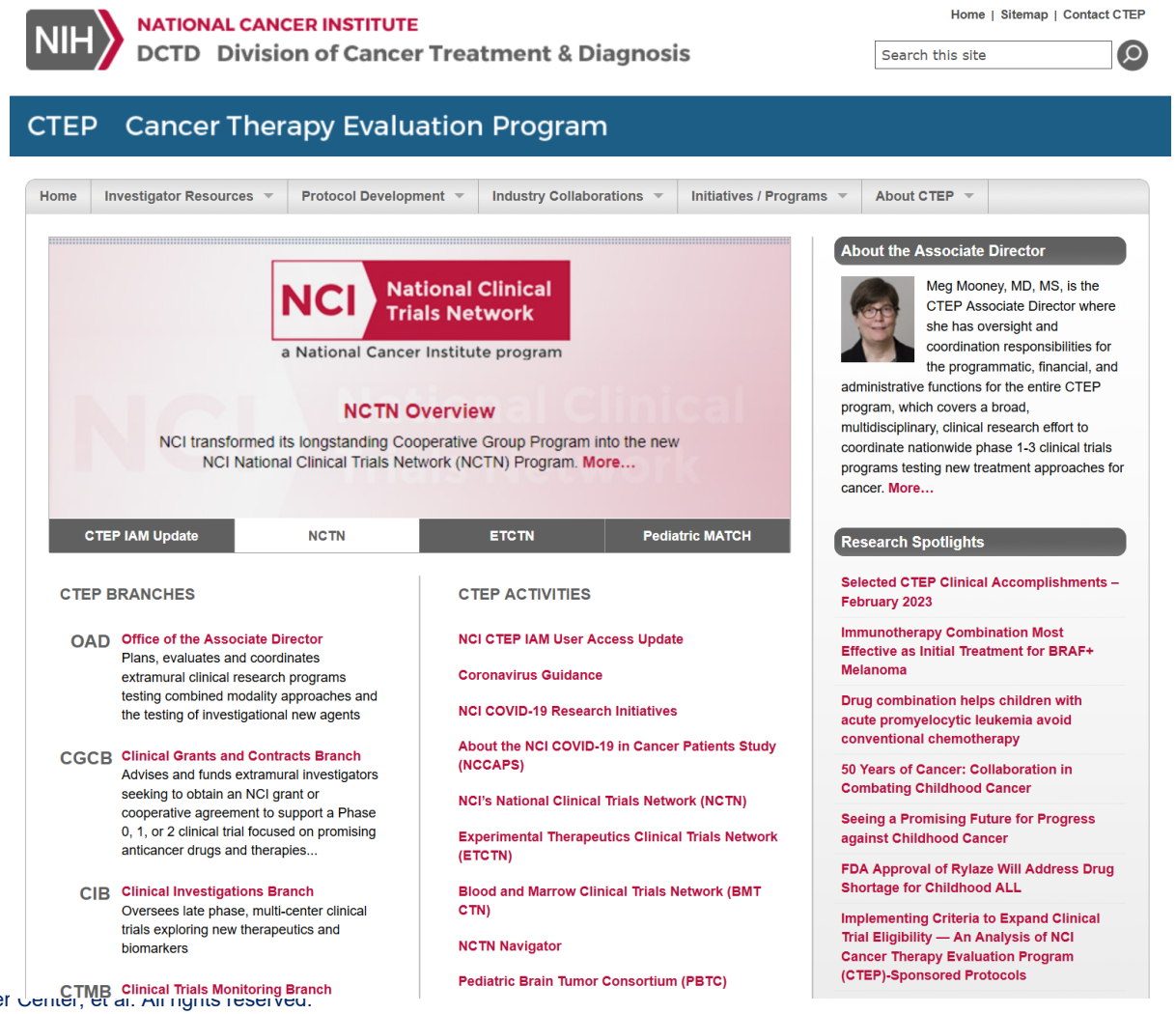
NCI: NCTN (the Cooperative Groups)



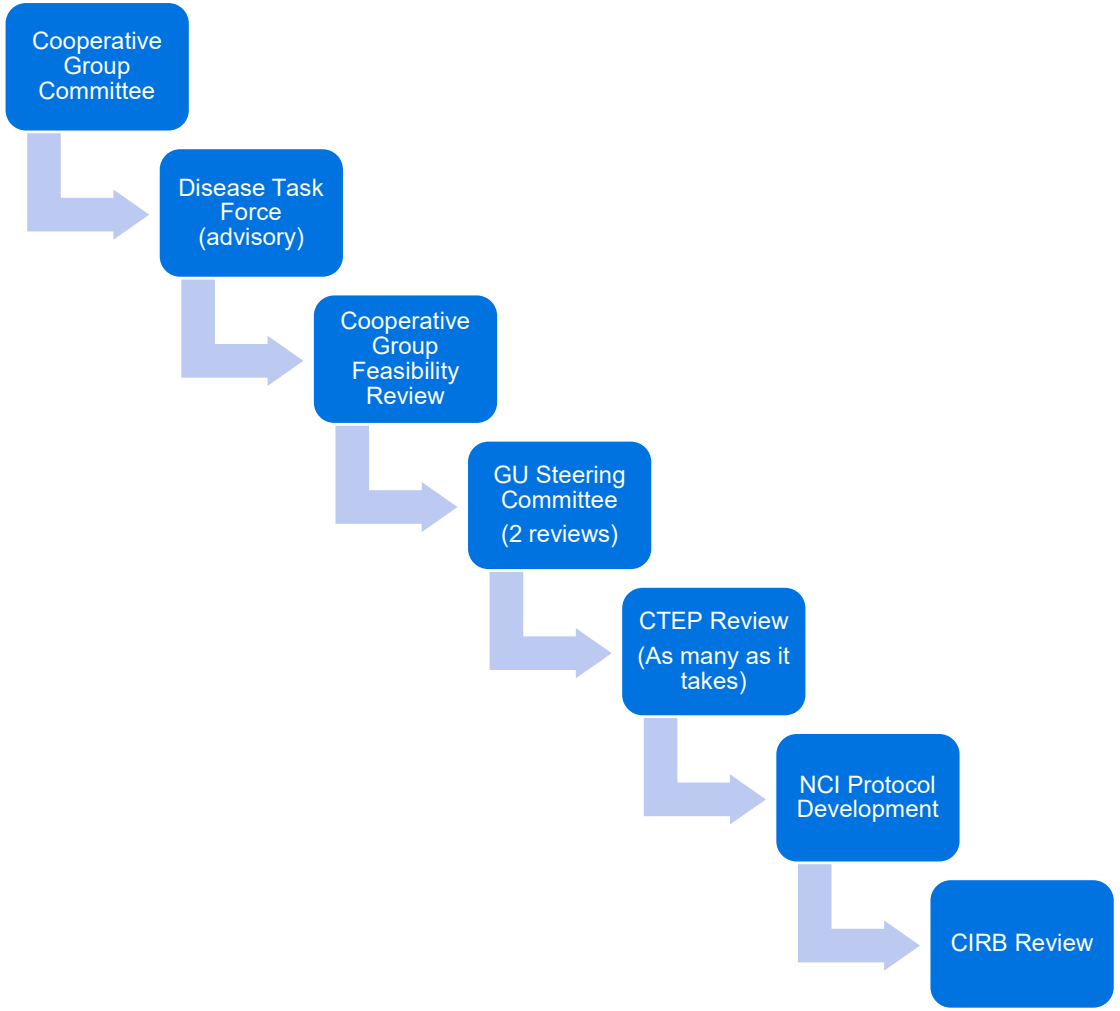
NCI sponsored studies

- Great opportunities for junior faculty to run large and practice-changing studies
- Great opportunities for collaboration
- Great opportunities for mentorship
- CTEP is the sponsor
- Cooperative Groups provide the administrative support
- Cooperative Groups provide editorial and statistical support
- NCI provides biospecimen storage
- NCI provides image storage
- Financial support to the institutions is less than industry sponsored studies
- The trial is run by the PI with administrative support from the Cooperative Group
- Significantly higher burden managing problems than with industry sponsored studies

CTEP will evaluate, support, and sponsor the trial. It will generally hold the IND.



Typical Review Process for GU Protocols in NCTN



General principles of review committees – academic and otherwise:

- Diverse levels of expertise and maturity
- Potentially conflicted
- The concept is the best one that you can get through
- Non-scientific issues may interfere with scientific review

Our History

The PCCTC was initiated in 2005 by the Prostate Cancer Foundation (PCF) and the U.S. Department of Defense (DOD) Prostate Cancer Research Program (PCRP) to address critically unmet needs in prostate cancer.

CDMRP
DEPARTMENT OF DEFENSE
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

PROSTATE CANCER FOUNDATION
PCF
CURING TOGETHER

pcctc
The Prostate Cancer Clinical Trials Consortium

Established as an independent entity in 2014, the PCCTC, LLC is now the nation's premier multicenter clinical research organization specializing in cutting-edge prostate cancer research.

Integrated Research Organization

Memorial Sloan Kettering Cancer Center
DF/HCC Dana-Farber/Harvard Cancer Center
Duke Cancer Institute
Johns Hopkins Medicine
Knight Cancer Institute, Oregon Health & Science University
UCSF Helen Diller Family Comprehensive Cancer Center
University of Washington
Carbone Cancer Center, University of Wisconsin School of Medicine and Public Health
Barbara Ann Karmanos Cancer Center
Weill Cornell Medical College
Columbia University Medical Center
MD Anderson Cancer Center
University of Michigan Comprehensive Cancer Center
The University of Chicago Medicine Comprehensive Cancer Center
Rutgers Cancer Institute of New Jersey
UCLA Jonsson Comprehensive Cancer Center
Sidney Kimmel Cancer Center at Thomas Jefferson University, NCI-designated
Masonic Cancer Center, University of Minnesota, Comprehensive Cancer Center designated by the National Cancer Institute
Mayo Clinic
UC San Diego Moores Cancer Center

Consortium

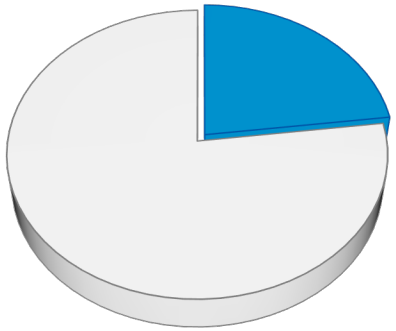
- PROJECT MANAGEMENT
- REGULATORY SERVICES
- QUALITY ASSURANCE
- CONTRACTS & BUDGETS
- CLINICAL DATA MANAGEMENT
- DATA SCIENCE & STATISTICAL ANALYSIS
- CORRELATIVE SCIENCE & LABORATORY SERVICES
- ADVISORY BOARDS
- MEDICAL COMMUNICATIONS & WRITING

CRO

A Global Network of Over 210 Participating Clinical Research Sites

Site Network

The PCCTC's Comprehensive Suite of Services and World-Class Scientific Expertise Streamlines and Accelerates the Activation, Accrual, and Completion of Multicenter Clinical Trials

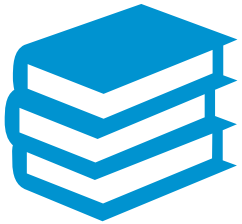


PCCTC investigator-led industry and IIT trials represent >22% of active early-phase prostate cancer clinical trials in the US.

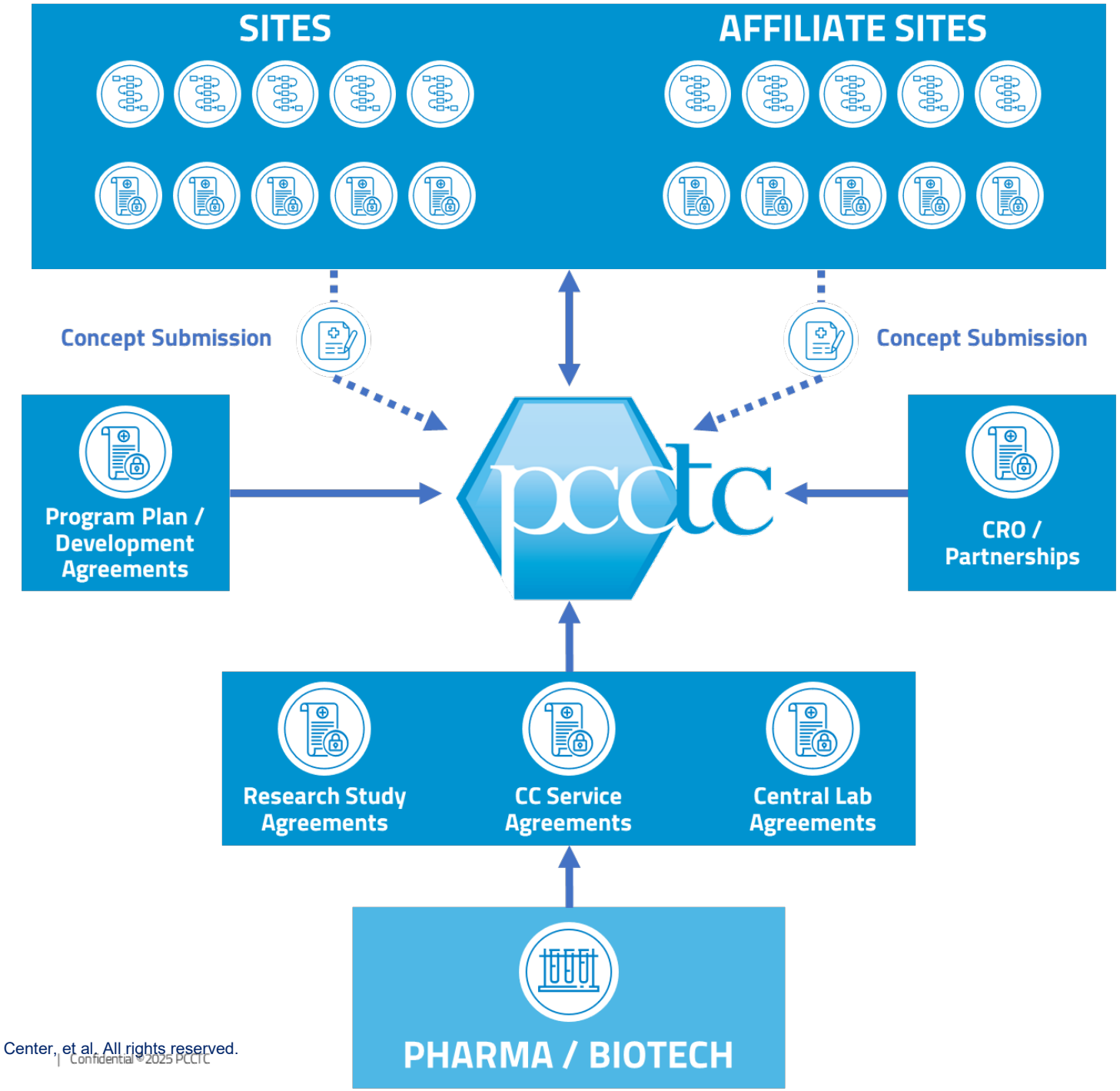
Over 16,500 participants have been enrolled onto 308 PCCTC studies.

FDA

The PCCTC has contributed to the advancement of 39 therapeutic candidates to phase 3 study, 12 of which are fully approved by the FDA.



PCCTC research has resulted in the publication of 523 abstracts and 191 academic papers.



CRO Business Model Evolving Top → Bottom to Bottom → Top

The Expanding Reach of the PCCTC

The PCCTC has a central role in the execution of translational treatment science, drug and biomarker development, and patient advocacy.

PCCTC Clinical Research Sites

US

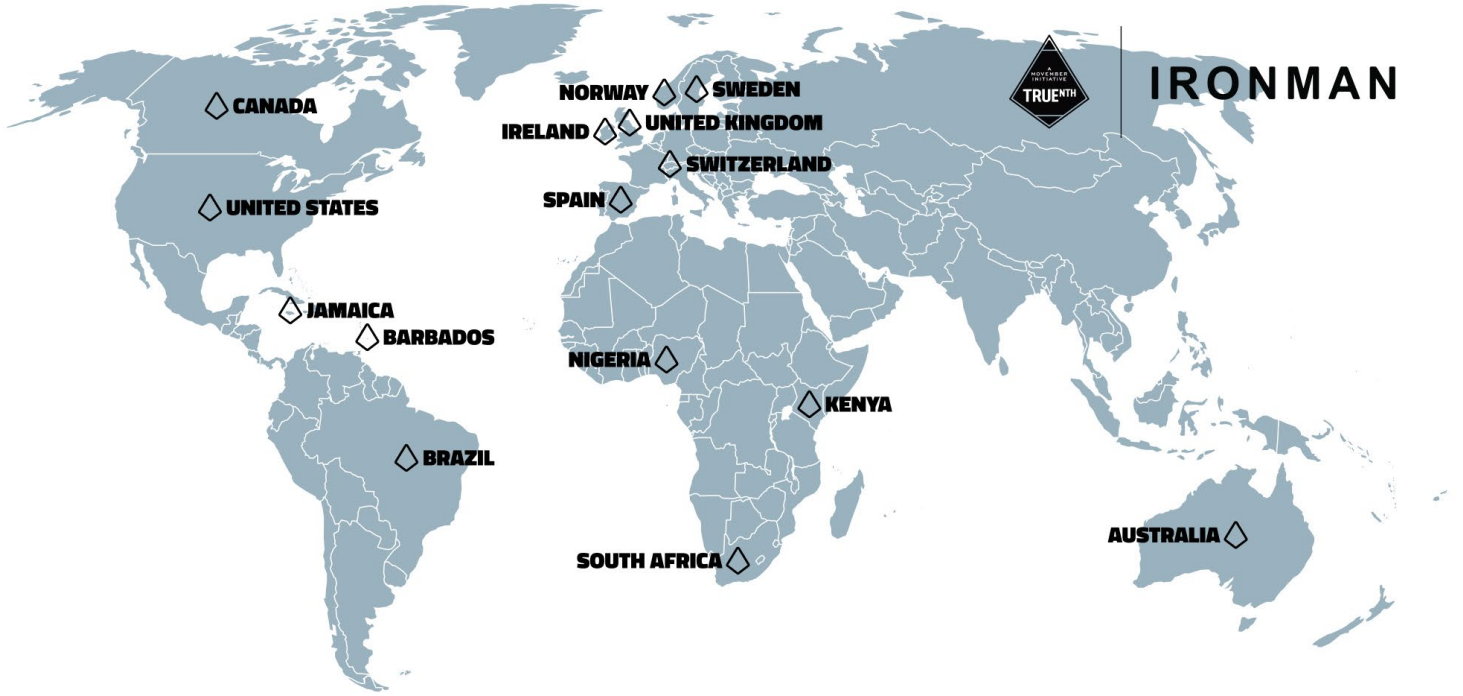
Arizona Urology Specialists
Atrium Health
Baptist Clinical Research Institute
Baylor College of Medicine
Boca Raton Hospital
California Research Institute
Carolina Urologic Research Center
Chesapeake Urology Research Associates
Christiana Care Health Services, Inc
City of Hope
Cleveland Clinic Foundation
Columbia University
Comprehensive Cancer Centers of Nevada
Dana-Farber Cancer Institute
Dayton Physician's Network
Delnor Cancer Center
Doylestown Health
Duke Cancer Institute
Durham VA Medical Center
Easton Hospital
Florida Urology Partners
Fox Chase Cancer Center - Temple Health
Hematology & Oncology Associates of the Treasure Cost
Houston Methodist Research Institute
Howard University
Indiana University
Johns Hopkins University Sidney Kimmel Comprehensive Cancer Center
Karmanos Cancer Institute
Kishwaukee Cancer Center
Lahey Clinic
Lifespan Health - Brown University
Mayo Clinic – Arizona
Mayo Clinic – Jacksonville
Mayo Clinic – Rochester
MD Anderson / Banner Health
MD Anderson / Cooper Health
Medical University of South Carolina
Memorial Sloan Kettering Cancer Center
Memphis VA Medical Center
Midlantic Urology
Millennium Oncologists
Moffitt Cancer Center
Morehouse School of Medicine
Mount Sinai Medical Center - Miami
Nebraska Cancer Specialists
Nevada Cancer Research Foundation (SNCRF)
New Jersey Urology / Summit Health
New Mexico Oncology & Hematology Consultants
New York University
NewYork–Presbyterian Brooklyn Methodist Hospital
NorthShore University Health System
Northwestern Medicine Warrenville & Delnor
Ochsner Health
Ohio State University
Oncology & Hematology Associates of Southwest Virginia
Oregon Health & Sciences University Knight Cancer Institute
Ralph H. Johnson VA Medical Center
Reading Health System
Rhode Island Hospital
Robert H. Lurie Comprehensive Cancer Center Northwestern University
Rocky Mountain Cancer Centers
Roswell Park Comprehensive Cancer Center
Rush University Medical Center
Rutgers University Cancer Institute of New Jersey
San Bernadino Urological Associates
SUNY Buffalo
Tennessee Cancer Specialists
The University of Chicago
Thomas Jefferson University - Sidney Kimmel Cancer Center
Tulane University
University Hospitals Cleveland Medical Center
University of Alabama-Birmingham
University of Alabama-Tuscaloosa
University of California, Davis
University of California, Los Angeles
University of California, San Diego
University of California, San Francisco
University of Cincinnati
University of Florida
University of Illinois at Chicago
University of Maryland
University of Massachusetts
University of Massachusetts Memorial Medical Center
University of Michigan
University of Minnesota
University of Mississippi Medical Center
University of New Mexico
University of North Carolina
University of Oklahoma Stephenson Cancer Center
University of Rochester Medical Center
University of Texas, Southwestern Medical Center
University of Utah
University of Virginia
University of Washington - Fred Hutch Cancer Center
University of Wisconsin - Carbone Cancer Center
Urology San Antonio - USA Clinical Trials
VA of Western New York Healthcare System
Virginia Cancer Specialists
Virginia Oncology Associates
Warrenville Cancer Center
Washington University in St. Louis
Weill Cornell Medical Center
William Jennings Bryan Dorn VA Medical Center
Winship Cancer Institute Emory University
XCancer Network
Yale University

INTERNATIONAL

A Beneficiência Portuguesa de São Paulo (Brazil)
Alfred Health (Australia)
Arthur J.E. Child Comprehensive Cancer Center (Canada)
Australian Prostate Centre (Australia)
Australian Urology Associates (Australia)
BC Cancer Agency (Canada)
Beacon Hospital (Ireland)
Canisius Wilhelmina Ziekenhuis (The Netherlands)
Centre Hospitalier de l'Université de Montréal (Canada)
Centro de Paulista de Oncologia (Brazil)
Centro de Pesquisa em Oncologia (Brazil)
Centro de Pesquisa São Lucas (PUCRS) (Brazil)
Chris O'Brien Lifehouse (Australia)
CHU de Québec-Université Laval (Canada)
Clatterbridge Cancer Centre NHS Foundation Trust (UK)
Consorci Hospitalari Provincial de Castelló (Spain)
Cross Cancer Institute (Canada)
Deventer Ziekenhuis (The Netherlands)
Eastern Health (Australia)
Ente Ospedaliero Cantonale (EOC) (Switzerland)
Epworth Healthcare (Australia)
Erasmus Medical Center (The Netherlands)
Federal Medical Centre Abeokuta (Nigeria)
Franciscus Gasthuis (The Netherlands)
Fundación Instituto Valenciano De Oncología (Spain)
Groote Schuur Hospital (South Africa)
Guy's and St Thomas' NHS Foundation Trust (UK)
Hospital 12 de Octubre (Spain)
Hospital Beneficência Portuguesa (Brazil)
Hospital Clínic de Barcelona (Spain)
Hospital Clinico San Carlos (Spain)
Hospital Das Clínicas Da Universidade Federal De Minas Gerais (HC-UFMG) (Brazil)
Hospital de Amor de Barretos (Brazil)
Hospital del Mar (Spain)
Hospital Erasto Gaertner (Brazil)
Hospital Israelita Albert Einstein (Brazil)
Hospital Moinhos de Vento (Brazil)
Hospital Universitario 12 de Octubre (Spain)
Hospital Universitario Central de Asturias (Spain)
Hospital Universitario La Princesa (Spain)
Hospital Universitario Miguel Servet (Zaragoza) (Spain)
Hospital Universitario Ramón y Cajal (Spain)
Hospital Universitario Virgen de la Victoria (Spain)
Hospital University Virgen del Rocio (Spain)
Hunting-St. Antonius (Netherlands)
IMIP Andrea Lopes (Brazil)
Institut Catalá d'Oncologia Badalona (Spain)
Instituto Brasileiro de Controle do Câncer (Brazil)
Instituto Câncer do Estado de São Paulo (Brazil)
Instituto do Câncer e Transplante (Brazil)
Instituto Valenciano de Oncología (Spain)
Isala Ziekenhuis (The Netherlands)
Jewish General Hospital (Canada)
Juravinski Cancer Centre (Canada)
Kantonsspital Grabünden (Switzerland)
Kantonsspital St. Gallen (Switzerland)
Lagos State University Teaching Hospital (Nigeria)
Lancashire Teaching Hospitals NHS Foundation Trust (UK)
Lister Hospital (UK)
Maasstad Ziekenhuis (The Netherlands)
Macquarie University Hospital (Australia)
MC Haaglanden (The Netherlands)
Mount Vernon Cancer Centre (UK)
Nederlands Kanker Instituut / Antoni van Leeuwenhoek Ziekenhuis (The Netherlands)
Noordwest Ziekenhuisgroep (NWZ) Alkmaar (The Netherlands)
Northern Health (Australia)
Onkozentrum Zürich (Switzerland)
Örebro University Hospital (Sweden)
Oslo University Hospital (Norway)
Ottawa Hospital Cancer Centre (Canada)
Peter MacCallum Cancer Centre (Australia)
Princess Alexandra Hospital (Australia)
Princess Margaret Cancer Center (Canada)
Prostate Cancer Centre (Canada)
Redland Hospital (Australia)
Rosebank Oncology (South Africa)
Royal Brisbane & Women's Hospital (Australia)
Servicio de Salud del Principado de Asturias, SESPA (Spain)
Sheffield Teaching Hospitals NHS Foundation Trust (UK)
Skåne University Hospital (Sweden)
Sligo University Hospital (Ireland)
Sociedade Campineira de Educação e Instrução (SCEI) (Brazil)
South Tyneside District Hospital (UK)
St. Vincent's Hospital Sydney (Australia)
St. Vincent's University Hospital (Ireland)
Steve Biko Academic Hospital (South Africa)
Stichting Amphia (The Netherlands)
Stichting Ziekenhuisgroep Twente (ZGT) (The Netherlands)
Sunderland Royal Hospital (UK)
Tacchini Hospital (Brazil)
Tallaght University Hospital (Ireland)
Ter Gooi Ziekenhuis (The Netherlands)
The Canberra Hospital (Australia)
The Christie NHS Foundation Trust (UK)
The Royal Marsden NHS Foundation Trust (UK)
The University of the West Indies – Cave Hill Campus (Barbados)
The University Of the West Indies – Mona Campus (Jamaica)
Umeå University Hospital (Sweden)
Universitätsspital Basel (Switzerland)
Universitätsspital Zürich (Switzerland)
University Hospital Southampton NHS Foundation Trust (UK)
University Hospitals of Morecambe Bay NHS Trust (UK)
University of Ilorin Teaching Hospital (Nigeria)
University of Maiduguri Teaching Hospital (Nigeria)
University of Nairobi (Kenya)
Vall D'Hebron Institut d'Oncologia (VHIO) (Spain)
Velindre Cancer Centre (UK)
Westmead Hospital (Australia)

International Registry for Men With Advanced Prostate Cancer (IRONMAN)

- IRONMAN is the ongoing PCCTC-managed prospective, international cohort of minimum 5,000 patients with advanced cancer, including patients with mHSPC and M0/M1 CRPC.
- Goal: To establish a population-based registry and recruit patients across academic and community practices across the globe.
- By collecting this information and blood samples, we will quickly understand which treatment and care practices deliver the best outcomes for patients with advanced prostate cancer. IRONMAN will then share this knowledge across the globe, so that all patients can benefit from this knowledge.



PROMISE Registry: A Prostate Cancer Registry of Outcomes and Germline Mutations for Improved Survival and Treatment Effectiveness

- PROMISE is a PCCTC-managed registry aiming to create a comprehensive nationwide registry of prostate cancer patients with germline pathogenic variants by prospectively screening ~5,000 subjects with a confirmed prostate cancer diagnosis.

- PROMISE is creating a coalition across institutions and building a genetic database directly from a grassroots network of patients so that every prostate cancer patient who is interested can better understand their genetic risk and potential treatment options.

Conclusions

- There are many different models by which to execute multicenter studies
  - Institutional
  - Industrial
  - NCI
  - Consortia

  - Pros and cons to each regarding
    - Autonomy of decision-making
    - Investigator input
    - Purpose of the study
    - Resources that determine feasibility

  - One size does not fit all