Unraveling the DCP Consortia

September 27, 2016

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Nurse Consultant

Prostate and Urologic Cancer Research Group

DCP, NCI, NIH, DHHS
# C2012 Web Seminar Series

<table>
<thead>
<tr>
<th>Date/Time</th>
<th>Webinar</th>
<th>Presenter</th>
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<tr>
<td>Sept. 27, 2016</td>
<td>Unraveling the DCP Consortia</td>
<td>Maggie House, RN, BSN</td>
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<tr>
<td>2pm – 3pm EST</td>
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<td>Oct. 27, 2016</td>
<td>The ABCs of Chemoprevention</td>
<td>Barbara Dunn, PhD, MD</td>
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<td>1pm – 2pm EST</td>
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<td>Dec. 8, 2016</td>
<td>Protocol Deviations</td>
<td>Vanessa Laroche, CCRC, CCRA, CIP, CQA</td>
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<td>Jan. 19, 2017</td>
<td>SAE Reporting</td>
<td>Gary Della-Zanna, DO, MSc</td>
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<td>1pm – 2pm EST</td>
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Do you need confirmation of attendance?

Please send your request to DCPhelpdesk@dcpais.com
The DCP Consortia - Hmmmm.....and I thought I was the biggest mystery!
We will discuss:

1. (where) Consortia program in relation to Federal framework
2. (what) Consortia program concepts and goals
3. (why) Consortia funding mechanism and infrastructure
4. (who) Consortia member roles and responsibilities
5. (how) Consortia protocol development process and funded studies
Federal Government
Executive Branch

President, VP, Cabinet Heads

DCP

Other Divisions
The National Institutes of Health

Office of the Director

NIA
NIAAA
NIAID
NIAMS
NIDCD
NIDDK
NIDA
NIEHS
NEI
NIGMS
NHGRI
NIMH
NINDS
NINR
NIBIB
NCAM
NCRR
NCMHD
CC
CIT

Source: http://www.nih.gov/
National Cancer Institute Organizational Structure
Division of Cancer Prevention Organizational Structure

DCP

Chemoprevention Agent Development
Organ Groups: Lung, Prostate, Breast, GI
Consortia

Community Oncology
Cancer Biomarkers
Early Detection
Nutrition Science
Biometry
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What is the Consortia Program?

The Consortia Program is a mechanism or program through which Phase 0/I/II Chemoprevention Clinical Trials are conducted.
Chemoprevention

Chemoprevention uses pharmacological agents to delay, arrest or reverse carcinogenesis at its earliest stages.

Development of Cancer - Opportunities for Intervention

DCP Early Phase Clinical Trials Consortia
Why is cancer prevention important?

- New cases/deaths double 20-40 years
  - Greatest in developing countries
  - Growth and aging of populations
  - Exogenous, modifiable risk factors
2016 Estimated US Cancer Cases*

Men 841,390

Prostate 21%
Lung & bronchus 14%
Colon & rectum 8%
Urinary bladder 7%
Melanoma of skin 6%
Non-Hodgkin lymphoma 5%
Kidney & renal pelvis 5%
Leukemia 4%
Oral cavity & pharynx 4%
Liver/intrahepatic Bile duct 3%
All other sites 22%

Women 843,820

29% Breast
13% Lung & bronchus
8% Colon & rectum
7% Uterine corpus
4% Non-Hodgkin lymphoma
3% Leukemia
3% Melanoma of skin
6% Thyroid
3% Kidney & renal pelvis
3% Pancreas
21% All Other Sites

*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.
Source: American Cancer Society, 2010.
What are the Consortia Program Goals

- Design/conduct early phase trials
  - Agent safety - AE/SAE monitoring
  - Chemoprevention agent efficacy

  Assess biological effects of intervention on molecular targets and endpoints associated with carcinogenesis (proliferation, apoptosis, growth factor expression, oncogene expression, etc.)

- Advance scientific insights of cancer prevention mechanisms through trial results

- Develop and test biomarkers as determinants of response
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Grant v. Contract Funding Mechanism

<table>
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<tr>
<th>Grant</th>
<th>Contract</th>
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<tr>
<td>Assistance mechanism to support research for the public good</td>
<td>Legally binding agreement to acquire goods or services for the direct use or benefit of the Government.</td>
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<tr>
<td>Peer review of broad criteria</td>
<td>Award based on stated evaluation factors</td>
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<tr>
<td>Limited Government oversight and control</td>
<td>More Government oversight and control</td>
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<tr>
<td>Annual Reports</td>
<td>Deliverables</td>
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DCP Early Phase Clinical Trials Consortia

- Program funded by contract
  - Solicitations sent out ~2x/year to 5 prime contractors, unsolicited proposals are accepted
  - Studies awarded to prime contractors, may take place in subcontract sites
  - Opportunity to add new sites
- Fills void between preclinical studies and Phase III
  - Emphasis on intervention effects on at-risk tissue – intensive tissue collections (e.g., biopsies), invasive biomarker monitoring
- Program pays for:
  - Core infrastructure (5 prime sites)
  - Participant accrual clinical costs
  - Partial salary support for main PI and one site coordinator per trial
  - Tissue collection and biomarker analysis costs
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“I understand your degree is in the sciences. However, if you’re hired your responsibilities will include but not be limited to lemonade quality assurance coordinator, budgetary overseer, inventory monitor, advertiser and recruiter for potential buyers, preparer of records for periodic health inspector visits, Excel datasheet manager, and completer and submitter of all Federal Government forms……..any interest?”
The Consortia Team

• DCP
• Consortia Lead Organizations (CLOs)
  • Participating Organizations (POs)
• Contractors
  • CCS Associates (CCSA)
  • Leidos Biomedical Research, Inc.
  • MRIGlobal
  • Technical Resources International (TRI), Inc.
• NCI Technology Transfer Branch
• NCI Cancer Prevention & Control (CPC)
  Central Institutional Review Board (CIRB)
• NCI Contracting Officers
The Consortia Team – DCP

DCP

- Dr. Ford – Associate Director for Clinical Research
- Dr. Szabo – DCP Consortia Program Head
- Mr. Johnsey – budget/administrative oversight
- DCP Medical/Scientific Monitors
- DCP Nurse Consultants
- Ms. Ryan – data management
- Protocol Information Office (PIO)
The Consortia Team
Consortia Lead Organizations (CLOs)

- Mayo Clinic – Cancer Prevention Network
- MD Anderson Cancer Center
- Northwestern
- University of Arizona
- University of Wisconsin
DCP Early Phase Clinical Trials Consortia

**Consortia Sites**
- 5 CLO contractors
- >50 member sites (POs)

**Goals:**
- Agent testing
- Biomarker identification
- Trial design optimization
Multi-institutional Consortia

- Each CLO forms its own stable consortium of institutions
- Efficiency increased by having multi-institutional consortia in place prior to solicitations for studies
- Numerous areas of expertise in each group
- Changes to consortium are allowed, with DCP permission (sites must be pre-qualified)
- Limited number of international sites
The Consortia Team – Contractors

- CCS Associates (CCSA)
  regulatory support

- Leidos Biomedical Research, Inc.
  biospecimen oversight

- MRIGlobal
  chemoprevention agent repository

- Technical Resources International (TRI), Inc.
  monitoring/auditing and informatics support
The Consortia Team – Other NCI Teams

- NCI Technology Transfer Center
- NCI Cancer Prevention & Control (CPC) 
  Central Institutional Review Board (CIRB)
- NCI Office of Acquisitions (Contracting Officers)
We will discuss:

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The Life Cycle of a Study: Concept Development

1. Concept idea from DCP staff
2. Submitted to Office of Acquisitions (OA, "Contracts")
3. Concept review meeting with DCP Organ System Groups, CADRG
4. OA releases Task Order Request for Proposals (TO – RFP)
5. Statement of Work, cost estimate (IGCE), background document
The Life Cycle of a Study: Proposal → Protocol Receipt → CIRB Review

TO – RFP responses received by Contracts

TO – RFP Review by DCP Organ System Groups
(with additional subject matter experts as appropriate)

Proposal approval

PSRC (Protocol and Safety Review Committee) Review

Protocol Approval
Protocol Disapproval

Submission to CIRB (and FDA, as appropriate)
## Protocols In-Development (10)

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<th>DCP Research Group</th>
<th>Agent</th>
<th>Cohort</th>
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<tr>
<td>Breast and Gynecologic Cancer Research Group</td>
<td>Oral Tamoxifen versus Transdermal 4-hydroxytamoxifen</td>
<td>DCIS</td>
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<td>9cUAB30</td>
<td>Early Stage Breast Cancer</td>
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<td></td>
<td>4-hydroxytamoxifen Topical Gel</td>
<td>Mammographically Dense Breasts</td>
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<td>Exemestane</td>
<td>Postmenopausal ER-Positive Breast Cancer</td>
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<td>HPV Vaccine</td>
<td>Renal Transplantation in Adult Women</td>
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<tr>
<td>Gastrointestinal and Other Cancers Research Group</td>
<td>Curcumin</td>
<td>Chronic Atrophic Gastritis and Gastric Intestinal Metaplasia</td>
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<td>Intermittent Aspirin Dosing</td>
<td>Colorectal polyps</td>
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<td>Erlotinib</td>
<td>Familial Adenomatous Polyposis</td>
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<td>Simvastatin</td>
<td>Liver Cirrhosis</td>
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<tr>
<td>Lung/Upper Aerodigestive Cancer Research Group</td>
<td>ACTOplus met XR</td>
<td>Carcinoma of the Oral Cavity or Oropharynx</td>
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Approved Protocols (22)

- Vaccines
  - MUC1 – newly diagnosed advanced adenomas
  - DNA Vaccine – chronic hepatitis C virus (HCV) infection
  - Nelipeimut-S Peptide vaccine – DCIS
  - PROSTVAC (prostate) vaccine – prostate cancer active surveillance
  - HPV vaccine – Prime and Deferred-booster Dosing in girls ages 9-11
  - DNA Plasmid Based Vaccine (WOKVAC) – breast cancer

- NSAIDs
  - Low dose ASA – CT – detected lung nodules
  - Intermittent v. continuous ASA – nasal epithelium gene expression smokers
  - Naproxen colorectal cancer
  - ASA – Barrett's Esophagus post radiofrequency ablation
  - Combined ASA and Zileuton (asthma drug) – biomarkers of tobacco-related carcinogenesis smokers
Approved Protocols (22)

- Epidermal Growth Factor Receptor (EGRF) inhibitors
  - Erlotinib – before bladder cancer surgery
  - Erlotinib – liver cirrhosis

- Bioactive food components and plant derivatives
  - DHA (omega 3 fatty acid) – breast cancer, premalignant lesions, or benign breast disease
  - Berberine (plant derivative) – ulcerative colitis
  - Pom-X (pomegranate derivative) – prostate cancer active surveillance
Approved Protocols (22)

- **Drug for other diseases**
  - Statin (lipid lowering) – pancreatitis
  - Metformin (diabetes) – oral cancer prevention
  - Inhaled Iloprost (pulmonary HTN) – lung cancer prevention former smokers
  - Linaclotide (irritable bowel) – dose finding study to maintain bioactivity in rectal mucosa

- **Novel compounds**
  - 9cUAB30 (retinoid) – Phase I dose-escalation study
  - Transdermal vs oral telapristone (selective progesterone receptor modulator) – mastectomy
Resources

DCP Consortia SOPs

SOPs

AQuiP website

AQuiP
http://www.dcpaquip.com
Acknowledgments

- CLOs and POs for their efforts in this important work
- Anne Ryan, Ellen Richmond, and Liz Walsh for their help with slides
- TRI for assisting with logistics for the webinar series