Cancer Immunotherapy Trials Network
iSBTc 25th Annual Meeting (Oct 4, 2010)
CITN: Vision

• To provide a highly collaborative structure to efficiently develop innovative, intelligent & biologically dictated immunotherapy regimens
Overall Strategy

• To design, develop & conduct important trials not otherwise possible
  – Best peer reviewed concepts
  – Optimal trial design, monitoring & trial sites provided by the CITN
  – Use of the best agents not generally available
    • Provided with the assistance of the NCI and/or industry.
Overall Strategy

• Tactics:
  – To be determined by Member Site PIs, External Advisory Board
    • With the PI & Co-Investigators

• My View:
  – To develop regimens that prospectively & predictably greatly increase the number of T cells specific for known and defined antigens
  – To develop “off the shelf” regimens that can be used by multiple investigators in multiple circumstances to serve as the backbone for further immunotherapy agent development
  – To focus on agents, antigens and regimens that have received consensus prioritization in previous workshops
Priority Agents
(from NCI Immunotherapy Agent Workshop)
(Bold agents - prioritized by the Immune Response Modifier Prioritization Working Group)

• T cell growth factors
  – IL-7, IL-15
• Dendritic cell activators
  – Anti-CD40, CD40L
• Dendritic cell growth factors
  – Flt3L
• Vaccine adjuvants
  – IL-12 CpG MPL, Poly I:C, Resiquimod, 852A
• T cell stimulators
  – 4-1-BB, Anti-GITR, Anti-OX40
• T cell attracting chemokines
  – CCL21
• Inhibitors of T cell checkpoint blockade
  – Anti-PD1 & PD1 Ligand, Anti-B7-H4, Anti-LAG-3, LIGHT
• Inhibitors
  – IDO immunosuppression (1-methyl tryptophan)
  – Signaling (Anti-TGF-b)
  – Inhibition (Anti-IL 10 & anti-IL 10R)
CITN: Basic Tenets

- Hybrid clinical trials model
  - Academic hypothesis-driven, peer-reviewed
  - Pharmaceutical-like efficiencies

- Proactively seek & initiate the best trials
  - Open submission of trials from any investigator
  - Selection by panel of successful immunologists & immunotherapists
    - Selection based on best science & likelihood of success in cancer therapy

- Design optimal trials using the best agents available
  - Will develop selected trials into “best” trials possible using combined Network skills & best agents available
  - To work with CTEP, industry & academic investigators to bring best agents together
CITN: Basic Tenets

• Provide key personnel and services for optimal trials
  – Protocol specialists, regulatory affairs, contracting, forms developer, statistician, etc.
• Set up and accrue trials rapidly
  – To provide experienced, preselected & precontracted trial sites
• Provide optimal immune response data
  – Centralized laboratory for validated immune response data
• Provide quality monitoring to assure quality outcome data
• Provide adequate, on-time funding
• Rapidly disseminate results
CITN: Organization

• COSC
  – (Central Operations & Statistical Center)
  – Based at the Fred Hutchinson Cancer Research Center (FHCRC)
  – To provide leadership & organizational resources
    • Infrastructure
    • Protocol coordination
    • Statistical support

• Up to 25 member institutions
  – To select & refine trials
  – To accrue patients
CITN: Leadership

• Mac Cheever – PI
  – Responsible for the Central Operations & Statistical Center (COSC)
    • Background – Principles of T cell therapy, cancer antigen discovery, industry cancer vaccine & therapeutic antibody product development, consensus prioritization of immunotherapy agents, antigenic targets, and regimens

• Dr. Mary L. “Nora” Disis - Co-Investigator
  – Responsible for immune monitoring
    • Background – Development, conduct and evaluation of phase I and II cancer vaccine and T cell therapy trials, development and application of novel techniques in immune monitoring.
    • PI of the University of Washington Clinical Translational Science Award (CTSA) Institute for Translational Health Science

• Kim Margolin - Co-Investigator
  – Shared responsible for organization & trial development
    • Background - Organizing, conducting and participating in multi-institutional trials as a leader of the Cytokine Working Group.
    • Expertise related to the FDA approval of immunotherapy agents as a past member of the Oncologic Drugs Advisory Committee (ODAC)
CITN: Leadership

- John Thompson
  - Consultant – Phase I/II protocol design
    - Director FHCRC/UW Phase I program
- Francesco Marincola
  - Consultant - Immune monitoring
    - Chief of the Infectious Disease and Immunogenetics Section in the Department of Transfusion Medicine at the Clinical Center of the NIH in Bethesda.
- Anna Karolina Palucka
  - Consultant - Analysis of blood transcriptional profiles and biomarker signatures
    - Investigator, Baylor Institute for Immunology Research
FHCRC – Extensive Experience Leading Coordinating Centers

- WHI - Clinical Coordinating Center for the Women’s Health Initiative
- EDRN - Early Detection Research Network - Data Management and Coordination Center
- SWOG - Southwest Oncology Group Statistical Center
- HVTN - HIV Vaccine Trials Network
- Center for Human Embryonic Stem Cell Research,
- TREC - Center for Ecogenetics/Environmental Health, the Transdisciplinary Research on Energetics and Cancer Coordinating Center,
- CARET - Carotene and Retinol Efficacy Trial (CARET) Coordinating Center,
- Northwest Genome Engineering Consortium,
- Center for Evaluation of Biomarkers for Breast Cancer.

- Standard processes and procedures for monitoring financial and regulatory aspect of Networks in place
CITN: Management in association with the HVTN (HIV Vaccine Trials Network)

- PI: Larry Corey – Director of FHCRC
- NIH NIAID funded multi-institutional multinational consortium
  - 28 trial sites in 17 countries on 4 continents
  - Conducted 44 vaccine trials
    - 17 first-in-human
    - 2 phase IIB large-scale “proof of concept” trials
    - Enrolled 8700 people
    - 10 trials to be initiated within the next 10 months
- To provide expertise in running early phase clinical trials with immunogens without having to establish a parallel infrastructure.
- HVTN personnel
  - 6 staff physicians for protocol design and safety monitoring
  - 6 PhD scientists for GLP immune monitoring assay
  - Statistical Center & Regulatory specialists
CITN: Trial Selection Process

- Peer-review process
  - Top scientists from the field
  - Assurance that all applicants are given thorough and fair consideration
- Open call for proposals
  - Year round
  - Investigator driven
  - Reviewed by Network personal and Site PIs
  - Emphasis on merit, significance, investigator experience and scientific merit
- Successful applicants submit a more detailed “Full Application”
  - Full applications to be developed by PI with assistance from Network
- Network to provide detailed conditions for acceptance including recommended changes
  - Protocol
  - Study design
  - Adjuvant & agents
  - Immunologic studies
  - Ethics processes
  - Etc
Trial Management: Comprehensive Support to be Provided to PI – From COSC & Member Site PIs

• Agents for “best trial possible” not otherwise possible
• Expertise and support for:
  – Protocol design
  – Regulatory approval
  – Collaborators/clinical site identification
  – Mechanistic study design
  – Site training
  – Patient recruitment
  – Protocol monitoring
  – Data acquisition
  – Immune response assays and marker studies and data analysis
  – Data analysis
  – Correlative studies
What can we expect?
How big is it?

• CITN - Projected 15 trials over 5 years
  – $17M total cost (direct & indirect)
  – < $1M/ trial
• Immune Tolerance Network (ITN)
  – Initiated with $140M direct costs over 7 years from NIAID
  – Renewal at $213M over 7 years
  – Receives considerable funding from non-NIH sources
    • 10% Industry
    • 10% Foundations
• HIV Vaccine Trials Network (HVTN)
  – Received >$250M over 9 years from NIAID
  – Key components supplemented by Gates Foundation
  – Some industry support
Prioritization is Mandatory!
Leveraged Support is Possible

• Funding from multiple sources will be facilitated by other organization desire for Network functions not readily available elsewhere:
  – “Best” trials possible based on biology
  – Immunologic & immunotherapy expertise
  – Efficient & cost effective trials

• Sources of leveraged funding
  – NCI – e.g., correlative studies / NExT / intramural collaboration
  – Industry
  – Non-governmental funding agencies & foundations
    • Disease focused organizations
  – Advocates & individual donations
Member Site Selection

• To be chosen based on
  – Past experience in leading or participating in Phase I and II immunotherapy trials
  – Capacity to contribute to the scientific leadership of the CITN

• Application due November 15, 2010
• LOI should be received by October 15, 2010

• CTEP web site for details

http://ctep.info.nih.gov/
T Cell Therapy: The Early Years
END