Cancer Vaccine
Clinical Trial Working Group

Final Workshop, 10 November 2005
CVCTWG Issues

- Cancer vaccines have unique developmental challenges.
- Some potential solutions exist.
- Not all potential solutions are widely understood.
- No consensus exists on potential solutions.
- No formal recommendations for a flexible and adequate clinical development path exist.
CVCTWG - The Initiative

• Collaborative Spirit
• Broad Expertise Contributed to Discussions:
  • Academic Leaders
  • Biotechnology/Pharmaceutical Drug Developers
  • Regulators
• > 60 International Participants
• Extensive Discussions in 4 Broad Areas
• Consensus Reached on Scientific Recommendations to Advance the Field of Cancer Vaccine Development
CVCTWG - Timelines 2004-2006

Nov. 2004 - April 2005
- Workstream Formation
- Initial Discussions
- Independent Workstream Activities

April 2005
- CVCTWG Interim Workshop
- Produce Results for Draft Manuscript

May - September 2005
- Draft Scientific Manuscripts
- Workstream Core Group Review

October 2005
- Circulate Scientific Manuscript for Review by Workshop Participants

November 2005
- Annual iSBTc Meeting
- CVCTWG Final Workshop
- Review and Finalize Manuscript

First Quarter 2006
- Publish Scientific Manuscript & Provide Manuscript to Regulatory Agencies
CVCTWG Workstreams

1. Clinical Endpoints to Support Product Efficacy
2. Design Methodologies for Cancer Vaccine Trials
3. Technical Challenges in Cancer Vaccine Trials
4. Enabling Technologies and Combinations of Investigational Agents
Workstream Participants

- **3 Leaders:** Industry, Academia, Regulatory
- **5 Core Members:** Industry, Academia
- **Associate Members** (as appropriate)
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<tr>
<th>Name</th>
<th>Institution/Company</th>
<th>Workshop</th>
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<tr>
<td>Giorgio Parmiani</td>
<td>Istituto dei Tumori, Milan</td>
<td>WS1</td>
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<td>Hans Loibner</td>
<td>Independent</td>
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<td>Peter Bross</td>
<td>CBER, FDA</td>
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<td>Axel Hoos</td>
<td>Bristol-Myers Squibb</td>
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<td>Alexander Eggermont</td>
<td>University of Rotterdam; EORTC</td>
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<td>Steven Hirschfeld</td>
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<td>Kristen Hege</td>
<td>CellGenesys</td>
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<td>Walter Urba</td>
<td>Earle Chiles Research Institute</td>
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<td>Keith Wonnacott</td>
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<td>Geoffrey Nichol</td>
<td>Medarex</td>
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<td>Mario Sznol</td>
<td>Yale University</td>
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<td>Ke Liu</td>
<td>CBER, FDA</td>
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CVCTWG Overall Goal

Provide a comprehensive scientific summary of critical issues for cancer vaccine clinical development and proposed solutions based on consensus between a wide number of experts representative for the cancer vaccine field.
Program Schedule, November 10, 2005

- 8:00am-8:30am  Welcome & Introductions
- 8:30am-10:30am Development of Cancer Vaccines: 5 Perspectives from Academia and Industry
- 10:45am-12:30pm Summary of Issues and Goals: Results of 4 Workstreams
- 12:30pm-2:45pm Parallel Sessions:
  1) State of the Field Lectures:
     - Measuring Residual Tumor Burden
     - Cancer Biometrics – Results from 2003 iSBTc Workshop
     - Bayesian Designs for Early Trials
  2) 4 Workstream Breakout Sessions
- 2:45pm-3:15pm  FDA Special Lecture
     - FDA Perspective on Preclinical Development of Cancer Vaccines
- 3:30pm-5:30pm  4 Breakout Session Reports & Discussions
- 5:30pm        Future Plans
Welcome!
Back-up
CVCTWG Workstream 1: Clinical Endpoints to Support Product Efficacy

- Conventional clinical oncology endpoints (measures of benefit)
- Discovery, standardization, and validation of surrogate endpoints for clinical benefit
- Immunological endpoints
- Novel experimental measures of minimal residual disease, such as circulating malignant tumor cells
- Other surrogate endpoints
CVCTWG Workstream 2: Design Methodologies for Cancer Vaccine Trials

- Adaptive trial designs for Phase 2 and 3 development and novel statistical approaches
- New standards/designs for Phase 1/2 trials versus Phase 3 trials
- Bridging the gap between Phase 2 and Phase 3 development
- Pivotal trial designs for autologous products
- Endpoints for early trials: toxicity, biological activity, clinical activity
- Surrogate endpoints (correlative tests and imaging) for clinical activity in early trials
- Designs for combination Phase 1 trials
- Results criteria for advancing to surgical adjuvant trials
- Standardization of study conduct and outcome review
CVCTWG Workstream 3:
Technical Challenges in Cancer Vaccine Clinical Trials

- Criteria for entering clinical development
- Product standardization and characterization for individualized vaccines
- Dose selection for early trials of cancer vaccines
- Definition of biological activity and biologically relevant clinical response parameters for early and late stage trials
- Patient selection (antigen expression, MHC expression, immune competence, others)
- Immunophenotyping and genotyping guidelines
- Funding issues
CVCTWG Workstream 4:
Enabling Technologies and Combinations of Investigational Agents

- Identification of key therapeutic agents (ie, cytokines, antibodies to cell surface co-stimulatory molecules, small molecules targeting immunologic signaling pathways)
- Regulatory issues (toxicology, IND requirements, registration) for combinations of investigational agents
- Intellectual property issues for combinations
- Phase 1 trial issues (endpoints, design, proof-of-concept, patient selection, tumor tissue typing, etc.)
- Later-stage development issues
- Funding for correlative studies
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<th>Steering Committee Members</th>
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<td>• Neil Berinstein</td>
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Aventis, EORTC, BioMira, FDA, Antigenics, iSBTc, Independent, Duke University, Medarex, Istituto dei Tumori, NCI, CTEP, Yale University.