

GTSAB REPORT

Recombinant DNA Advisory Committee

September 12, 2012



Protocols Submitted for 3rd Quarter 2012

▶ **13 Total submissions**

Disease indications for the protocols not selected:

- **11 Cancer**
- **1 Heart Failure**

Vectors:

- **2 Adenovirus**
- **1 Plasmid**
- **3 Retrovirus**
- **2 Lentivirus**
- **1 Modified bacteria**
- **1 VSV**
- **1 AAV**
- **1 RNA transfer**

Serious Adverse Events

26 serious adverse events were reviewed by the GTSAB from 19 protocols, including initial and follow-up reports.



Opening of New Protocols 3rd Quarter 2012

- ▶ **10 Protocols notified OBA of enrollment (MIC1 submission).**
- ▶ **Two of the 10 were reviewed at a public meeting.**
 - **One of the two provided responses to the issues raised following public review. (Other trial received no recommendations following public review.)**
- ▶ **Information on trials not selected will be available with these slides on OBA's Website after the meeting.**

Phase I Trial of Attenuated Vaccinia Virus (GL-ONC1) Delivered Intravenously with Concurrent Cisplatin and Radiotherapy in Patients with Locoregionally Advanced Head and Neck Carcinoma (OBA Protocol #1089 Reviewed June 2011)

- ▶ **Enrollment will not be limited to those who have already failed chemo/radiation. However, only those who are not eligible for resection or have an unfavorable risk will be enrolled.**
- ▶ **Subjects with newly diagnosed salivary cancer will also be eligible.**
- ▶ **Historical data will be used to aid in the interpretation of safety data as chemo/radiation will likely lead to a number of toxicities independent of the gene transfer.**
- ▶ **The virus will be infused by the trained oncology staff in a negative pressure room. All staff are offered the smallpox vaccine.**

Gene Therapy Recommended for Approval in Europe

- ▶ **The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) made a recommendation that alipogene tiparvovec be approved as a therapy.**
- ▶ **This product uses an AAV vector encoding for the lipoprotein lipase (LPL) gene and is intended for patients with LPL deficiency who have severe or multiple attacks of pancreatitis despite dietary fat restrictions.**
- ▶ **Carlos R. Camozzi, M.D., Ph.D., Vice President and Chief Medical Officer, uniQure B.V., will speak about the development of this product and the regulatory process tomorrow at the workshop on Gene Therapy and Rare Diseases (this conference will be webcast - <http://videocast.nih.gov/default.asp>).**

University of Pennsylvania and Novartis Form Alliance to Expand Use of T Cell Immunotherapy for Cancer

- ▶ **In August 2012 the University of Pennsylvania (Penn) and Novartis announced a research and licensing agreement aimed at expanding the use of personalized T cell therapy using chimeric antigen receptors (CARs) for cancer.**
 - ▶ **Penn and Novartis will build a Center for Advanced Therapeutics (CACT) on the Penn campus.**
 - ▶ **The CACT will be devoted to discovery, development and manufacturing of adoptive T cell immunotherapy.**
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University of Pennsylvania and Novartis Form Alliance (continued)

- ▶ The agreement follows a 2011 publication by a Penn research team, led by Dr. Carl June, demonstrating significant clinical responses to this personalized immunotherapy technique in several chronic lymphocytic leukemia (CLL) patients, who had already received multiple standard chemotherapy treatments (*N. Eng. J. Med* 2011;365:725-733).
- ▶ Novartis will have an exclusive global licensing to the technologies used in an ongoing trial of patients with CLL as well as future CAR-based therapies developed through the collaboration.

Gene Therapy for Adenosine Deaminase-Deficient Severe Combined Immune Deficiency: Clinical Comparison of Retroviral Vectors and Treatment Plans

Fabio Candotti¹, Kit L. Shaw², Linda Muul¹, Denise Carbonaro², Robert Sokolic¹, Christopher Choi², Shepherd H. Schurman¹, Elizabeth Garabedian¹, Chimene Kesserwan¹, G. Jayashree Jagadeesh¹, Pei-Yu Fu², Eric Gschweng², Aaron Cooper³, John F. Tisdale⁴, Kenneth I. Weinberg⁵, Gay M. Crooks⁶, Neena Kapoor⁷, Ami Shah⁷, Hisham Abdel-Azim⁷, Xiao-Jin Yu⁷, Monika Smogorzewska⁷, Alan S. Wayne⁸, Howard M. Rosenblatt⁹, Carla M. Davis¹⁰, Celine Hanson¹⁰, Radha G. Rishi¹¹, Xiaoyan Wang¹², David Gjertson^{6,12}, Otto O. Yang¹³, Arumugam Balamurugan¹³, Gerhard Bauer¹⁴, Joanna A. Ireland⁷, Barbara C. Engel¹⁵, Gregory M. Podsakoff¹⁶, Michael S. Hershfield¹⁷, R. Michael Blaese¹⁸, Robertson Parkman⁷, and Donald B. Kohn^{2,19*}

Blood E-pub 091212

QUESTIONS?



▶ **PROTOCOLS NOT REVIEWED AT A PUBLIC MEETING.**

- **A Phase I Trial of Oncolytic Measles Virotherapy in Malignant Pleural Mesothelioma (OBA Protocol #1033)**
- **A phase 1 trial to evaluate the safety and immunogenicity of an IL-12 pDNA enhanced HIV-1 multiantigen pDNA vaccine delivered intramuscularly with electroporation, as a prime for an HIV-1 rVSV vaccine boost, in healthy HIV uninfected adult participants (OBA Protocol #1041)**
- **A Randomized Phase II Study to Assess the Activity of TroVax® (MVA-5T4) Plus Docetaxel Versus Docetaxel Alone in Subjects with Progressive Hormone Refractory Prostate Cancer (OBA Protocol #1043)**
- **Phase I Study of the Administration of T lymphocytes Expressing the CD30 Chimeric Antigen Receptor for relapsed CD30+ Hodgkin's Lymphoma and CD30+ Non-Hodgkin's Lymphoma (OBA Protocol #1066)**

▶ **PROTOCOLS NOT REVIEWED AT A PUBLIC MEETING.**

- **A Phase I/IIa Dose Escalation Safety Study of Subretinally Injected UshStat®, Administered to Patients with Retinitis Pigmentosa Associated with Usher Syndrome Type 1B (OBA Protocol #1102)**
- **A Multi-Center, Open-Label, Randomized, Phase 2b Study to Evaluate the Efficacy and Safety of BC-819 and Gemcitabine versus Gemcitabine Alone in Treatment-Naïve Patients with Locally Advanced Pancreatic Adenocarcinoma (OBA Protocol #1115)**
- **Phase II Trial of Intratumoral pIL-12 Electroporation in Advanced Stage Cutaneous and in Transit Malignant Melanoma (OBA Protocol #1135)**
- **Phase I/II Study of Metastatic Cancer Using Lymphodepleting Conditioning Followed by Infusion of Anti-mesothelin Gene Engineered Lymphocytes (OBA Protocol #1139)**