

GTSAB REPORT

Recombinant DNA Advisory Committee

June 19, 2012



Protocols Submitted for 2nd Quarter 2012

▶ **19 Total submissions**

Disease indications for the 17 protocols not selected:

- **13 Cancer**
- **1 Peripheral Artery Disease**
- **1 Infectious Disease-HIV**
- **1 Oral Mucositis**
- **1 Monogenic Congenital Retinal Disease-Achromatopsia**

Vectors:

- **5 Adenovirus**
- **3 Plasmid**
- **3 Retrovirus**
- **2 Lentivirus**
- **2 Modified bacteria**
- **1 Vaccinia**
- **1 AAV**

Serious Adverse Events

20 serious adverse events were reviewed by the GTSAB from 12 protocols, including initial and follow-up reports. Summaries will be available on meeting website by next quarter.



Opening of New Protocols 2nd Quarter 2012

- ▶ **13 Protocols notified OBA of enrollment (MIC1 submission).**
- ▶ **Five of the 13 were reviewed at a public meeting.**
 - **Three of the five provided responses to the issues raised following public review.**
- ▶ **Information on these trials and summaries of the responses to RAC review will be available on OBA's Website after the meeting.**

Gene Transfer and Rare Diseases Workshop

**Co-sponsored by NIH OBA and
Office of Rare Disease Research**

September 13, 2012

Session I: Clinical Experience

- Hemophilia
- Leber Congenital Amaurosis and Other Eye Disorders
- Blood Cell Disorders

Session II: Defining Opportunities for Data Sharing Across Protocols

- Common pharm/tox studies
- Vector platforms

Session III: Resources

- Rare Diseases Clinical Research Network
 - National Gene Vector Biorepository
 - Bridging Interventional Development Gaps
 - Gene Therapy Resource Program
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QUESTIONS?



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

- **Pilot Study of Redirected Autologous T Cells Engineered to Contain Anti-CD19 Attached to TCR ζ and 4-1 BB Signaling Domains in Patients with Chemotherapy Resistant Or Refractory CD19+ Leukemia and Lymphoma (OBA Protocol #793)**
- **A Phase I/II Randomized Double-Blind, Placebo Controlled Dose Escalation Study To Evaluate The Safety And Efficacy of JVS-100 Administered By Direct Intramuscular Injection To Cohorts Of Adults With Critical Limb Ischemia (OBA Protocol #1070)**
- **A Phase I/II Study of the Safety and Biological Activity of Intraperitoneal EGEN-001 (IL-12 Plasmid Formulated with PEG-PEI-Cholesterol Lipopolymer) Administered Alone and in Combination with Standard Chemotherapy in Colorectal Peritoneal Carcinomatosis Patients Who Had Previously Received Cytoreductive Surgery plus HIPEC Therapy (OBA Protocol #1090)**
- **Administration of an Allogeneic Myeloma GM-CSF Vaccine in Conjunction with a Lenalidomide Containing Regimen in Myeloma Patients with Near Complete Remission (OBA Protocol #1107)**

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

- **Phase II Trial of Adjuvant bi-shRNA^{furin} and GM-CSF Augmented Autologous Tumor Cell Vaccine (FANG™) Integrated with Bevacizumab for Patients with Recurrent/Refractory Ovarian Cancer Participating in Study CL-PTL 105 (OBA Protocol #1111)**
- **A Phase 1/2a Dose-escalation Study of JX-594 (Thymidine Kinase-Deactivated Vaccinia Virus plus GM-CSF) Administered by Multiple Intravenous (IV) Infusions Followed by Intratumoral (IT) Boosts Alone and in Combination with Irinotecan in Patients with Metastatic, Refractory Colorectal Carcinoma (OBA Protocol #1113)**
- **A Phase 1 Double-Blind, Randomized, Placebo-Controlled Trial to Evaluate the Safety and Immunogenicity of a Multi-antigen HIV (HIV-MAG) plasmid DNA (pDNA) Vaccine Co-administered with Recombinant Human IL-12 pDNA (GENEVAX® IL-12) Followed or Preceded by Recombinant Ad35-GRIN/ENV HIV Vaccine in HIV-Uninfected, Healthy Volunteers (OBA Protocol #1124)**
- **Phase I Trial of Intratumoral Bi-functional shRNA Stathmin 1-knockdown Lipoplex in Patients with Advanced and/or Metastatic Cancer (OBA Protocol #1138)**

Phase I Clinical Intramuscular Gene Therapy Of rAAV.FS344 Trial To Patients With Becker Muscular Dystrophy And Sporadic Inclusion Body Myositis (OBA Protocol #1074 Reviewed December 2010)

- ▶ Inclusion criteria were modified to more clearly define what is meant by quadriceps muscle “weakness.”
- ▶ Definition of a dose limiting toxicity was modified to include any grade III (instead of grade II) event that is possibly, probably, or definitely related to the study agent.
- ▶ Follistatin expression can potentially affect cardiac muscle and has been linked to malignancy, in particular hepatocellular carcinoma. Echocardiograms will be performed at the baseline visit and at three months post vector administration. In addition, liver function testing and alpha fetoprotein (a marker for liver cancer) testing will be performed at baseline and at all follow-up visits for two years.

A Phase 1 Ascending Dose Trial of the Safety and Tolerability of Toca 511, a Retroviral Replicating Vector, Administered to Subjects at the Time of Resection for Recurrent High Grade Glioma and Followed by Treatment with Toca FC, Extended-Release 5-FC (OBA Protocol #1120 Reviewed September 2011)

- ▶ The protocol has been modified to indicate that research participants who develop viremia or healthcare workers that have been accidentally exposed (e.g., needlestick injury) will be given at least two antiretrovirals to avoid the development of antiviral resistance if treatment with just azidothymidine (AZT) provided.
- ▶ To address the risk of cancer resulting from insertional mutagenesis with this retroviral vector, research participants will be monitored for new malignancies and if new tumors develop tumor tissue will be examined for the presence of the vector
- ▶ The recommendation that subjects be offered antivirals if persistent viremia occurs (at least one month) will not be implemented as the risk of insertional mutagenesis from such viremia is likely out-weighted by the risk of the mortality from the tumor. Antivirals will be given if there is evidence that the tumor is not responding.

A Phase I Trial of the Safety and Immunogenicity of a DNA Plasmid Based Vaccine Encoding the Amino Acids 1-163 of IGFBP-2 in Patients with Advanced Ovarian Cancer (OBA Protocol #1122, Reviewed December 2011)

- ▶ A subject's immune response to this vaccine may vary due to several factors, including the baseline immune response to IGFBP-2 prior to vaccination; expression of the protein in the tumor; and circulating levels of the protein. The analysis of the immune response rate will examine these factors.
- ▶ Since IGFBP-2 is expressed on normal as well as tumor cells, a toxicity to this vaccine may be autoimmunity. If evidence of autoimmunity detected steroids will be administered. However, since premature steroid administration may abrogate the immune response, the clinical protocol has been revised to indicate the criteria for initiating steroid treatment and the doses to be used.