

# GTSAB REPORT

## Recombinant DNA Advisory Committee

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RAC Chair

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# Protocols Submitted for Third Quarter 2015

## 30 total submissions

- Three were selected for public review
- Protocols not selected this quarter include:

Diseases (n=27)		
24 Oncology	1 Peripheral artery disease	1 Eye disorder
1 Monogenic diseases		

Vectors (n=27)		
5 Retroviruses	5 Plasmids	2 Adenoviruses
3 Lentiviruses	1 AAV	2 attenuated <i>Listeria monocytogenes</i>
2 RNA	5 HSV	1 DNA
1 vaccinia virus		

# Serious Adverse Events

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

# Opening of New Protocols Third Quarter 2015

**15 protocols notified NIH of enrollment (MIC1 submission)**

- **Six publicly reviewed**

# Protocols Initiated this Quarter

(publicly reviewed)

- **Phase I Trial of Intratumoral Injection of Vesicular Stomatitis Virus Expressing Human Interferon Beta in Patients with Sorafenib Refractory/Intolerant Hepatocellular Carcinoma and Advanced Solid Tumors with Liver Predominant Locally Advanced/Metastatic Disease (*0810-946 Reviewed December 2008*)**
- **Phase I Study of an Active Immunotherapy for Asymptomatic Phase Lymphoplasmacytic Lymphoma with DNA Vaccines Encoding Antigen-Chemokine Fusion (*1007-1050 Reviewed September 2010*)**
- **Phase I Study of an Active Immunotherapy for Asymptomatic Phase Lymphoplasmacytic Lymphoma with DNA Vaccines Encoding Antigen-Chemokine Fusion (*1007-1050 Reviewed September 2010*)**

# Protocols Initiated this Quarter

(publicly reviewed - continued)

- **A Phase I Study of Chimeric Antigen Receptor Modified T-cells Targeting NKG2D-Ligands in Patients with Acute Myeloid Leukemia/Advanced Myelodysplastic Syndrome and Multiple Myeloma (*1406-1319 Reviewed September 2014*)**
- **Pilot Study of Autologous T-cells Redirected to Mesothelin and CD19 with a Chimeric Antigen Receptor in Patients with Metastatic Pancreatic Cancer (*1410-1352 Reviewed December 2014*)**
- **Phase I, Randomized, Open-Label, Active-Controlled, Dose Escalation Study to Evaluate the Safety, Tolerability, and Immunogenicity of INO-1800 Alone or in Combination With INO-9112 Delivered IM followed by Electroporation in Select Nucleos(t)ide Analogue-Treated, HBeAgPositive, Chronic Hepatitis B Patients (*1411-1357 Reviewed March 2015*)**

# Protocols Initiated this Quarter

(not publicly reviewed)

- **A Phase I Study of Autologous T- Cells Genetically Modified at the CCR5 Gene by Zinc Finger Nucleases SB-728 in HIV Infected Patients Pre-treated or Not with Cyclophosphamide (1304-1228)**
- **Pilot Study of Autologous T Cells Redirected to EGFRvIII with a Chimeric Antigen Receptor in Patients with EGFRvIII+ Glioblastoma (1310-1267)**
- **Phase I Study of Cellular Immunotherapy Using Central Memory Enriched T Cells Lentivirally Transduced to Express an IL13Ra2-Specific, Hinge-Optimized, 41BB-Costimulatory Chimeric Receptor and a Truncated CD19 for Patients with Recurrent/Refractory Malignant Glioma (1310-1271)**
- **Phase I clinical trial of autologous CART-meso cells in patients with mesothelin expressing cancers (1311-1277)**
- **Administration of TGF-Beta Resistant Cytotoxic T-Lymphocytes to Patients with EBV-Positive Nasopharyngeal Carcinoma (RESIST-NPC) (1312-1282)**

# Protocols Initiated this Quarter

(not publicly reviewed)

- **A Phase 1b Randomized Clinical Trial to Evaluate the Safety and Immune Response to a Mammaglobin-A DNA Vaccine in Breast Cancer Patients Undergoing Neoadjuvant Endocrine Therapy (1406-1322)**
- **A Phase 1b Study Evaluating the Safety, Tolerability and Immunogenicity of CMB305 (Sequentially Administered LV305 and G305) in Patients with Locally Advanced, Relapsed, or Metastatic Cancer Expressing NY-ESO-1 (1408-1344)**
- **A Phase II, Single Arm, Multicenter Trial to Determine the Efficacy and Safety of CTL019 in Pediatric Patients with Relapsed and Refractory B-Cell Acute Lymphoblastic Leukemia (1410-1351)**
- **Phase I/II Study in WT1-Expressing Non-Small Cell Lung Cancer and Mesothelioma, Comparing Cellular Adoptive Immunotherapy with Polyclonal Autologous Central Memory to Naïve CD8+ T Cells that have been Transduced to Express a WT1-Specific T-Cell Receptor (1502-1388)**

# Recent Publications

## **4-1BB costimulation ameliorates T cell exhaustion induced by tonic signaling of chimeric antigen receptors.**

Long AH, Haso WM, Shern JF, Wanhainen KM, Murgai M, Ingaramo M, Smith JP, Walker AJ, Kohler ME, Venkateshwara VR, Kaplan RN, Patterson GH, Fry TJ, Orentas RJ, Mackall CL. *Nat. Med.* 2015 Jun; 21(6): 581-90

### **Results:**

- CD28 costimulation augments, whereas 4-1BB costimulation reduces, exhaustion induced by persistent CAR signaling
- CD19 CAR T cells incorporating the 4-1BB costimulatory domain are more persistent than those incorporating CD28 in clinical trials

# Recent Publications

## **NY-ESO-1–specific TCR–engineered T cells mediate sustained antigen-specific antitumor effects in myeloma.**

Rapoport AP, Stadtmauer EA, Binder-Scholl GK, Goloubeva O, Vogl DT, Lacey SF, Badros AZ, Garfall A, Weiss B, Finklestein J, Kulikovskaya I, Sinha SK, Kronsberg S, Gupta M, Bond S, Melchiori L, Brewer JE, Bennett AD, Gerry AB, Pumphrey NJ, Williams D, Tayton-Martin HK, Ribeiro L, Holdich T, Yanovich S, Hardy N, Yared J, Kerr N, Philip S, Westphal S, Siegel DL, Levine BL, Jakobsen BK, Kalos M, June CH. *Nat. Med.* 2015 Aug; 21(8): 914-21

### **Results:**

- NY-ESO-1 TCR-engineered T cells were safe, trafficked to marrow and showed extended persistence that correlated with clinical activity against antigen-positive myeloma.
- Encouraging clinical responses were observed in 16 of 20 patients (80%) with advanced disease, with a median progression-free survival of 19.1 months

**QUESTIONS?**