IBC Meeting Minutes

Meeting Minutes
10/2/2025

Voting Members Present
Biana Godin, PhD Chair
Daniel Kiss, PhD
Sasha Azar, PhD Vice Chair
Chas Gray, RPh
Jillian Chahal
Nagendran Tharmalingam, PhD
Vicente Zuno, BSO
Wenhao Chen, PhD
Tamara Steele
Anjana Tiwari, PhD
Francesca Taraballi, PhD
Joan Nichols, PhD
Jiangyong Shao

Other Non-Voting Attendees:
Malissa Mayer-Diaz
Leola Griffin
Prince Agyapong
Shane Wilson
Perla J. Rodriguez
Rebecca Corrigan
Joylise Mitchell
Enid Burns

Voting Members Absent:
Sachin Thakkar, PhD
Edward Graviss, PhD, MPH
Dimitrios L. Wagner, MD, PhD
Tanya Herzog, PhD

Non-Voting Members Present:
Leon Brown, M.S
Brenda Hartman, B.S
Astrid Quiroga
Gretchen Gotlieb

Call to Order:

The Institutional Biosafety Committee convened a virtual meeting via Microsoft Teams on October 2, 2025. The meeting was called to order at 11:03 a.m. with 13 members in attendance, exceeding the quorum requirement of 9 members.

Reports:

- **Office of Research Protection**
    - Discussion regarding generic IBC title updates. ORP will consult with IBC members to create a template for investigators.
- **Biosafety Officer Report**
    - None to report

Conflict of Interest:

Committee members were reminded by the IBC Chair to recuse themselves in the event of any conflicts of interest.

Old Business:

- A list of approved protocols was shown to committee members during the meeting.

New Business:

- A list of approved amendments via designated member review was shown to the committee members during the meeting.
- A list of approved administrative amendments was shown to the committee members during the meeting.
- A list of approved continuing reviews via designated member review was shown to the committee members during the meeting.

Minutes Review:

- The meeting minutes from September 4, 2025, were reviewed. A motion to approve was made and seconded, and the minutes were subsequently approved.
- **Motion: Approved**
    - Yes votes: 13
    - No votes: 0
    - Abstained: 0

AGENDA ITEMS

IBC NEW APPLICATIONS

IBC00002460
Title: Expanded Access Program of Cretostimogene Grenadenorepvec in Patients with Non-Muscle Invasive Bladder Cancer Unresponsive to Bacillus Calmette-Guerin
Principal Investigator: Raj Satkunasivam

Study Overview: This clinical trial is an Expanded Access Program for Cretostimogene Grenadenorepvec, intended for patients with non-invasive muscle bladder cancer that has not responded to standard treatment. The investigational agent is a recombinant, conditionally replication-competent adenoviral vector (serotype 5), engineered to act as an anti-tumor therapy. Its design allows it to selectively infect and replicate within cancer cells, initiating the lytic cycle only in those cells, while leaving normal cells unaffected. Key genetic modifications include:

Replication Control: The viral replication machinery is regulated by human promoters rather than viral ones. Specifically, the E1a promoter has been replaced with the E2F1 gene, which is transcriptionally inactive in normal cells. It becomes active only in cells with a defective retinoblastoma (Rb) pathway, a common feature in bladder cancer cells.
Immune Activation: The viral E3 gene has been removed and replaced with the human granulocyte-macrophage colony-stimulating factor (GM-CSF) gene. This modification helps recruit immune cells to the site of viral replication, enhancing the immune system's ability to recognize and respond to tumor antigens. The goal of this therapy is to achieve targeted destruction of cancer cells while stimulating a localized immune response.
Dosing Schedule: $1x10^{12}$ viral particles every week for six treatments.

- **Training**: All staff members have completed and are current with their required training.
- **Applicable NIH Guidelines**: Section III-C-1
- **Containment Conditions to be implemented**: BSL2
- **Risk assessment and Discussion**: Adenoviral vectors, like wild-type adenovirus, are easily transmissible. Potential routes of exposure include inhalation of aerosolized droplets, contact with mucous membranes, parenteral inoculation, and ingestion. Pregnant or breastfeeding individuals, as well as those who are immunocompromised or immunosuppressed, should not: Prepare, administer, or handle the study agent or any potentially contaminated materials; provide direct care to treated subjects exhibiting symptoms potentially related to the agent for at least two weeks post-treatment or until symptoms fully resolve. **Agent Handling and Transport:** The agent is received in frozen vial form. The pharmacy team will follow a specific protocol for thawing and preparation, which includes: performing all work within a glove box; placing the prepared syringe into a zip-lock bag, which is then transported in an igloo container to hospital care areas. **Documentation:** The provided Safety Data Sheet (SDS) is dated 2021. If a more current version is available, it should be submitted to ensure up-to-date safety information.
- **Comments sent to the PI for clarification**:
    - **Section Summary of Proposed Research**: The attached SDS is dated March 2, 2021. If a more recent version is available, please attach it.
    - **Exposure Management – Pharmacy**: Under engineering controls, update the reference from "BSC Class II Type A1/A2" to "Glove Box". Pharmacy

staff have indicated this is the equipment used for their work.

Motion: Approve by Administrative Review

- Yes Votes: 13
- No Votes: 0
- Abstained: 0

IBC00002372
Title: Phase 2 Open-label Multicenter Study of RP2 Oncolytic Immunotherapy Plus 2nd-line Therapy in Patients W/ Locally Advanced Unresectable, Recurrent, &/or Metastatic Hepatocellular Carcinoma
Principal Investigator: Maen Abdelrahim

Study Overview: The study team resubmitted this application for review after it was tabled by the IBC on August 7, 2025. This study evaluates the safety and efficacy of Oncolytic Immunotherapy RP2 in combination with atezolizumab and bevacizumab for the treatment of hepatocellular carcinoma (HCC). RP2 is an investigational oncolytic immuno-gene therapy derived from a modified herpes simplex virus (HSV), designed to selectively infect and destroy tumor cells and stimulate immune response.

- **Key Features of RP2:**
  - Engineered HSV with deletions (ICP34.5, ICP47) for tumor selectivity and enhanced antigen presentation.
  - Upregulation of US11 gene to support viral replication in tumors.
  - Expression of GM-CSF to promote dendritic cell activity.
  - Expression of GALV-GP R- to enhance tumor cell killing and immunogenic cell death.
  - Expression of anti-CTLA-4 antibody-like molecule to boost immune activation.
- **Dosing Schedule:**
  - **RP2**: Intratumoral administration up to 8 doses (Q2W for first 4 doses, then Q3W for up to 4 additional doses).
  - **Bevacizumab**: IV at 10 mg/kg Q2W for first 3 doses, then 15 mg/kg Q3W.
  - **Atezolizumab**: IV at 840 mg Q2W for 2 doses starting with RP2 dose 2, then 1200 mg Q3W starting with RP2 dose 3.
  - Combination dosing of atezolizumab and bevacizumab occurs on the same day, with bevacizumab administered at least 10 minutes after atezolizumab. All combination treatments must be given within 72 hours of RP2 dosing when scheduled in the same week.

- **Training**: All staff members have completed and are current with their required training.
- **Applicable NIH Guidelines**: Section III-C-1
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion**: While the study team has provided some of the missing information, several key items remain unresolved: the agent's name in the application should clearly indicate that it is an *oncolytic immuno-gene therapy based on herpes simplex virus;* specific contact information must be provided for staff in case of accidental exposure to the agent; the study team must respond to all questions in the *Clinical Trial Site* section, the *Engineering Controls* listed in both the *Pharmacy* and *Hospital Exposure Management* sections need to be appropriately updated.

- **Comments sent to the PI for clarification**:
    - **Sponsor Information:** Please add sponsor information and not just a phone number. Who can Employee Health contact if there is an accidental exposure?
    - **Hazard Identification:** The agent name needs to be updated to "RP2-oncolytic immuno-gene therapy based on HSV" - updating the name here will update the name in all other sections.
    - **Human Clinical Trials:** Under "For Human Gene Transfer protocols where HMRI is the initial clinical trial site, please answer the questions below:" While it was previously asked to clear the questions, please provide answers to questions 4-6.
    - **Exposure Management Pharmacy:** Please confirm which engineering control will be used. BSC class II Type A1 & A2 Recirculating are currently listed; however, pharmacy personnel indicated that a glove box is what is used for their work.
    - **Exposure Management Hospital:** Please confirm if BSC's are available in the hospital areas- under engineering controls, BSC Class II Type A2 vented are listed.
- **The motion to approve the study through designated member review was seconded and passed.**

Motion: Approvable by designated member review

- Yes Votes: 13
- No Votes: 0
- Abstained: 0

IBC AMENDMENTS

IBCA00001362
Title: Hazard Amendment 4 for Control of immune responses in transplantation
Principal Investigator: Xian Li

- *Dr. Wenhao Chen exited the meeting due to conflict of interest and did not vote. Quorum was maintained.*

- **Amendment Overview**: The study team seeks to add mouse tumor cell line TRAMP-C1, which will be injected subcutaneously into mice. The study team will also add mouse T cells that have been transduced in vitro with replication-incompetent retroviral vectors which will be injected intravenously into mice. **Genes of Interest**: Ezh2-/- TEa cells overexpressing WT EZH2 or SET domain-deleted EZH2, TEa cells overexpressing Tcf7, Id3, Klf2, or Lef1, and Cas9 Ezh2-/- TEa cells with deletion of Tcf1, Id3, Klf2, or Lef1). **Subcutaneous Tumor Growth Model:** The study team proposes to culture TRAMP-C1 cells under sterile conditions. Once harvested and resuspended in PBS, the cells will be injected subcutaneously—typically into the flank region of mice—to establish tumor growth. The progression of tumors and associated immune responses will be monitored and evaluated throughout the study. **Intravenous Injection of Transduced T Cells:** T cells will be transduced using either the pMYs-IRES-GFP or pLMPd-Ametrine retroviral vectors. Following transduction, cells expressing fluorescent markers (GFP or Ametrine) will be sorted via flow cytometry. The sorted cells will then be washed, counted, and injected intravenously into mice as part of transplantation models. The study will assess the fate and functional changes of the injected T cells in recipient animals.

- **Training**: All staff members have completed and are current with their required training
- **Applicable NIH Guidelines**: Section III-D-2
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion:** TRAMP-C1 cells are being acquired from ATCC, and the associated Product Sheet has been appended to the protocol. An amendment to the IACUC protocol is currently pending to reflect the use of TRAMP-C1 cells, which will be administered subcutaneously at a dose of 1–10 million cells in 100 µL PBS per mouse within ABSL1 containment. TRAMP-C1 is a murine prostate cancer cell line and does not pose a risk to human health, as it is non-pathogenic to humans. Standard personal protective equipment and appropriate engineering controls are in place to ensure safe handling. An updated Transport Protocol has also been provided. Additionally, the dose for the virally transduced mouse T cells is specified as less than 1 million cells per mouse.

- **The motion to approve the amendment was seconded and passed. The IBC subsequently approved the amendment.**

Motion: Approved

- Yes Votes: 12
- No Votes: 0
- Abstained: 0

Adjournment:

- The meeting adjourned at 11:58 am.
