IBC Meeting Minutes

Meeting Minutes
8/7/2025

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

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

Voting Members Absent:
Sachin Thakkar, PhD

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

Call to Order:

The Institutional Biosafety Committee convened a hybrid meeting via Microsoft Teams on August 7, 2025. The meeting was called to order at 10:08 a.m. with 15 members in attendance, exceeding the quorum requirement of 9 members.

Reports:

- **Biosafety Officer Report**
    - None reported

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 was shown to the committee members during the meeting.

Minutes Review:

- The meeting minutes from July 10, 2025, were reviewed. A motion to approve was made and seconded, and the minutes were subsequently approved.
- **Motion: Approved**
    - Yes votes: 15
    - No votes: 0
    - Abstained: 0

AGENDA ITEMS

IBC NEW APPLICATIONS

IBC00002369
Title: Phase 2 Study of Adjuvant V940 (mRNA-4157) + Pembrolizumab vs Placebo + Pembrolizumab in High-Risk Muscle-Invasive Urothelial Carcinoma Post-Radical Resection (Randomized, Double-Blind, Controlled)
Principal Investigator: Raj Satkunasivam

- **Study Overview**:
  This clinical trial investigates the safety and efficacy of V940 (mRNA-4157), a personalized mRNA-based neoantigen therapy, in combination with pembrolizumab, with or without enfortumab vedotin, in patients with muscle-

invasive urothelial carcinoma who are ineligible for cisplatin-based chemotherapy.
Cohorts:
- Adjuvant Cohort: ~200 participants post-radical resection. Primary objective is to compare disease-free survival (DFS) between V940 + pembrolizumab vs. placebo + pembrolizumab.
- Perioperative Cohort: ~30 participants receiving treatment in both neoadjuvant and adjuvant settings.
V940 Details:
V940 is a custom-manufactured mRNA therapy encoding patient-specific tumor neoantigens, formulated in lipid nanoparticles. It is administered as a sterile injectable dispersion and stored frozen. Each participant receives up to 9 doses across treatment periods.
Dosing Schedule:
- Adjuvant Cohort: V940 or placebo every 3 weeks for 9 doses.
- Perioperative Cohort: Dosing begins in the neoadjuvant period and continues post-surgery to complete 9 total doses.

- **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**: BSL1
- **Risk assessment and Discussion**: As an mRNA molecule with a large molecular weight, little to no systemic absorption is expected to occur in a workplace setting. It is also expected to rapidly degrade in the digestive tract following accidental ingestion. Ribonucleotides in water are expected to degrade rapidly in the environment. No special precautions are needed. Overall, the weight of evidence indicates that the genotoxic risk to humans is considered low due to minimal systemic exposure following intramuscular administration, limited duration of exposure, and negative in vitro results.
- **The motion to approve the study was seconded and passed. The IBC subsequently approved the study**

Motion: Approve

- Yes Votes: 15
- No Votes: 0
- Abstained: 0

IBC00002339
Title: Phase 2, randomized, open-label, controlled study to assess efficacy & safety of rapcabtagene autoleucel vs comparator in severe, refractory idiopathic inflammatory myopathy participants

Principal Investigator: Sarah Kazzaz

- **Study overview:** This study evaluates the safety and efficacy of rapcabtagene autoleucel (YTB323), a CD19-directed CAR-T cell therapy, in patients with severe, refractory, active idiopathic inflammatory myopathies, including Dermatomyositis (DM), Anti-Synthetase Syndrome (ASyS), and Immune-Mediated Necrotizing Myopathy (IMNM), with or without secondary Interstitial Lung Disease (ILD). Idiopathic inflammatory myopathies are autoimmune diseases characterized by autoantibody production by B cells, leading to muscle and organ damage. Current therapies inadequately target these autoantibody-producing B cells, leaving a significant unmet medical need.
  Rapcabtagene autoleucel (YTB323) is an investigational autologous CAR-T therapy manufactured using the T-Charge process, which preserves naïve and stem cell memory T cells, potentially enhancing therapeutic efficacy and persistence. The therapy uses a third-generation lentiviral vector (CTL019) to transduce patient-derived T cells with an anti-CD19 chimeric antigen receptor.
  Dosing:
  • T cells are collected from patients and shipped to Novartis for processing.
  • The final product is cryopreserved in bags ranging from 10–30 mL, depending on dose and transduction efficiency.
  • Recommended dose range: 1.0–3.0 × 10^9 CD3+ cells, not exceeding 20.0 × 10^9 total nucleated cells (TNC).
- **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**:
  - The study team should specify the doses to be administered. The text in section hazard identification states the amount of cells that are to be shipped to Novartis for IP production.
  - The Investigational Brochure's safety cut-off date is 5-15-24. An updated document should be provided.
  - Clinical protocol approval and IRB approval need to be provided when available.
  - Oxford BioMedica (Third party vendor) is mentioned as the source, while in other parts of the protocol states Novartis.
- **Comments sent to the PI for clarification**:
  - **Summary Of Proposed Research:** In the statement: "Then we take these cells to the sponsor's manufacturing facility and we modify them so they can attack and destroy other immune cells, the B cells, that contribute to the myositis pathogenesis. We modify the T cells so they can target the CD19 protein that is expressed in the B cells. To achieve this, we transfer genetic material in the cells in the lab using a carrier virus. After the process is completed in the manufacturing facility, the cells are shipped back to the site and the patients will receive back their own modified T cells, called now

YTB323, CAR-T cells, via an intravenous infusion" - The language should be amended to make it clear that the study team is NOT modifying the T cells, but only using the end product. Please also specify the doses to be administered here - The text in section hazard identification states "Total viable total nucleated cells is recommended to not exceed 20.0 x 10e9 TNC for a range between 1.0 - 3.0 x 10e9 CD3+ cells. These cells will be shipped to Novartis for IP production.
The finished product bags/cryobags range in volume from 10 to 30 mL depending on the target dose and transduction efficiency of the T cells." Please include the administration dose or dose range. Additionally, the Investigational Brochure's safety cut-off date is 5-15-24. An updated document should be provided.

- **Human Clinical Trials:** IRB protocol in HMH is still under review. Please attach the IRB approval when it is available. For the Novartis protocol attached it says "Content final Date: 17-May-2024" – if the protocol expires, please provide an updated protocol.
- **Viral Studies:** Here, Oxford BioMedical (Third party vendor) is mentioned, while in other parts of the protocol it says Novartis. Please clarify.

- **The motion to approve the study through designated member review was seconded and passed.**

Motion: Approvable by designated member review

- Yes Votes: 15
- No Votes: 0
- Abstained: 0

IBC00002249
Title: In-vivo effect of Oncomagnetic Device on Implanted Tumor
Principal Investigator: Martyn Sharpe

- **Study Overview**: The study aims to investigate the role of thymidine kinase (TK) in modulating the effects of acyclovir on tumor progression and the immune response in brain tumors. The objective is to identify key immune components involved in the brain tumor microenvironment.
Mouse glioma GL-261 cells will be genetically modified to overexpress the thymidine kinase enzyme using commercially available lentiviral particles. These transformed cells will then be injected intracranially into Black6 or C57BL/6 mice. Tumor development will be monitored using MRI scans with gadolinium contrast. Following tumor confirmation, mice will be divided into two groups: one receiving acyclovir (50–150 mg/kg/day) via oral gavage, and the other receiving a placebo. After 10 days of treatment, a second MRI scan will be conducted. All animals will then be euthanized, and brain tissues will be collected for histological and immunohistochemical analysis.

- **Training**: All staff members are currently up to date with their training.
- **Applicable NIH Guidelines**: Section III-D-1
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion**:
    - Regarding the animal studies, the ABSL indicated for GL1261 mouse cell line overexpressing thymidine kinase must be updated to ABSL2.
    - Given that the title includes "oncomagnetic device", there should be a description or summary regarding how the oncomagnetic device is related to the proposed research.
    - It's unclear whether the lentiviral constructs are being used in the same manner or if they serve distinct purposes.
    - Since MRI studies are indicated, the radiation safety committee application must be filled and completed.

- **Comments sent to the PI for clarification**:
    - **Summary of Proposed Research**: Given that the title includes "oncomagnetic device", there should be a description or summary regarding how the oncomagnetic device is related to the proposed research. Are both lentiviral constructs being used in the same way or are they distinct? Please provide a diagrammatic workflow of the lentiviral experimental procedures for clarity.
    - **Animal Sections**: The ABSL indicated for GL1261 mouse cell line overexpressing thymidine kinase must be updated to ABSL2
    - **Other Agents**: Since MRI studies are indicated, please answer "yes" under "*Will you be using any Radioactive Materials / X-Rays / Lasers in the course of the work listed in this application?"* and link the associated RSC application RSC00000830
- **The motion to approve the study after designated member review was seconded and passed.**

Motion: Approve after Designated Member Review

- Yes Votes: 15
- No Votes: 0
- Abstained: 0

IBC00002321
Title: Phase 1 Study of NKX019, a CD19 Chimeric Antigen Receptor Natural Killer Cell Therapy, in Subjects with Autoimmune Disease
Principal Investigator: Myriam Guevara

- **Study overview**: This Phase 1 study assesses the safety and tolerability of NKX019, an allogeneic CAR-NK cell therapy, in patients with active lupus nephritis

or primary membranous nephropathy. Participants undergo lymphodepletion with fludarabine and cyclophosphamide prior to receiving NKX019 on Days 0, 3, and 7. Each dose is followed by a 24-hour observation period, after which participants are discharged with home monitoring instructions. Dose-limiting toxicities are monitored through Day 28, with oversight by a Data Safety Monitoring Board. NKX019 is manufactured from $CD56^{+}CD3^{-}$ NK cells sourced from screened healthy donors. Cells are expanded and transduced with a γ-retroviral vector encoding a CAR and membrane-bound IL-15. The final product undergoes rigorous release testing for identity, potency, sterility, and viral safety. The investigational agent is processed at the Ann Kimball & John W. Johnson Center for Cellular Therapeutics and transported to the bedside in a labeled biohazard cooler via off-stage elevators.

- **Training**: All staff members are currently up to date with their training.
- **Applicable NIH Guidelines**: Section III-C-1
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment and Discussion**:
    - This study is appropriately classified as Risk Group 2 (RG2) and requires BSL-2 containment. Exposure to NKX019 presents risks similar to handling human blood. NKX019 is manufactured using a γ-retroviral vector to introduce a transgene into donor-derived NK cells. To mitigate the risk of residual replication-competent retrovirus (RCR), each batch of NKX019 undergoes quantitative PCR testing for rare recombination events. Additionally, all γ-retroviral vector batches are screened for retroviral contaminants. While integration of the vector into the NK cell genome carries a theoretical risk of insertional mutagenesis, any transformed cells would likely be cleared by the host immune system due to the allogeneic nature of the product. Universal precautions will be followed to minimize exposure risk to personnel handling the agent.
- **The motion to approve the study was seconded and passed. The IBC subsequently approved the study.**

Motion: Approved

- Yes Votes: 15
- 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**: 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 and Discussion:** Several critical items are either missing or inadequately addressed in the submitted protocol.
  - **Sponsor Contact Information**: The protocol must include complete contact details for the study sponsor, including a phone number
  - **Drug Handling and Administration Details**: Clarify who will be responsible for transferring, handling, and administering the investigational drug (RP2). This should include roles such as pharmacists, nurses, and other study personnel handling the agent.
  - **Universal Precautions Statement**: A statement emphasizing the necessity of universal precautions when handling RP2 needs to be included. Specifically:
    - Personnel must not have open skin lesions when handling RP2 or

contaminated materials.
        - All individuals handling RP2 must follow institutional safety protocols.
        - Pregnant study personnel must not handle RP2.
    - **Replication Characteristics**: RP2 replicates selectively in tumor tissue and is attenuated in normal tissue
    - **Host Range and Target Cells**: Host range is human, as stated on page 25 of the pharmacy manual. The target cells are tumor cells, not human T cells.
    - **Transmission Risks**: Potential transmission routes include:
        - Accidental parenteral inoculation
        - Droplet exposure to mucosal membranes
        - Contamination of broken skin
    - RP2 is sensitive to thymidine kinase inhibitors, including acyclovir, Famciclovir, & Cidofovir. Information regarding medical treatment and hazards should be included as written in the pharmacy manual
- **Comments sent to the PI for clarification**:
    - **Staff Identification:** Provide information related to who will transfer the drug, transport the drug, handle the drug and administer the drug. (-) If the research nurse will be administering the drug, she must first complete the required credentialing process. Once credentialed, she should be added to the study staff section, as she may be exposed to the RP2 drug during the course of the study.
    - **Hazard Identification:** Pharmacy services have been indicated throughout the protocol. Please select "pharmacy" and fill out the corresponding section "Exposure Management- Pharmacy". In this section, provide a transport SOP that describes transport from the Pharmacy to the patient care areas.
    - **Sponsor Information:** Please provide contact information for the company. If there is an accidental exposure the institutional representative will need to call the sponsor.(-) Under "Other sponsor information" include the sponsor phone number
    - **Summary Of Proposed Research:** Spell out IDS pharmacy. Is this the pharmacy at Houston Methodist? Please add a statement regarding the need for use of universal precautions when handling RP2. That means, pharmacists, nurses and other study staff should ensure that:
      They do not have open skin lesions when handling RP2 or materials that have come into contact withP2; all personnel handling the virus or material contaminated with it must observe safety precautions per institutional standards. Study personnel who are pregnant should not handle RP2.
    - **Risk Assessment:** The agent is actually RP2, an oncolytic immuno-gene therapy based on herpes simplex virus (HSV). Please make this change.
    - **Human Clinical Trials:** Regarding questions #4-6- RP2 - is derived from

a new clinical isolate of HSV resulting from a comprehensive screen of clinical strains for their ability to infect & kill human tumor cells. Is this the first-time use in human subjects? If not, please clear all answers in questions #4-6.

- **DNA Studies:** There are several genes that have been added or modified. Please list these genes and not just RP2. For example: The HSV gene encoding ICP34.5 was deleted to enhance tumor selectivity, HSV US11 gene upregulated to overcome the reduction in replication in tumors otherwise resulting from deletion of ICP34.5; ICP47 deleted to prevent inhibitions of antigen presentation (ICP47 blocks TAP); expression of GM-CSF –promotes dendritic cell expansion & maturation; expression of a potent fusogenic protein (GALV-GP R-) which substantially increases tumor killing & immunogenic cell death, thereby intended to maximize Signal 1; expression of an anti-CTLA-4 antibody-like molecule to block the B7/CTLA-4 negative feedback interaction, enhancing both Signal 1 & Signal 2. Provide transport protocol from pharmacy to patient care areas. If there is an accidental exposure, the safety team will need to know where to go.
- **Viral Studies**: **Replication and Tissue Specificity**: RP2 selectively replicates in tumor tissue and is attenuated in normal tissue. This should be clearly stated in the protocol. **Host Range**: HSV has a broad host range, but in this study, the relevant host is human. Page 25 of the pharmacy manual confirms human host range—please revise the protocol to reflect this and ensure consistency with the manual. **Recipient and Target**: The intended recipient is a human subject, with RP2 administered indirectly into tumor tissue. The target is cancer cells, not human T cells. This distinction should be clearly reflected in the protocol.
- **Exposure Management- Clinic/Hospital:** Include that transmission can be accidental parenteral inoculation, droplet exposure to mucosal membranes or contamination of broken skin. Drug susceptibility- RP2 should be sensitive to thymidine kinase inhibitors acyclovir, famciclovir and cidofovir. Pg 26 of the pharmacy manual provides medical treatment and hazards that should be included in this section.

- **The motion to Table the study was seconded and passed.**

Motion: Table

- Yes Votes: 15
- No Votes: 0
- Abstained: 0

IBC AMENDMENTS

IBCA00001277

Title: Hazard Amendment 2 for IBC for Effect of over-expression of antioxidant enzymes in brain cells on spin oscillating magnetic field (sOMF) induced toxicity
Principal Investigator: Santosh Helekar

- **Amendment Overview**: To evaluate the effects of oncomagnetic treatment in animal models, including large animal models, a lentiviral system carrying the gene of interest will be used to achieve stable expression of genes or shRNAs in human, mouse, and pig cells. These modified cells will be used to mimic gene expression profiles characteristic of human glioblastoma
- **Training**: All staff members have completed and are current with their required training
- **Applicable NIH Guidelines**: Section III-D-1-3
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion:**
    - The lab has experience performing this work with mouse GLB cells and they will use the same safety and containment procedures. The cells will be injected surgically, so the PI needs to remove the reference in the animal section that states the cells will be handled in a BSC. The IACUC protocol has not been updated to add these experiments in pigs.
- **Comments sent to the PI for clarification**:
    - **Exposure management- Animal Facility**: The cells will be injected surgically. The PI needs to remove the reference in the animal section that states the cells will be handled in a BSC. Select “other” and include the information under “if other, please describe.”
    - **Exposure management- Animal Areas**: Transport protocol expires in September 2025 (refer to target review date). Please provide an updated transport SOP and update the target review date.

- **The motion to approve the amendment by designated member review was seconded and passed.**

Motion: Approved by Designated Member Review

- Yes Votes: 15
- No Votes: 0
- Abstained: 0

Adjournment:

- The meeting adjourned at 10:52 am.