THOMAS JEFFERSON UNIVERSITY
MINUTES
INSTITUTIONAL BIOSAFETY COMMITTEE
DATE: June 18, 2025
Re-scheduled from June 13, 2025

Attendance: Total Attending: # 7 **Voting Members Present**: #7

Called to Order: 09:02 a.m.

Name	Expertise	Present
Linda Cassidy, MS	Non-Voting Member	
Sue Gotta, MS	rDNA; Select Agents	X
Gerald Grunwald, PhD	rDNA; Biochemistry; Cellular & Developmental Biology	X
Douglas C. Hooper, PhD	rDNA; Immunology; Gene Transfer	X
Botond Igyarto, PhD	Microbiology	X
Loretta Kelly, Esq.	Non-affiliate Community Member	X
Kathleen "Kitty" Kono	Non-Affiliate Community Member	
Phil LaTourette, DVM	Laboratory Animal Sciences	
Sara Meyer, PhD	Cancer Biology	
Fabienne Paumet, PhD	Cellular Biology & Biochemistry	X
Zia Rahman, PhD	Microbiology	
Yuri Sykulev, PhD	Microbiology	X

MINUTES REVIEWED:
May's minutes were not presented for review.

NEW PROTOCOLS:

1. Principal Investigator EB
IBC Control#25-04-944 "*Discovery, validation, and translation of acquired and intrinsic resistance to anticancer therapy"*

A motion was made and seconded to defer this protocol to our next meeting so that the PI can provide additional information. The motion was unanimously approved.

This protocol was reviewed under NIH Category E and assigned BSL2. The principal risks identified were:
Human lung, sarcoma, and connective tissue cell lines
Organoid models of cancer
Replication incompetent lentivirus
CRISPR-Cas9
The risks were adequately identified by the Principal Investigator and a final assessment regarding appropriate mitigation will be made upon review of the revised protocol.

Protocol Summary:

The purpose of the study is to learn how cancers become resistant to treatments and ways to overcome that resistance. Cell culture and organoid models of cancer will be used. Traditional therapies will be given to the cells/organoids to study the development of resistance. Then combinatorial drug strategies or genetic manipulations of the cell lines to their

tumor suppressor pathways or oncogenes will be done to see if this resistance can be overcome. Lentiviral vectors, CRISPR-Cas9, and small molecular inhibitors will be used to accomplish these genetic manipulations.

Discussion/Clarifications Requested:

- **Protocol Summary:**
  - The summary is sufficient but additional methodological detail is needed.
- **Biological Agents:**
  - The table in question #1 needs to be completed correctly.
  - Question #3, the abbreviation "TU" needs to be defined.
  - Question #10 is answered "yes," but there was nothing in the protocol summary referring to the use of irradiation.
- **Recombinant:**
  - Questions #3a-c needs to be modified if using lentiviral vectors.
- **Toxins:**
  - Page needs to be deleted as no toxins are used in the protocol.
- **Facilities:**
  - Question 1b should also have 70% EtOH checked.
  - Question #4 needs to be appropriately answered.
- **Attachments:**
  - SOP: A spill in the BSC needs to be followed up with 70% EtOH.

2. Principal Investigator UG

IBC Control#25-04-949 "*A Phase 1/2 Multi-Center Study Evaluating the Safety and Efficacy of LYL314, a CD19/CD20 Dual-Targeting Chimeric Antigen Receptor T-Cell Therapy in Participants with Aggressive B-Cell Non-Hodgkin Lymphoma"* at CC.

A motion was made and seconded to provisionally approve this protocol pending minor clarifications that will be administratively reviewed. The motion was unanimously approved.

This protocol was reviewed under NIH Category C. The principal risks identified were:
CAR-T cells
Lymphodepleting therapy
The risks were adequately identified by the Principal Investigator and appropriate mitigation was described in the protocol.

Protocol Summary:

The purpose of this study is to evaluate the safety and efficacy of LYL314, a CD19/CD20 dual-targeting CAR-T cell therapy, in patients with aggressive B-Cell Non-Hodgkins Lymphoma. LYL314 is an autologous T-cell product transduced with a lentiviral vector to express a dual-targeting CAR targeting CD19 and CD20. This CAR construct is designed to increase the complete response rate in participants with B-cell lymphoma and to prolong the duration of response.

Discussion/Clarifications Requested:

- **Lay Summary:**
  - Specify B-cell cancers vs cancer.
- **Biological Agents:**
  - Question #4, CAR-T cells are replication competent, so this should be checked "yes."
- **Recombinant**
  - Question #2b, the cell description needs to be corrected, the CAR-T isn't GPRC5D but CD19 and CD20.

3. Principal Investigator UG

IBC Control#25-05-454 "*A Phase 1/2 Multi-Center Study Evaluating the Safety and Efficacy of LYL314, a CD19/CD20 Dual-Targeting Chimeric Antigen Receptor T-Cell Therapy in Participants with Aggressive B-Cell Non-Hodgkin Lymphoma"* at LVHN

A motion was made and seconded to provisionally approve this protocol pending minor clarifications that will be administratively reviewed. The motion was unanimously approved.

This protocol was reviewed under NIH Category C. The principal risks identified were:
CAR-T cells
Lymphodepleting therapy
The risks were adequately identified by the Principal Investigator and appropriate mitigation was described in the protocol.

Protocol Summary:

The purpose of this study is to evaluate the safety and efficacy of LYL314, a CD19/CD20 dual-targeting CAR-T cell therapy, in patients with aggressive B-Cell Non-Hodgkins Lymphoma. LYL314 is an autologous T-cell product transduced with a lentiviral vector to express a dual-targeting CAR targeting CD19 and CD20. This CAR construct is designed to increase the complete response rate in participants with B-cell lymphoma and to prolong the duration of response.

Discussion/Clarifications Requested:

- **Lay Summary:**
  - Specify B-cell cancers vs cancer.
- **Biological Agents:**
  - Question #4, CAR-T cells are replication competent, so this should be checked "yes."
- **Recombinant**
  - Question #2b, the cut and paste error needs to be corrected, the CAR-T isn't GPRC5D but CD19 and CD20.

4. Principal Investigator UG
IBC Control#25-04-948 "*A Phase 2, Open-Label, Multicenter Study of Arlocabtagene Autoleucel (BMS-986393), a GPRC5D-directed CAR T Cell Therapy in Adult Participants with Relapsed or Refractory Multiple Myeloma (QUINTESSENTIAL)"*

A motion was made and seconded to provisionally approve this protocol pending minor clarifications that will be administratively reviewed. The motion was unanimously approved.

This protocol was reviewed under NIH Category C. The principal risks identified were:
CAR-T cells
Lymphodepleting therapy
The risks were adequately identified by the Principal Investigator and appropriate mitigation was described in the protocol.

Protocol Summary:

This trial aims to evaluate efficacy and safety of BMS-986393 in both triple and quadruple-class exposed Multiple Myeloma (MM), a cancer of blood plasma, i.e. the participant population have received at least 3 or 4 prior lines of therapy (LOT). BMS-986393 is an investigational CAR-T cell product that consists of autologous T-cells that have been transduced ex-vivo with a genetically engineered replication-incompetent, third-generation, self-inactivating lentiviral vector encoding a G protein-coupled receptor class C, group 5, member D (GPRC5D)-specific chimeric antigen receptor (CAR). GPRC5D-specific CAR, expressed on the T-cell surface, provides signals for T cell activation and co-stimulation upon antigen binding, eliciting T cell proliferation and cytokine secretion, and redirecting cytolytic activity against

GPRC5D-expressing cells. Due to integration of the viral vector into the host genome, these sequences will be present as a stable, integral part of the host DNA in transduced T cells during the duration that the cells persist following infusion. The vector does not encode any pathogenic genes and is not itself handled at the clinical site. The lentiviral vector used to transduce the autologous T lymphocytes is replication-incompetent, self-inactivating. It is not capable of replicating in human cells and therefore cannot form progeny virions that would result in the spread of a replicating virus or recombination with other retroviruses.

Discussion/Clarifications Requested:

- **Lay Summary:**
  - The last sentence needs to be simplified, and the technical terms defined.
- **Biological Agents:**
  - Question #4, CAR-T cells are replication competent, so this should be checked "yes."
- **Recombinant**
  - Question #2b, the plasmid encodes for more than GPRC5D, please list the other CAR components.

5. Principal Investigator MS

IBC Control#25-04-945 "*A Phase 1/2 Study of EG-70 as an Intravesical Administration to Patients with BCG-Unresponsive Non-Muscle Invasive Bladder Cancer (NMIBC) and High-Risk NMIBC Patients who are BCG Naïve or Received Incomplete BCG Treatment"*

A motion was made and seconded to provisionally approve this protocol pending minor clarifications that will be administratively reviewed. The motion was unanimously approved.

This protocol was reviewed under NIH Category C. The principal risks identified were:
Recombinant plasmid within nanoparticles
Human material
The risks were adequately identified by the Principal Investigator and appropriate mitigation was described in the protocol.

Protocol Summary:

This clinical trial evaluates detalimogene voraplasmid (EG-70), a non-viral, intravesically administered gene therapy. The goal of the trial is to assess the safety, tolerability, and preliminary efficacy of EG-70 in patients with high-grade non-muscle invasive bladder cancer (NMIBC). The ongoing Phase 2 portion of the study is designed to determine EG-70's ability to elicit complete responses and prevent recurrence or progression. A new cohort was added in Phase 2 to include patients with high-grade papillary-only disease, which means tumors that protrude from the bladder lining but without coexisting carcinoma in situ (CIS). Papillary tumors are generally easier to visualize and remove, whereas CIS presents as flat, more aggressive lesions that are difficult to detect and treat. This addition helps to assess EG-70's efficacy in a broader population.

EG-70 is a non-viral gene therapy composed of plasmid DNA (pDNA) encoding human interleukin-12 (IL-12) subunits (p35 and p40) and RIG-I agonists, which are synthetic RNA elements that activate innate immune responses. These plasmids are packaged in proprietary nanoparticles formed from two polymers: RXG and PEG-b-PLE. This nanoparticle delivery system enables localized uptake by bladder urothelial cells and expression of the immunostimulatory proteins. The plasmid is non-replicating, non-integrative (it does not insert into the human genome), non-viable, and non-infectious. The study includes the collection of human biological specimens including blood, urine, and, when clinically indicated, bladder tissue biopsies. These specimens will be processed for pharmacokinetic analysis, immune response markers, and exploratory biomarkers by an outside laboratory.

Discussion/Clarifications Requested:

- **Recombinant**
  - Question #2b, should also include the short repeating bovine elastin sequence linking p35 and p40.

- **Safety**
  - Are needles involved in reconstituting the plasmid for the instillation process. If so, and an accidental needlestick occurs, what would the risk be to the personnel?

ADMINISTRATIVELY APPROVED ITEMS:
The KSI database indicates the following items have been given administrative approval since our last meeting:

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Protocol #	PI	Form type	Comments
22-10-594	LC	CR	No changes
21-08-423-1	YK	CR	No changes
24-07-873	DM	CR	No changes
21-06-395-1	JM	CR	Personnel updated
24-05-846	JM	CR	Personnel updates
24-07-871	MD	CR	No changes
22-04-498-1	MR	CR	Personnel updates
24-07-875	DT	CR	No changes
24-02-809	NN	CR	No changes
23-08-716	TC	CR	No changes
22-07-525-1	KB	CR	Personnel updates
22-12-614	MT	Amendment	Personnel updates, human primary PBMCs added
24-09-886	MO	Amendment	Updated IB and Injection manual added
23-10-731	JL	Amendment	Hazardous chemical added
22-08-534	AS	Amendment	Whole platelets added
21-11-459	AF	Amendment	No changes
23-05-681	AF	Amendment	Personnel updates
24-04-837	BE	CR	No changes
22-04-505-1	LL	CR	No changes
22-03-493-1	AS	CR	No changes
21-03-355	RP	Amendment	Personnel updates, new human cell lines added
24-05-855	RS	Amendment	Updated IB as well as package inserts for standard of care drugs added
21-07-403-1	FB	CR	New human cell lines added
22-12-614	MT	Amendment	Personnel updates, new recombinant DNA added
24-05-850	DT	CR	No changes
21-12-462-1	SM	CR	No changes

OTHER BUSINESS:

- Institutional Biosafety Office Sue Gotta reported that the room 352 JAH project is waiting for the final go-ahead, and that should be given shortly. Basically, the project is about 3 months behind the original schedule.
- Ms. Gotta also reported that the 5 West JAH project is nearing completion and is to be occupied July/August. She has also initiated an EM exercise with the students from TJU's Emergency and Disaster Management M.S. Program for this area. It will be held on July 17th.
- IBC Chair Dr. Grunwald gave a brief update on the grant funding situation.

Meeting Adjourned: approximately 09:35 a.m.

Respectfully submitted for the IBC,

/s/Gerald Grunwald, PhD
Chair, Institutional Biosafety Committee

GG/sg