

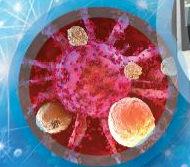
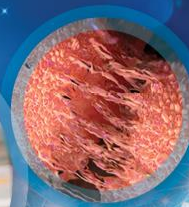
AACR

American Association
for Cancer Research®

**ANNUAL
MEETING**

2023

APRIL 14-19 • #AACR23



A novel combination therapy of arenavirus vectors and PD1-IL2v strongly potentiates tumor specific T cell responses resulting in synergistic anti-tumor efficacy

Judith Strauss, PhD

Hookipa Pharma, New York, NY

Judith Strauss

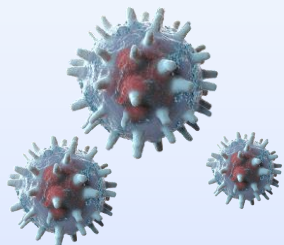
I have the following relevant financial relationships to disclose:

Employee of: **Hookipa Pharma**

Stockholder in: **Hookipa Pharma**

Hookipa's replicating arenaviral vector technology drives CD8⁺ T cell killing of tumors

Engineered arenaviral vectors
infect and activate (but do not kill)....



- Replication competent, attenuated
- Non-oncolytic
- Encoding tumor associated antigens for active immunization
- Two different vectors (artLCMV and artPICV) allow alternating administration

Infect

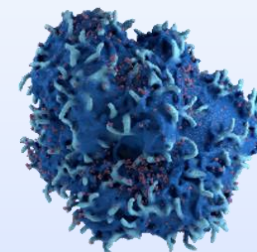
...Antigen presenting cells,
which **express and present** the
vector-encoded antigens to....



- Dendritic cells, Monocytes, Macrophages

Activate

...CD8⁺ T cells, which get
activated and **kill tumor cells**



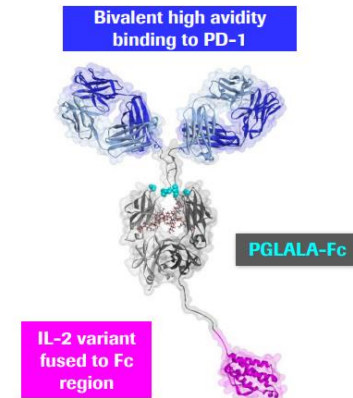
- High frequency CD8⁺ T cell responses in mice and humans

GOAL

Maximize the therapeutic efficacy of arenaviral vectors by combining with other therapeutic modalities

PD1-IL2v

- Delivers IL-2v in cis to PD-1⁺ T cells whilst blocking PD-1
- Preferentially targets conventional CD8⁺ effector T cells over CD4⁺ regulatory T cells
 - IL-2v does not bind IL-2R α (predominantly on Tregs)
 - PD-1 is expressed on activated T cells
- PD1-IL2v treatment generates better effector cells (more cytotoxic, less exhausted) than PD-1/-L1 blockade alone (Codarri et. al, 2022)



Roche template, 2021

Does therapeutic cancer vaccination with arenavirus vectors synergize with PD1-IL2v?

Vectors & Tumor Models

artLCMV-TRP2 (B16.F10 model)
= tumor-associated self antigen

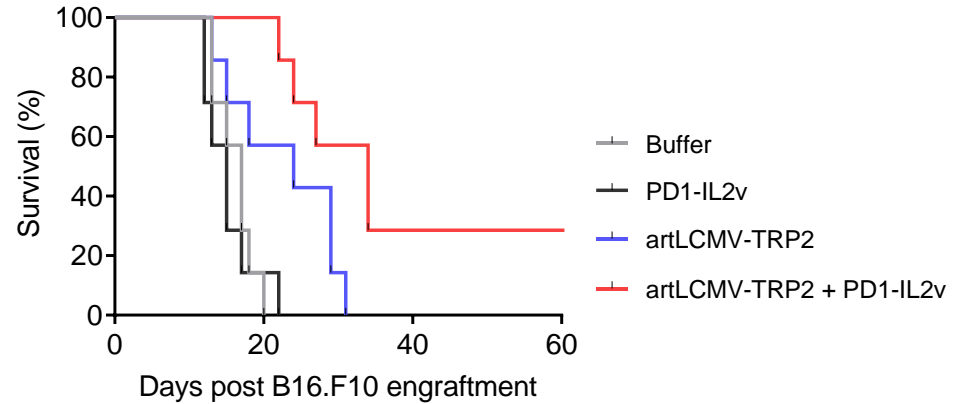
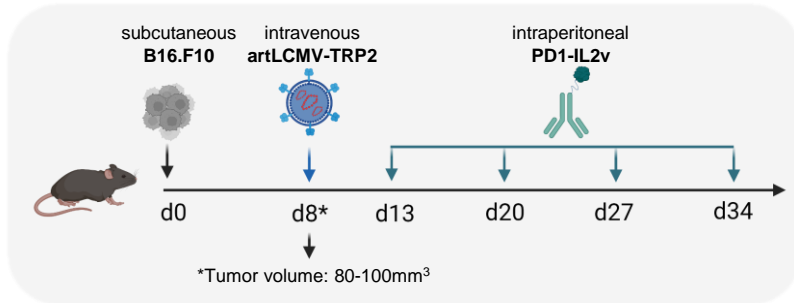


artLCMV-E7E6 (HPV16+ cancers, TC-1 model)
= oncoviral antigen

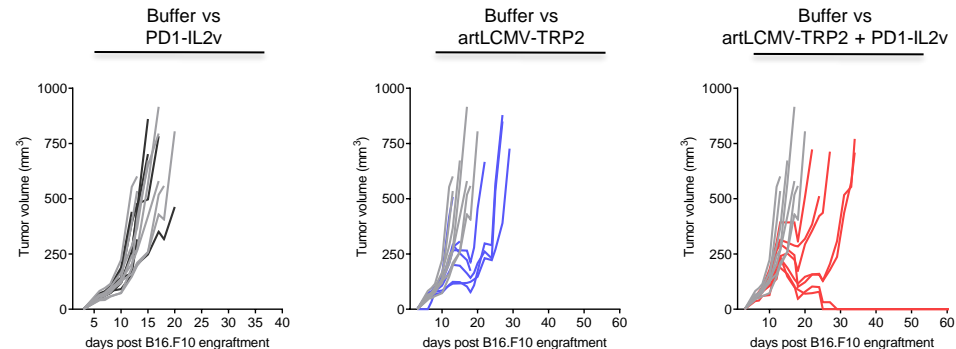
artLCMV-TRP2 + PD1-IL2v combination therapy synergistically improves tumor clearance

DO NOT POST

APRIL 14-19 • #AACR23

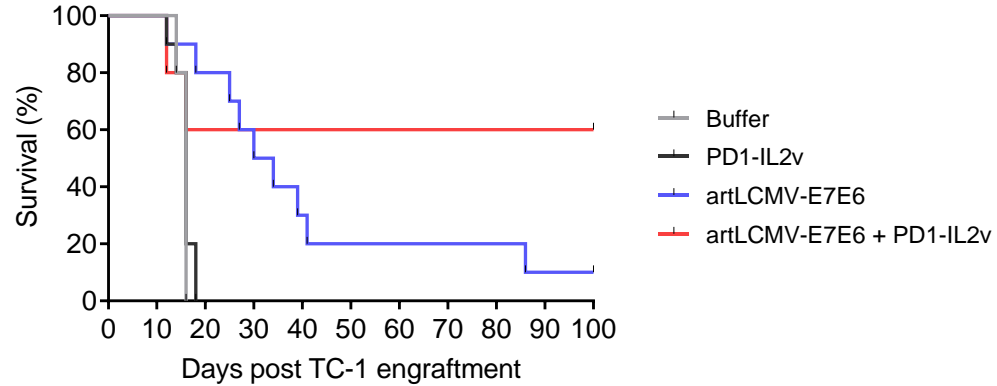
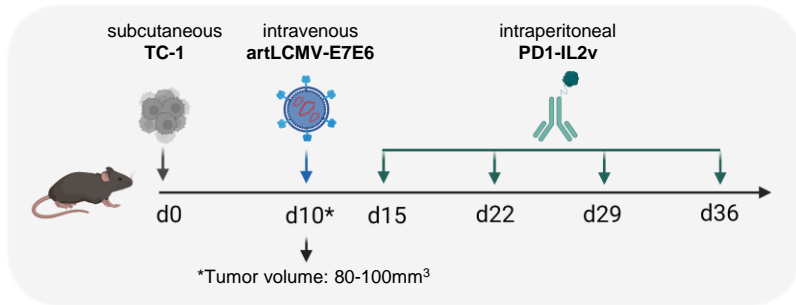


- **Increased survival time and tumor control** in artLCMV-TRP2 monotherapy
- **~30% tumor eradication** in combination therapy

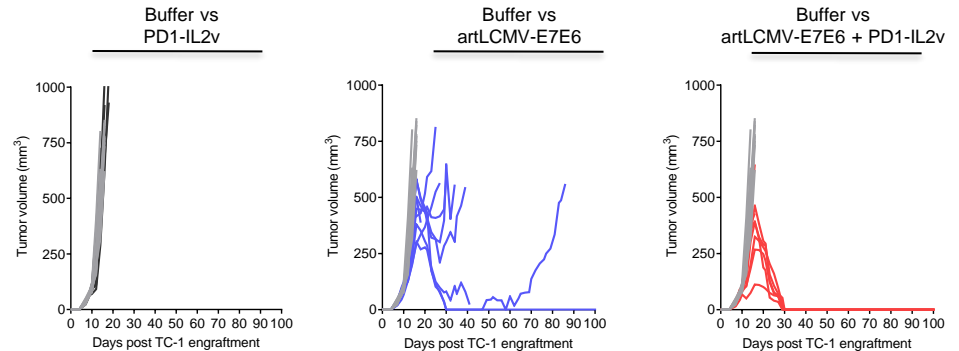


artLCMV-E7E6 + PD1-IL2v combination therapy eradicates tumors in HPV-associated cancer model

DO NOT POST



- 60% tumor eradication upon artLCMV-E7E6 + PD1-IL2v combination therapy



Combination therapy fully protects animals against re-challenge in both tumor models

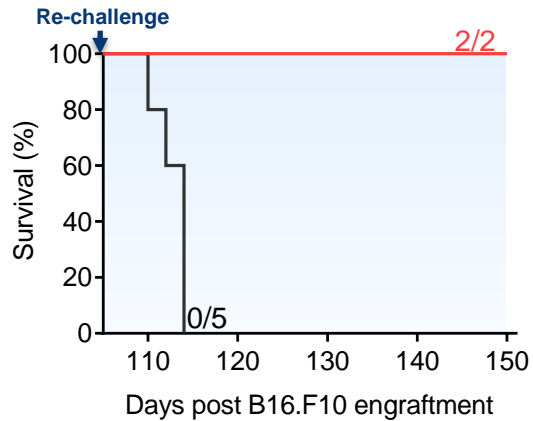
DO NOT POST



ANNUAL MEETING 2023

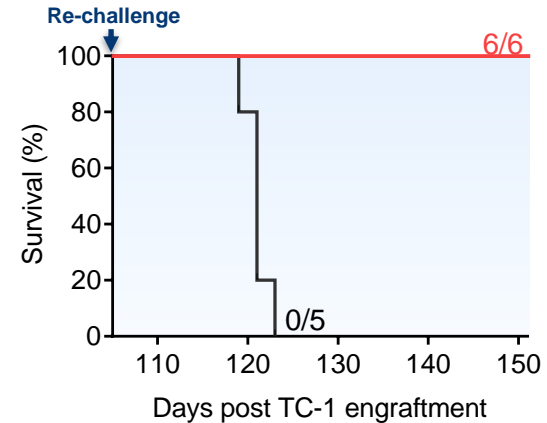
APRIL 14-19 • #AACR23

artLCMV-TRP2
B16.F10 model



— tumor-free after artLCMV+ PD1-IL2v
— Re-challenge control

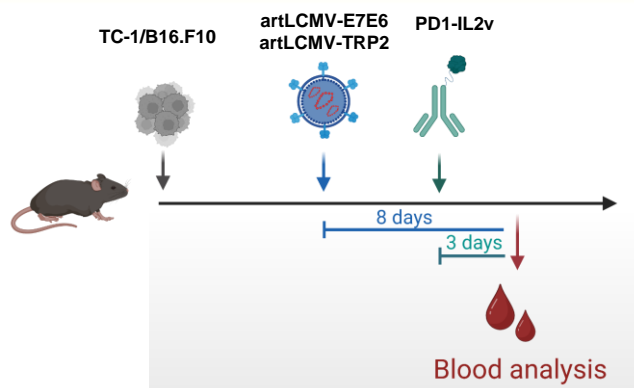
artLCMV-E7E6
TC-1 model



Long-term protection against tumor re-challenge indicates protective **CD8⁺ T cell memory**

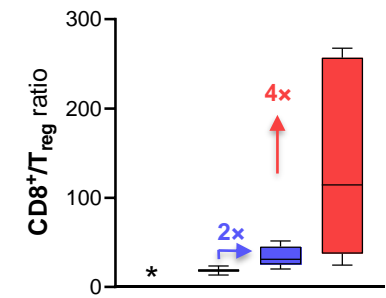
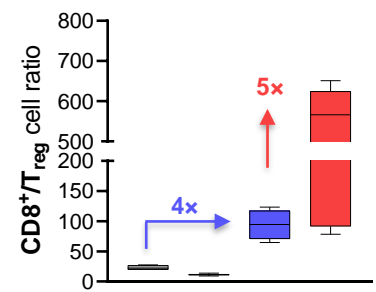
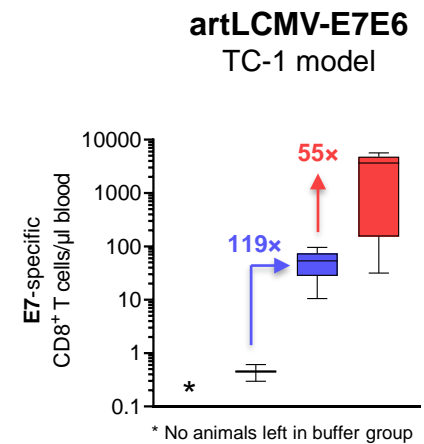
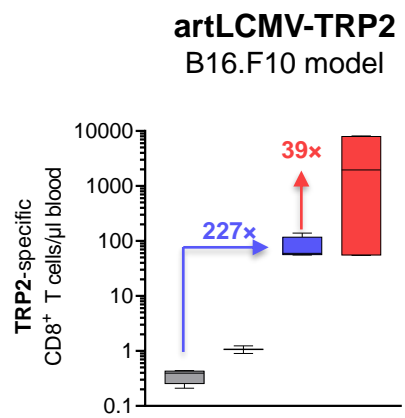
artLCMV induces a strong tumor-antigen specific CD8⁺ T cell response which is further enhanced by PD1-IL2v

DO NOT POST



- Buffer
- PD1-IL2v
- artLCMV
- artLCMV + PD-1IL2v

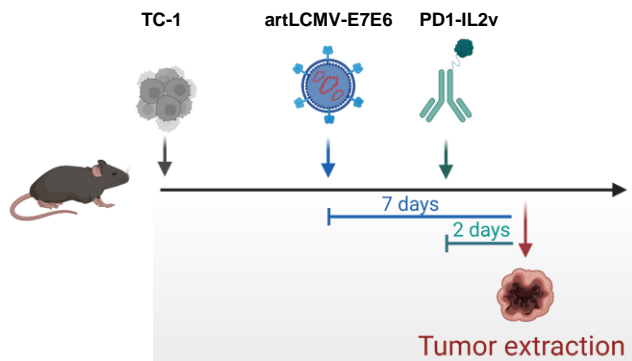
- **artLCMV** treatment induces high peripheral **tumor-antigen specific CD8⁺ T cell responses** which are further augmented by PD1-IL2v
- **CD8⁺/Treg cell ratio increased** upon artLCMV monotherapy and further elevated by combination therapy
- **PD1-IL2v monotherapy** did not trigger substantial anti-tumor CD8⁺ T cell responses



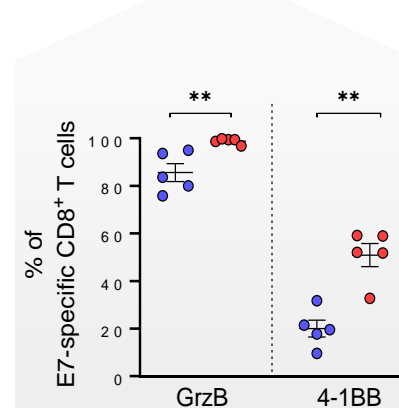
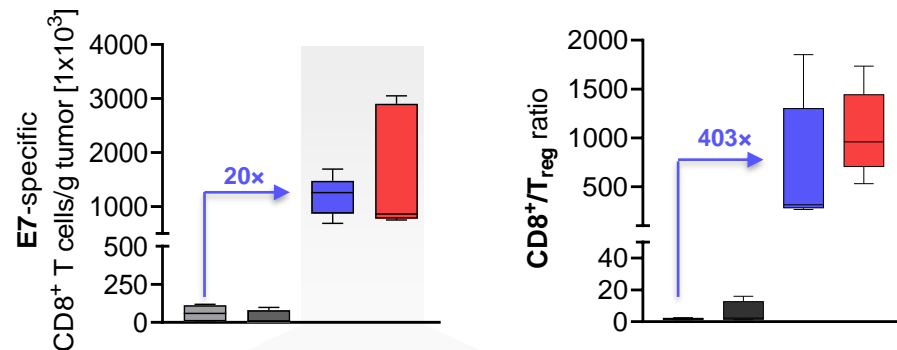
artLCMV+PD1-IL2v combination therapy enhances functionality of intratumoral CD8⁺ T cells

DO NOT POST

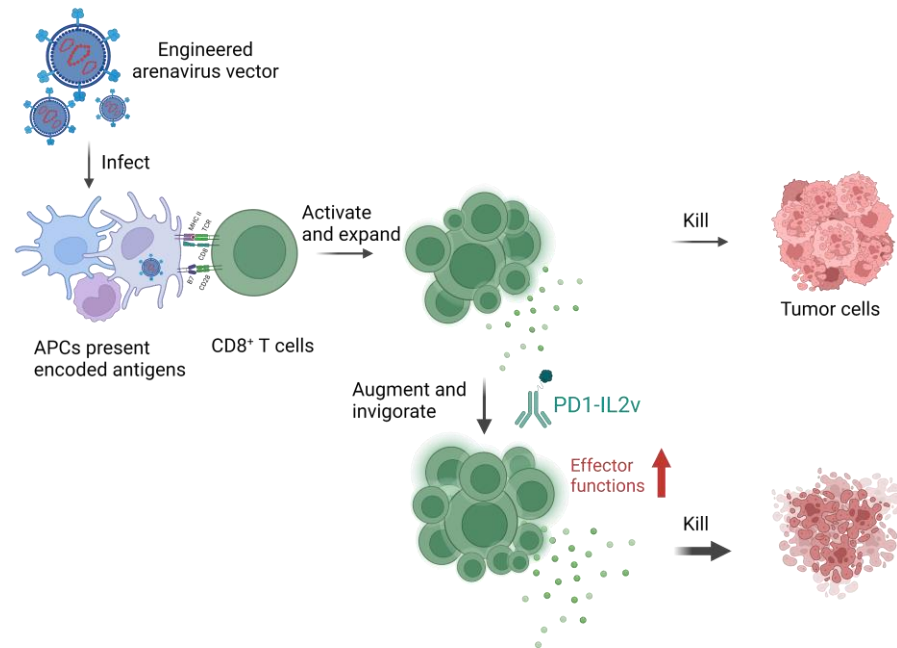
APRIL 14-19 • #AACR23



- Strong **tumor infiltration** of **E7-specific** CD8⁺ T cells upon artLCMV-E7E6 monotherapy
- Increased CD8⁺/Treg cell ratio** within the TME upon artLCMV-E7E6 monotherapy
- artLCMV-E7E6+PD1-IL2v combination therapy enhances the **functionality** of tumor-infiltrating CD8⁺ T cells



Summary



artLCMV+PD1-IL2v combination therapy...

- leads to **high tumor cure rates** in preclinical models
- elicits a **massive tumor antigen-specific CD8⁺ T cell** response which
 - efficiently **infiltrates tumors**
 - exhibits **increased functionality**
- induces a protective **T cell memory** against tumor rechallenge
- represents a very promising combination for **clinical applications**

Acknowledgements

Hookipa Pharma

Diana Reckendorfer

Kimberly Pojar

Josipa Raguz

Henning Lauterbach

Klaus Orlinger

Roche

Laura Codarri Deak

Valeria Nicolini

Roger Sutmuller

Christian Klein

Pablo Umaña