



Neoantigen-targeting TCR engineered cellular therapy for TP53, EGFR and RAS-mutant tumors

Hawaii Global Summit for Thoracic Malignancies

June 30, 2023

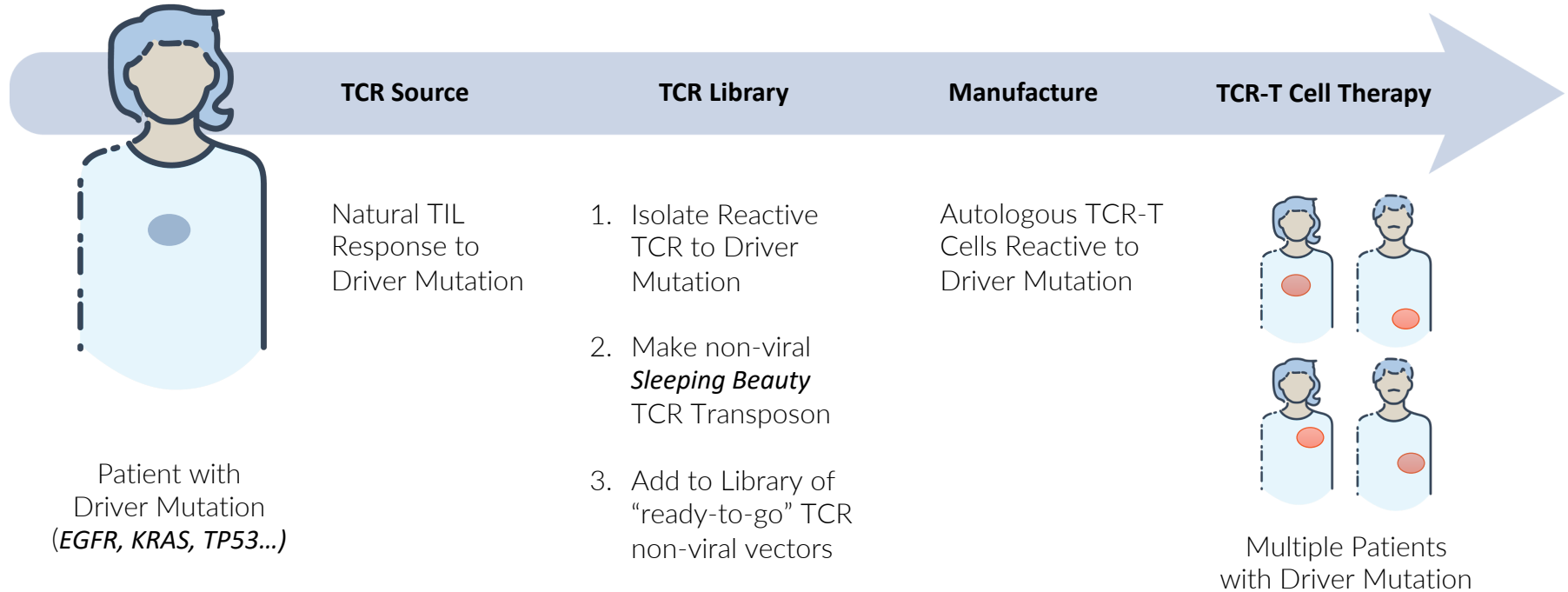
PRESENTED BY

Matthew Collinson-Pautz, PhD, Director Translational Sciences

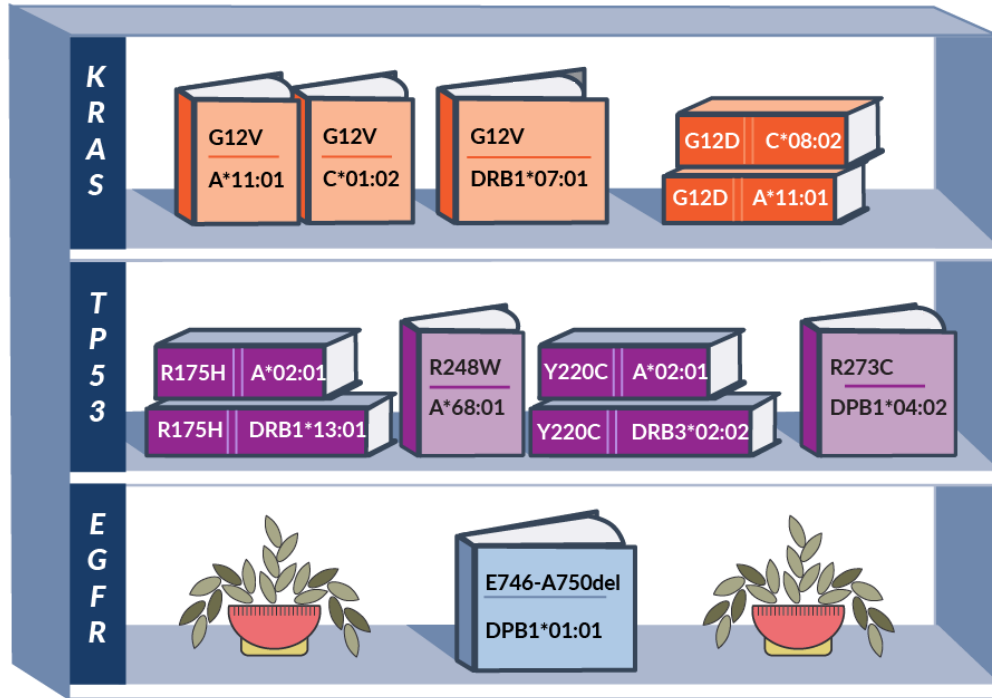
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Differentiated Approach to Convert Natural T-Cell Responses into Mutation-Targeted TCR-T Cell Therapy in Solid Tumors



Industry Leading TCR Library Captures Both High Frequency Mutations and HLA Types



- ◀ In over 700 patients screened, 15% match rate to a TCR in our library
- ◀ Our TCR library contains mutations from genes that are known to drive cancer and are highly expressed by tumors
- ◀ Mutations in our library are among the most frequent and most mutated genes in solid tumors
- ◀ HLAs that present our mutations are prevalent in the United States
- ◀ Two-pronged library expansion strategy:
 1. Add more HLAs to existing mutations
 2. Add more mutations to KRAS, TP53, EGFR

Confirmed Responses from Leading Academic Institutions Corroborate Targeting Driver Mutations with TCR-T Cells

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Neoantigen T-Cell Receptor Gene Therapy in Pancreatic Cancer

Rom Leidner, M.D., Nelson Sanjuan Silva, B.S., Huayu Huang, M.S., David Sprott, B.S., Chunhong Zheng, Ph.D., Yi-Ping Shih, Ph.D., Amy Leung, B.S., Roxanne Payne, M.N., Kim Sutcliffe, B.S.N., Julie Cramer, M.A., Steven A. Rosenberg, M.D., Ph.D., Bernard A. Fox, Ph.D., Walter J. Urba, M.D., Ph.D., and Eric Tran, Ph.D.

Greater than 70% tumor reduction of metastatic pancreatic cancer six months after infusion of **KRAS-G12D and HLA-C*08:02** reactive TCR-T cells

CANCER IMMUNOLOGY RESEARCH | RESEARCH ARTICLE

Adoptive Cellular Therapy with Autologous Tumor-Infiltrating Lymphocytes and T-cell Receptor-Engineered T Cells Targeting Common p53 Neoantigens in Human Solid Tumors

Sanghyun P. Kim¹, Nolan R. Vale¹, Nikolaos Zacharakis¹, Sri Krishna¹, Zhiya Yu¹, Billel Gasm², Jared J. Gartner¹, Sivasish Sindiri¹, Parisa Malekzadeh¹, Drew C. Deniger¹, Frank J. Lowery¹, Maria R. Parkhurst¹, Lien T. Ngo¹, Satyajit Ray¹, Yong F. Li¹, Victoria Hill¹, Maria Florentin¹, Robert V. Masi¹, Biman C. Paria¹, Noam Levin¹, Alakesh Bera¹, Elizabeth A. Hedges¹, Agnes Choi¹, Praveen D. Chatani¹, Anup Y. Parikh¹, Shoshana Levi¹, Samantha Seitter¹, Yong-Chen Lu¹, Zhili Zheng¹, Todd D. Prickett¹, Li Jia³, Jonathan M. Hernandez⁴, Chuong D. Hoang⁵, Paul F. Robbins¹, Stephanie L. Goff¹, Richard M. Sherry¹, James C. Yang¹, and Steven A. Rosenberg¹

55% tumor reduction of metastatic breast cancer six months after infusion of **TP53-R175H and HLA-A*02:01** reactive TCR-T cells

Alaunos is the only company in the clinic with these TCRs in its library

First-in-Human TCR-T Clinical Trial Actively Enrolling with Innovative TCR Library Approach at MD Anderson

Phase 1

- Defines safety and dose with any TCR and any of six indications
- Enrolling in one of three dose cohorts: 5, 40 and 100 billion TCR-T cells

Phase 2

- Defines efficacy at recommended dose with any TCR in library
- Each cancer type will be a distinct cohort

Pivotal

- Selected indications and selected TCRs with efficacy in Phase 2
- Expansion into other indications/TCRs during Phase 2 for lead candidates

First-in-Human Clinical Experience in Solid Tumors by TCR-T Cell Therapy with Manageable Safety and Evidence of Efficacy

SAFETY

Manageable safety profiles to date

Gr1 – 3 CRS observed (fever, hypoxia, hypotension)

Lymphodepletion-related lymphopenia, neutropenia, thrombocytopenia

Anemia requiring transfusion

No ICANS, No DLTs

PERSISTENCE

Persisting TCR-T cells (20%-30%) in blood in the absence of IL-2

Evidence of potential T-cell activation post-infusion

TCR-T cells trafficking to tumor

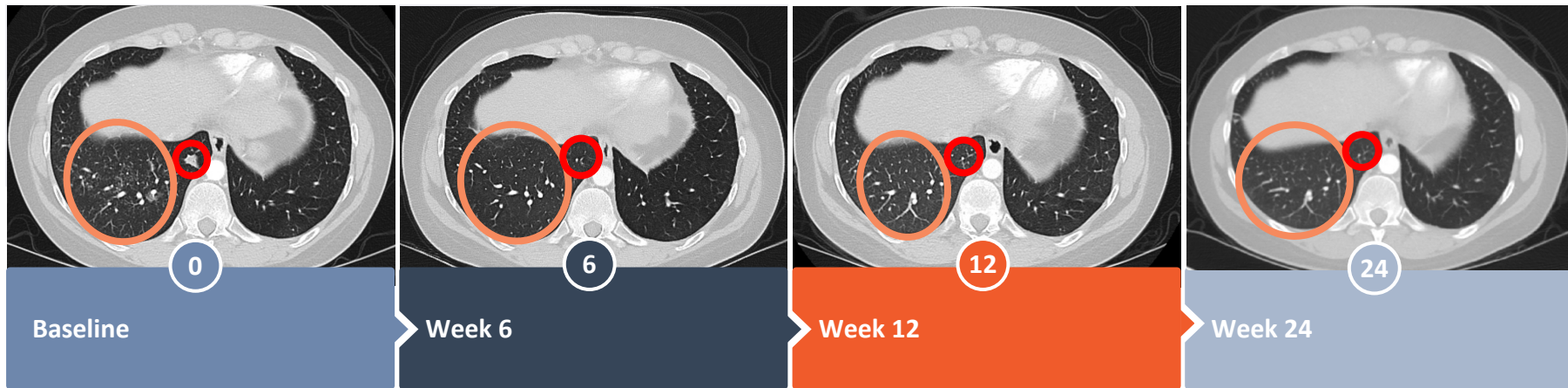
EFFICACY

First TCR-T cell response in checkpoint inhibitor refractory NSCLC (>50% reduction)

Six-month progression-free survival in Patient 1 (NSCLC) with Partial Response

Best overall responses in Patient 2 (CRC) and Patient 3 (PDAC), Stable Disease and Progressive Disease

Patient 1 Showed Confirmed Partial Response of KRAS-G12D Mutant Lung Adenocarcinoma with 6 Month PFS



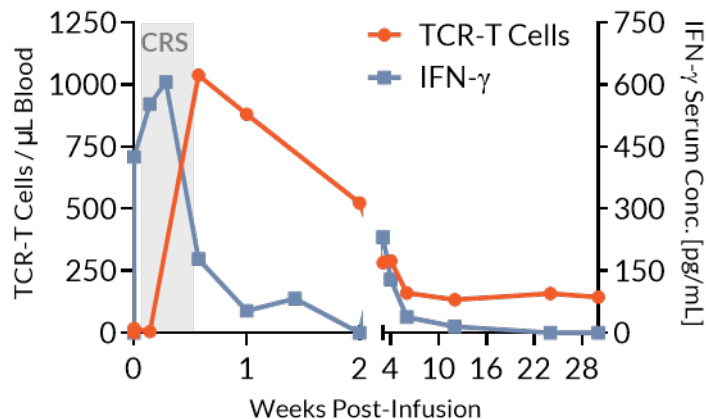
- Patient 1 had multiple lines of prior therapy and was refractory to checkpoint inhibitors
- Treated with 9 billion TCR-T cells (dose level 1) targeting KRAS-G12D and HLA-A*11:01 with manageable safety profile
- Confirmed partial response; patient is off-study after six-month progression-free survival

Red circles represent target lesions, orange circles represent non-measurable disease

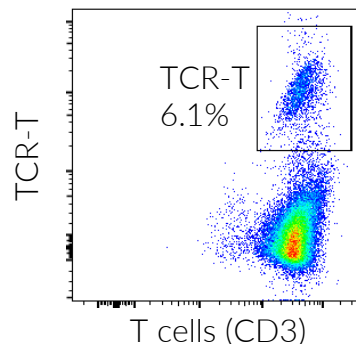
Patient 1 case report presented: [Negrao MV et al. CRI-ENCI-AACR International Cancer Immunotherapy Conference 2022](#)

TCR-T Cells Persist in Blood and Traffic to Tumor Microenvironment

TCR-T Cell Expansion and Persistence in Blood
Patient 1



Seven-month Tumor Biopsy
Patient 1



TCR-T cells expanded and were detectable in peripheral blood at last follow-up



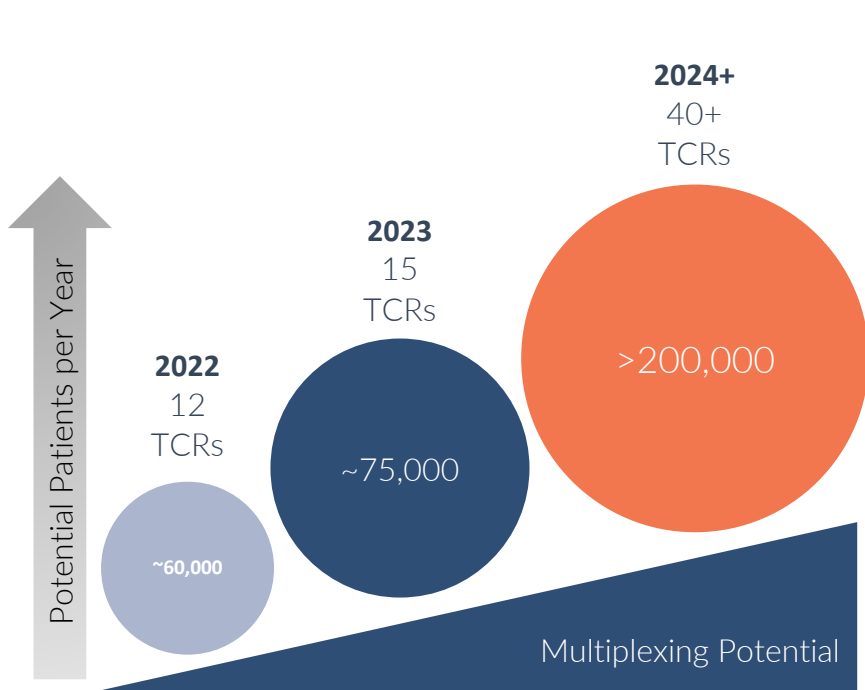
Elevated Th1 effector cytokines during TCR-T expansion phase



Tumor trafficking seven months after infusion observed

(Left) CRS – Cytokine release syndrome. Patient 1 experienced self-limiting Grade 2 CRS following TCR-T administration.
(Right) TCR-T cells from biopsy taken at seven months post-infusion from Patient 1 were grown in lab before analysis

hunTR[®] Expands TCR Library, Extends Patient Reach and Enables Multiplexed TCR-T Cell Therapy



Add new HLAs to existing mutations and add more key mutations within *EGFR*, *KRAS*, *TP53*



Matching data from clinical efforts inform which HLA/mutation combinations to prioritize



Sleeping Beauty expected to allow for cost-effective and efficient expansion of TCR library for clinic



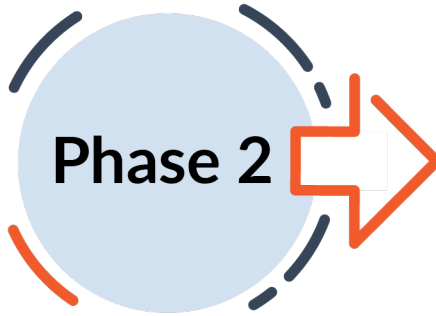
Expect out-licensing opportunities of selected proprietary TCRs

Driving Towards The Future of Mutation-Targeted TCR-T Cell Therapy For Solid Tumors



Designed to Target Tumors
Their Root

Evidence of Efficacy with TCR-T
Targeting Mutations



Advancing TCR-T Library Trial
to Phase 2



hunTR®
Expand TCR Library to Reach
More Patients

Data-Driven Discovery to
Target the Most Tumors

Thank You

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Phase 1/2 TCR-T Clinical Trial NCT05194735