

Precigen R&D Day

November 4, 2021

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Today's Agenda

AGENDA

UltraCAR-T® Platform

- PRGN-3006 UltraCAR-T® in AML and MDS
- PRGN-3005 UltraCAR-T® in Ovarian Cancer
- PRGN-3007 UltraCAR-T® in Hematological & Solid Cancers

AdenoVerse™ Platform

- PRGN-2012 AdenoVerse™ in RRP
- PRGN-2009 AdenoVerse™ in HPV+ Cancers

Q&A

PARTICIPANTS



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President and CEO
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A lead investigator for the PRGN-3006 clinical study



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A lead investigator for the PRGN-2009 clinical study



Clint T. Allen, MD

Principal Investigator with the Section on Translational Tumor Immunology at the National Institutes of Health
A lead investigator for the PRGN-2012 clinical study

Welcome & Introduction

Helen Sabzevari, PhD
President and CEO, Precigen

UltraCAR-T[®] Platform

Helen Sabzevari, PhD

President and CEO, Precigen

PRGN-3006 UltraCAR-T®

David Sallman, MD

Assistant Member in the Department of Malignant Hematology,
H. Lee Moffitt Cancer Center & Research Institute

ACUTE MYELOID LEUKEMIA (AML)

- AML starts in the bone marrow, but most often moves into the blood
- AML is the most common acute leukemia in adults

MYELOYDYSPLASTIC SYNDROMES (MDS)

- MDS are cancerous conditions of the bone marrow generally found in adults in their 70s

CURRENT TREATMENT PARADIGM

- Approximately 50% of the AML patients relapse^{4,5}
- Prognosis is very poor for relapsed or refractory (r/r) AML patients

DISEASE SNAPSHOT



HIGH UNMET NEED

5-year survival
as low as 5%
for AML patients
over 65³

>11K estimated
deaths from AML
in 2021¹



>20K US

Newly
diagnosed
AML patients
per year¹

>10K US

Newly
diagnosed
MDS patients
per year²

¹American Cancer Society. Key Statistics for Acute Myeloid Leukemia (AML).

²American Cancer Society. Key Statistics for Myelodysplastic Syndromes.

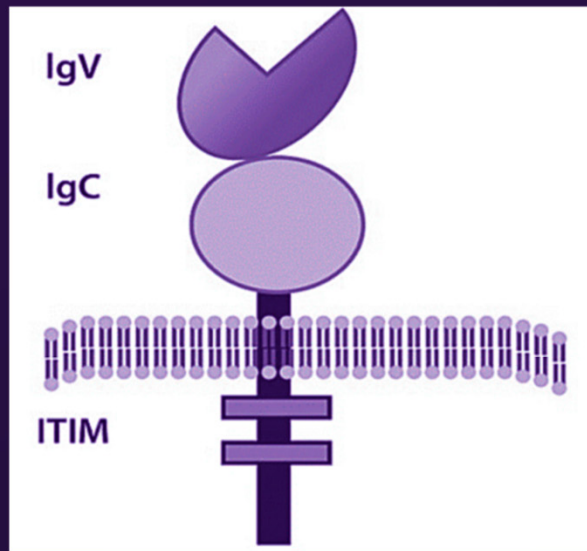
³Thein, M., et al., Outcome of older patients with acute myeloid leukemia: an analysis of SEER data over 3 decades. Cancer, 2013. 119(15): p.2720-7.

⁴Dohner H, et al., Blood (2010);115:453-474.

⁵Burnett A, et al., J Clin Oncol (2011);29:487-494

PRGN-3006 TARGETS CD33

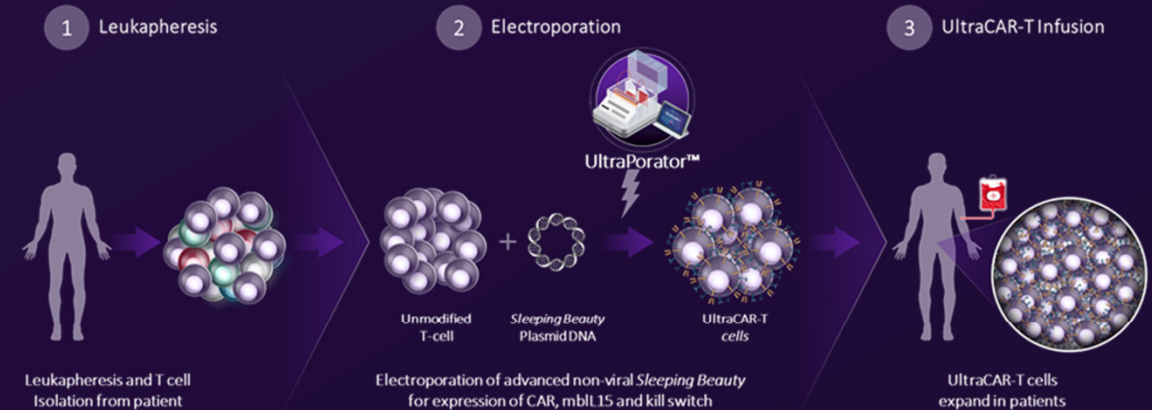
- CD33 is overexpressed on myeloid leukemia and leukemic stem cells
- 85-90% of AML patients show expression of CD33 on blast cells¹
- Minimal expression outside of hematopoietic system



Modified from: <https://www.openaccessgovernment.org/cd33-directed-therapy/47313/>

PRGN-3006: MULTIGENIC DESIGN and OVERNIGHT MANUFACTURING

- Non-viral system to simultaneously express CD33 CAR, mbIL15 and kill switch
- Overnight, decentralized manufacturing process

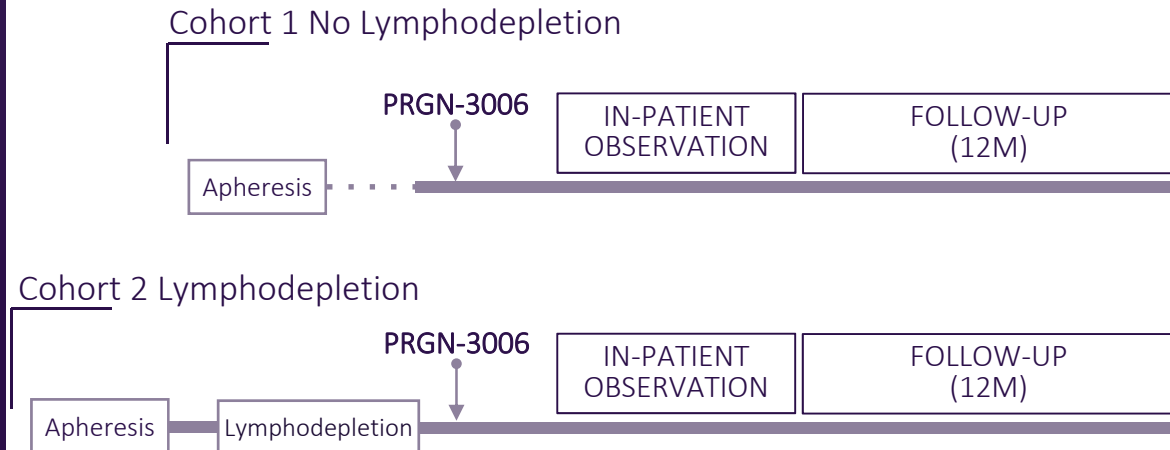


¹Molica M et al., *Cancers* 2021

FIRST-IN-HUMAN, TWO-ARM, DOSE ESCALATION STUDY EVALUATING SAFETY AND EFFICACY OF PRGN-3006

ELIGIBILITY

- r/r AML, high risk MDS or CMML with >5% blasts
- ALC > 0.2 k/ μ L
- Prior HSCT allowed



SAFETY MONITORING

- CRS
- Neurotoxicity (ICANS)
- Management via ASTCT guidelines

DISEASE RESPONSE

- ELN Criteria (AML)
- IWG 2006 criteria (MDS)

CORRELATIVES

- PRGN-3006 persistence/expansion
- Immune phenotype, biomarkers

STUDY OBJECTIVES

Primary

- Evaluate the safety and determine the maximum tolerated dose (MTD) of PRGN-3006 delivered via intravenous (IV) infusion with or without lymphodepletion

Secondary

- To evaluate *in vivo* persistence and anti-tumor activity of PRGN-3006

- Phase 1/1b study in collaboration with the H. Lee Moffitt Cancer Center

PRGN-3006 Phase 1 Cohort 1 (No Lymphodepletion): Baseline Patient Characteristics and Safety Summary

PATIENT CHARACTERISTICS

	N=9
Median age (range), years	63 (33-77)
Male	5 (56%)
Female	4 (44%)
Prior treatments	
<ul style="list-style-type: none"> Median (range) 	4 (1-6)
<ul style="list-style-type: none"> HMA + venetoclax 	6/6 (100%)
<ul style="list-style-type: none"> Intensive chemo 	8/9 (89%)
<ul style="list-style-type: none"> Prior allo-HSCT 	3/9 (33%)
Baseline disease	
<ul style="list-style-type: none"> AML 	9/9 (100%)
<ul style="list-style-type: none"> Extramedullary sole site 	0/9 (0%)
<ul style="list-style-type: none"> ELN intermediate 	3/9 (33%)
<ul style="list-style-type: none"> ELN adverse 	6/9 (67%)

SAFETY SUMMARY

CAR-T Cell Toxicity (N=9)		
Dose Limiting Toxicity	CRS (number of subjects, %)	Neurotoxicity (number of subjects, %)
<ul style="list-style-type: none"> 0 DLTs 	<ul style="list-style-type: none"> CRS, any grade: 4/9 (44%) CRS, Grade 1-2: 3/9 (33%) CRS, Grade 3: 1/9 (11%) Use of tocilizumab: 2/9 (22%) Use of kill switch: 0/9 (0%) 	<ul style="list-style-type: none"> Neurotoxicity, any grade: 0% (0/9)

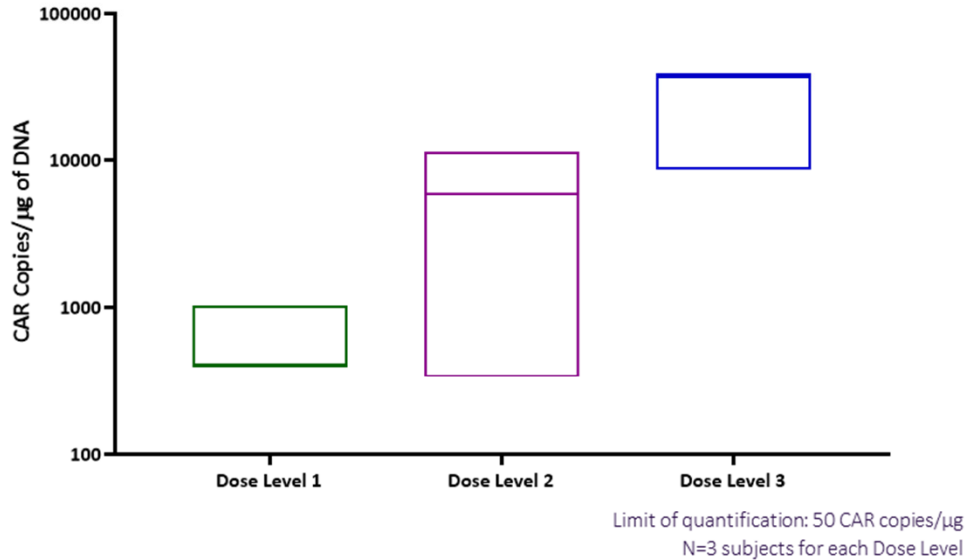
PRGN-3006 UltraCAR-T DOSES ADMINISTERED

Dose Level (DL)	Subjects	Dose Range (UltraCAR-T Cells/kg)	Total UltraCAR-T Dose Administered
DL1	N=3	>3x10 ⁴ to ≤1x10 ⁵	1.8 – 7.1 x10 ⁶
DL2	N=3	>1x10 ⁵ to ≤ 3x10 ⁵	24 – 29 x10 ⁶
DL3	N=3	>3x10 ⁵ to ≤ 1x10 ⁶	34 – 50 x10 ⁶

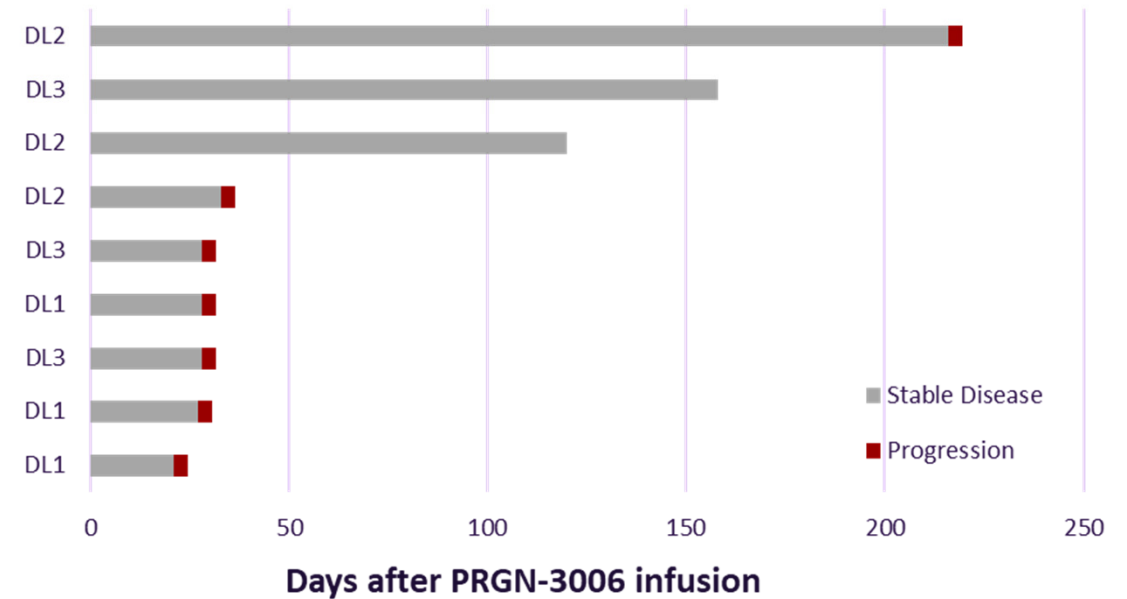
PRGN-3006 treatment was well-tolerated with no incidences of DLTs or neurotoxicity

PRGN-3006 Phase 1 Cohort 1 (No Lymphodepletion): UltraCAR-T Expansion, Persistence and Summary of Responses

PRGN-3006 PEAK EXPANSION IN BLOOD (NO LYMPHODEPLTION COHORT)



SUMMARY OF RESPONSES



- Dose-dependent expansion of PRGN-3006 observed

PRGN-3006 UltraCAR-T DOSES ADMINISTERED

Dose Level (DL)	Subjects	Dose Range (UltraCAR-T Cells/kg)	Total UltraCAR-T Dose Administered
DL1	N=3	>3x10 ⁴ to ≤1x10 ⁵	1.8 – 7.1 x10 ⁶
DL2	N=3	>1x10 ⁵ to ≤ 3x10 ⁵	24 – 29 x10 ⁶
DL3	N=3	>3x10 ⁵ to ≤ 1x10 ⁶	34 – 50 x10 ⁶

PRGN-3006 Phase 1 Cohort 2 (Lymphodepletion): Baseline Patient Characteristics and Safety Summary

PATIENT CHARACTERISTICS

	N=6
Median age (range), years	56 (38-64)
Male	2 (33%)
Female	4 (67%)
Prior treatments	
<ul style="list-style-type: none"> Median (range) HMA + venetoclax Intensive chemo Prior allo-HSCT 	<p>3 (1-7)</p> <p>5/6 (83%)</p> <p>4/6 (67%)</p> <p>3/6 (50%)</p>
Baseline disease	
<ul style="list-style-type: none"> AML Extramedullary sole site ELN intermediate ELN adverse 	<p>6/6 (100%)</p> <p>1/6 (17%)</p> <p>2/6 (33%)</p> <p>3/6 (50%)</p>

SAFETY SUMMARY

CAR-T Cell Toxicity (N=6)

Dose Limiting Toxicity	CRS (number of subjects, %)	Neurotoxicity (number of subjects, %)
<ul style="list-style-type: none"> 0 DLTs 	<ul style="list-style-type: none"> CRS, any grade: 3/6 (50%) CRS, Grade 1-2: 3/6 (50%) CRS, Grade 3: 0/6 (0%) Use of tocilizumab: 0/6 (0%) Use of kill switch: 0/6 (0%) 	<ul style="list-style-type: none"> Neurotoxicity, any grade: 0% (0/6)

PRGN-3006 UltraCAR-T DOSES ADMINISTERED

Dose Level (DL)	Subjects	Dose Range (UltraCAR-T Cells/kg)	Total UltraCAR-T Dose Administered
DL1	N=3	>3x10 ⁴ to ≤1x10 ⁵	4.4 - 10 x 10 ⁶
DL2	N=3	>1x10 ⁵ to ≤ 3x10 ⁵	18 - 28 x 10 ⁶

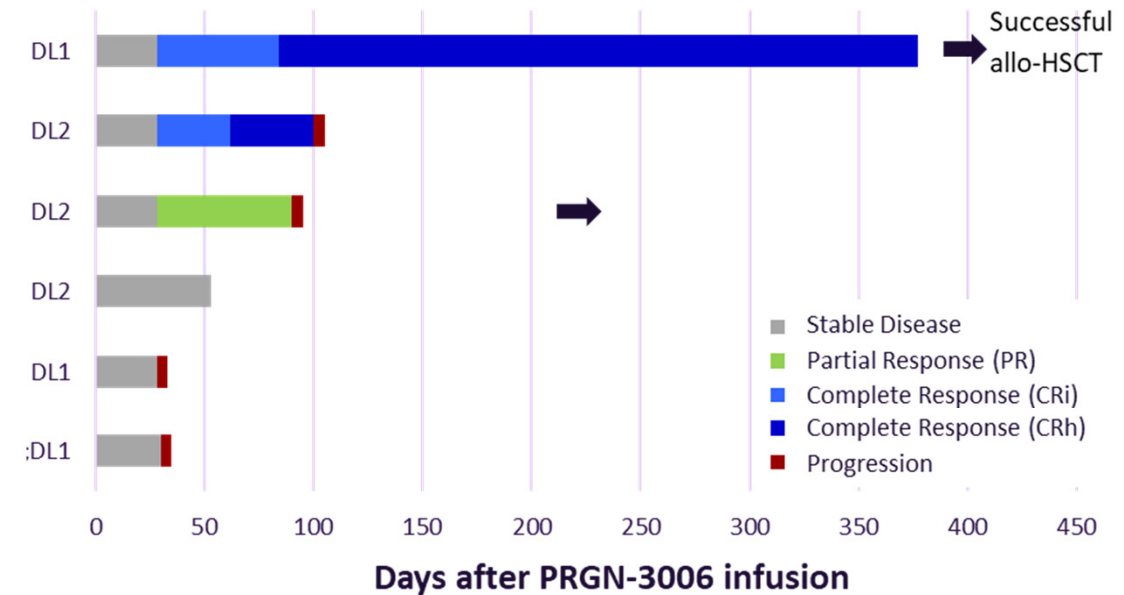
PRGN-3006 treatment was well-tolerated with no incidences of DLTs or neurotoxicity

PRGN-3006 Phase 1 Cohort 2 (Lymphodepletion): Summary of Responses

50% ORR in Patients Treated at the Two Lowest Dose Levels

SUMMARY OF RESPONSES

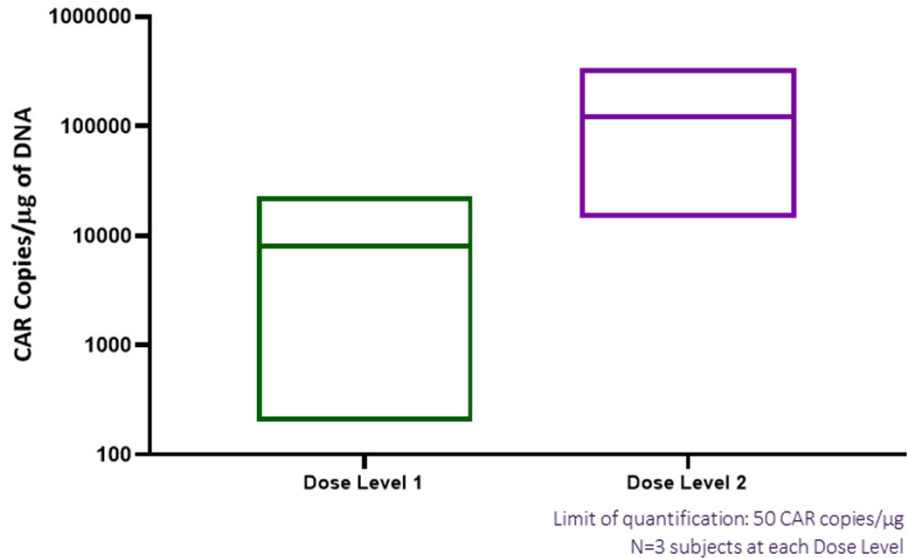
Dose Level (DL)	DL1 (N=3)	DL2 (N=3)
Dose Range	>3x10 ⁴ to ≤1x10 ⁵ /kg	>1x10 ⁵ to ≤ 3x10 ⁵ /kg
Total UltraCAR-T Dose Administered	4.4 – 10 x 10 ⁶	18 - 28 x 10 ⁶
ORR (%)	33%	67%



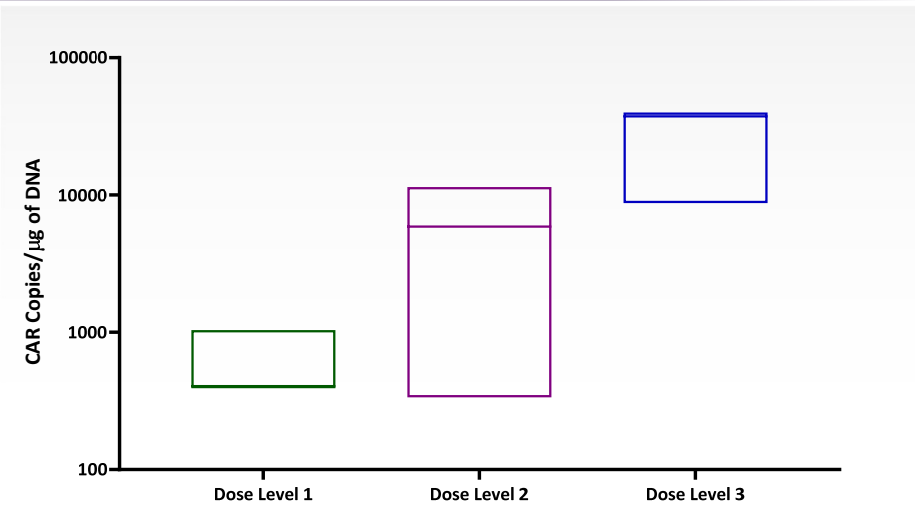
50% (3/6) Objective Response Rate (ORR) in patients treated at the two lowest Dose Levels

PRGN-3006 Phase 1 Cohort 2 (Lymphodepletion): UltraCAR-T Expansion and Persistence

PRGN-3006 PEAK EXPANSION IN BLOOD (LYMPHODEPLETION COHORT)



PEAK EXPANSION IN BLOOD (NO LYMPHODEPLETION COHORT)



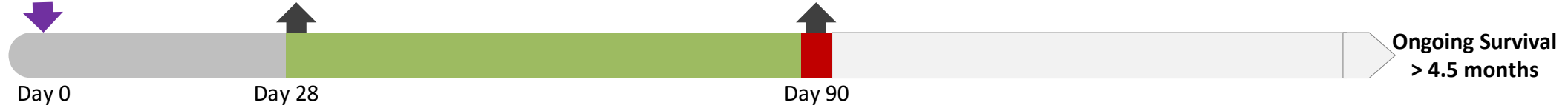
PRGN-3006 UltraCAR-T DOSES ADMINISTERED

Dose Level (DL)	Subjects	Dose Range (UltraCAR-T Cells/kg)	Total UltraCAR-T Dose Administered
DL1	N=3	$>3 \times 10^4$ to $\leq 1 \times 10^5$	$4.4 - 10 \times 10^6$
DL2	N=3	$>1 \times 10^5$ to $\leq 3 \times 10^5$	$18 - 28 \times 10^6$

- Dose-dependent expansion of PRGN-3006 observed in all treated patients
- Persistence up to 3 months post infusion for the two lowest Dose Levels with Lymphodepletion
- Substantially higher peak expansion in the Lymphodepletion Cohort compared to the No Lymphodepletion Cohort

Case Study: Partial Response in Patient with Extramedullary AML after PRGN-3006 Infusion (Cohort 2: Lymphodepletion, Dose Level 2)

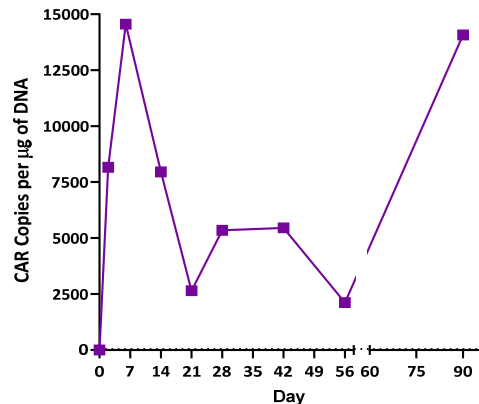
PRGN-3006 Dose:
28 x 10⁶ (DL2)



PATIENT BASELINE CHARACTERISTICS

- 53 year old male with extramedullary AML as sole site of disease
- 7 prior lines of therapy including: intensive chemo, vidadia, venetoclax, FLAG, anti-IDH1, and allo-HSCT
- Soft tissue masses in mesentery, retroperitoneum, pelvis, gallbladder, large left pelvic mass involving iliac bone and SI joint, and lower extremities
- Single infusion of 28 x 10⁶ PRGN-3006 (Dose Level 2) after lymphodepletion

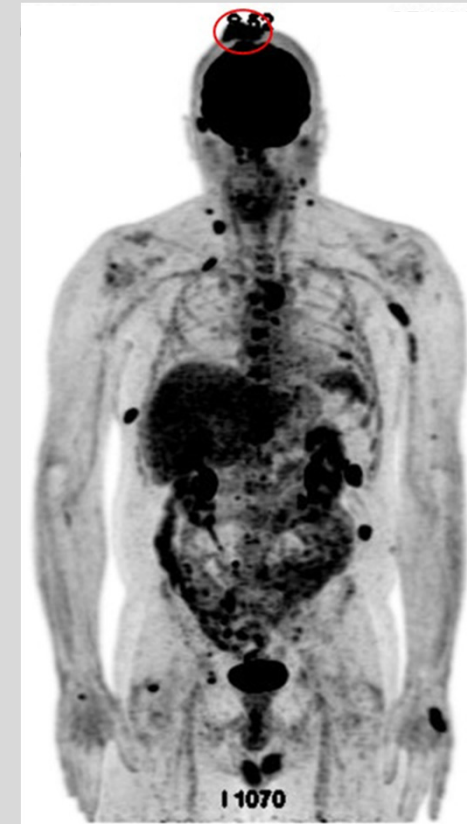
EXPANSION IN BLOOD



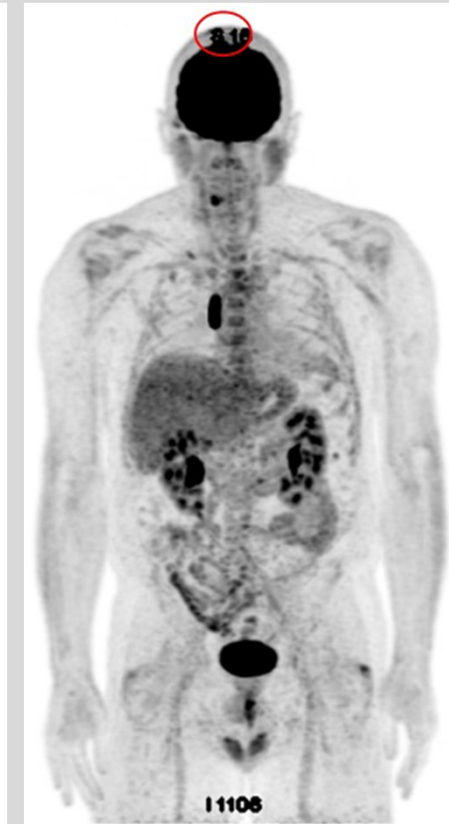
SAFETY AND EFFICACY DATA

- No incidence of CRS, neurotoxicity or DLT
- Achieved PR at Day 28 by RECIST v1.1
 - Clearance of all lesions except a small lesion on the scalp (red circle)
- Day 90 PET/CT demonstrated PD with new soft tissue nodes on head/neck and skull

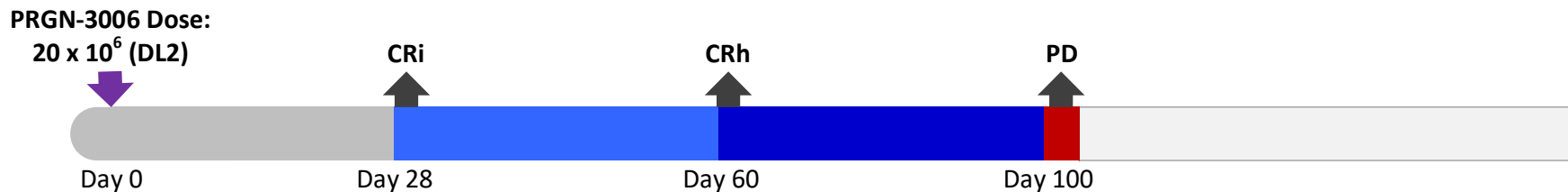
Baseline



Day 28



Case Study: Complete Response in AML Patient after PRGN-3006 Infusion (Cohort 2: Lymphodepletion Dose Level 2)



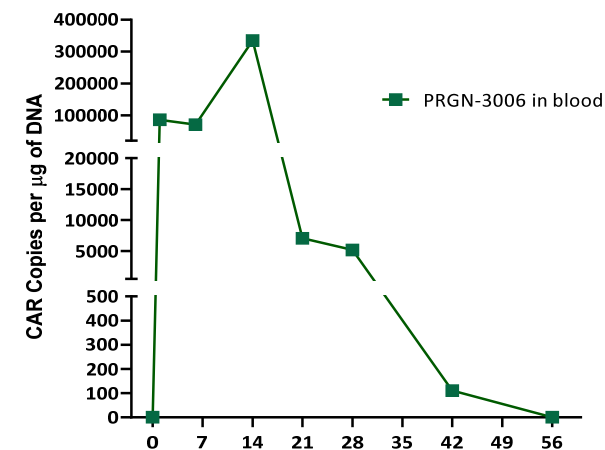
PATIENT BASELINE CHARACTERISTICS

- 61 year old female with AML
 - Cytogenetics : t(1;3)(p36.3q21); NGS Myeloid Panel: KRAS, PHF6
- 4 prior treatments: vyxeos, HMA+venetoclax, allo-HSCT
- Single infusion of 20×10^6 PRGN-3006 (Dose Level 2) after lymphodepletion

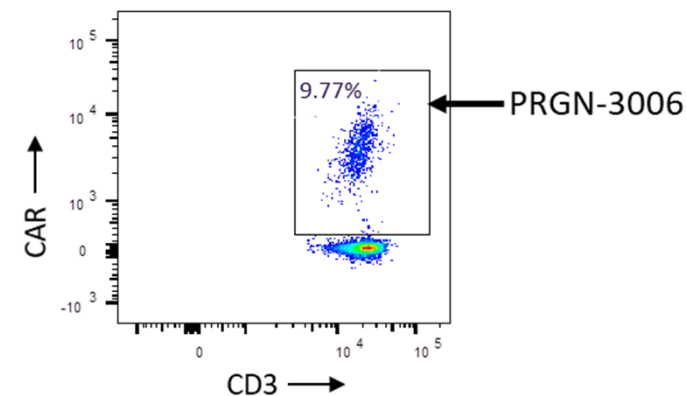
SAFETY AND EFFICACY DATA

- CRS grade 1, with SAE skin rash (possible GVHD)
- Complete Response with incomplete hematologic recovery (CRi) at Day 28
- Complete Response with hematologic recovery (CRh) at Day 60
- Patient survived > 6 months

EXPANSION IN BLOOD

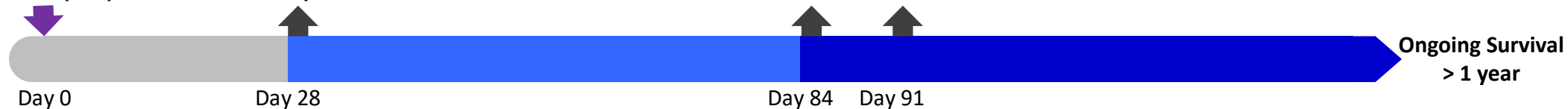


Flow cytometry (Blood, Day 14)



Case Study: Complete Response in AML Patient after PRGN-3006 Infusion (Cohort 2: Lymphodepletion, Dose Level 1)

PRGN-3006 Dose:
 8.7×10^6 (DL1)



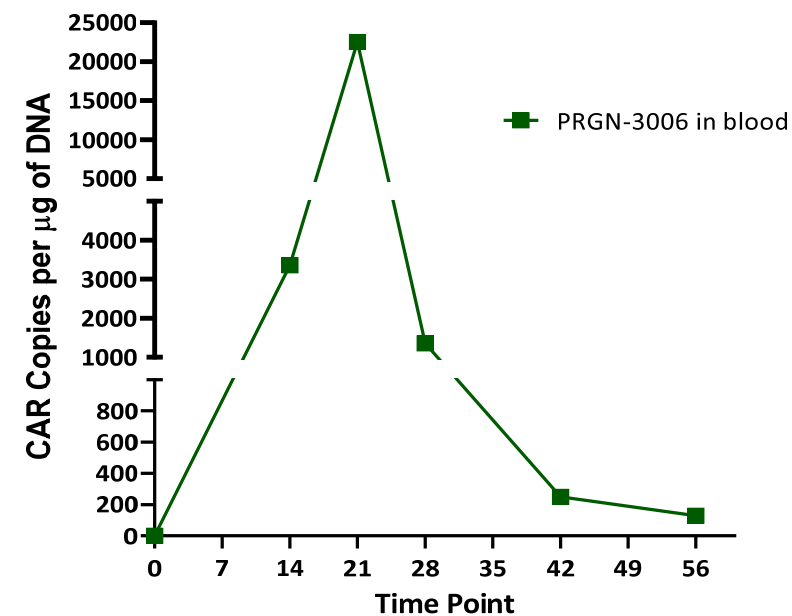
PATIENT BASELINE CHARACTERISTICS

- 60 year old female with persistent AML
 - Cytogenetics: Intermediate risk/normal; NGS Myeloid Panel: +CBL, TET2, U2AF1
- Prior treatments include CLAG and HiDAC
- Patient infused on 8.7×10^6 PRGN-3006 cells (Dose Level 1) after lymphodepletion

SAFETY AND EFFICACY DATA

- No incidence of CRS, neurotoxicity or DLT
- Complete Response with hematologic recovery (CRh) by Day 84
- Subsequently received a successful allo-HSCT
- Ongoing survival at > 1 year post-infusion

EXPANSION IN BLOOD



PRGN-3006 UltraCAR-T: Summary

PRGN-3006 was well-tolerated with or without lymphodepletion. No DLTs or neurotoxicity observed

Results demonstrate feasibility of overnight, decentralized manufacturing

Excellent dose-dependent expansion and persistence of over 3 months observed

Objective Response Rate (ORR) of 50% in patients treated at the two lowest Dose Levels in the Lymphodepletion Cohort

PRGN-3006 UltraCAR-T: The Road Ahead

- Complete dose escalation in Phase 1 No Lymphodepletion Cohort
- Complete dose escalation in Phase 1 Lymphodepletion Cohort
- Opportunity to evaluate repeat dosing, if needed
- Initiate Phase 1b dose expansion trial
- Registration study strategy

PRGN-3005 UltraCAR-T[®]

Mary L. (Nora) Disis, MD

University of Washington (UW) Professor of Medicine, Director of UW Center for Translational Medicine, Professor in the Clinical Research Division at Fred Hutch

OVARIAN CANCER

- Ovarian cancer is the most lethal of the gynecologic malignancies⁶



HIGH UNMET NEED

Stage IV survival as low as 20%³



300K WW/22K US

Newly diagnosed patients per year^{1, 2}

CURRENT TREATMENT PARADIGM

- The current standard of care for ovarian cancer is surgery, followed by chemotherapy with a combination of platinum agents and taxanes⁴
- Recurrence of the disease occurs in most patients after initial treatment, resulting in a cycle of repeated surgeries and additional rounds of chemotherapy
- Low overall response rate (< 10%) with anti-PD1 treatment⁵

MUC16 IS OVEREXPRESSED IN VARIOUS SOLID TUMORS

MUC16 expression (% patients)^a



Ovarian Cancer

Addressable Patient Population: 24,000



Breast Cancer

Addressable Patient Population: 117,000



Pancreatic Cancer

Addressable Patient Population: 33,000



Endometrial Cancer

Addressable Patient Population: 42,000



Lung Cancer

Addressable Patient Population: 144,000

¹World Health Organization, International Agency for Research on Cancer, Global Cancer Observatory, Cancer Today, Estimated number of new cases in 2018, worldwide, both sexes, all ages.

²American Cancer Society Ovarian Cancer Special Section.

³American Cancer Society, Survival Rates for Ovarian Cancer, by Stage.

⁴C. Della Pera et al., Chin. J. Cancer 34, (2015).

⁵Bartl, T. et al. Current state and perspectives of checkpoint inhibitors in ovarian cancer treatment. memo 13 (2020).

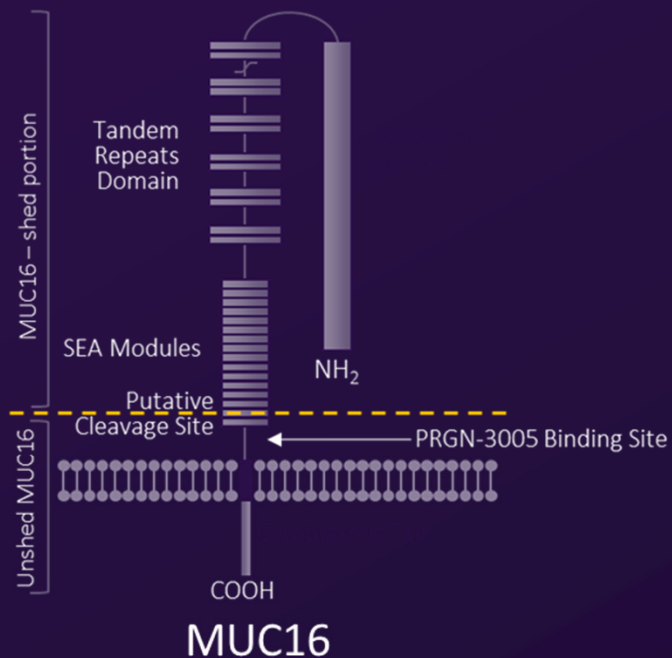
⁶Giannone G. et al., AnnTransl Med (2019).

^aWHO International Agency for Research on Cancer dataset

^bHuman Protein Atlas MUC16 Protein Expression Summary

PRGN-3005 TARGETS UNSHED PORTION OF MUC16

- MUC16 is overexpressed on >80% of ovarian tumors¹
- Limited expression found on healthy tissues
- Initial target is advanced stage platinum resistant ovarian cancer

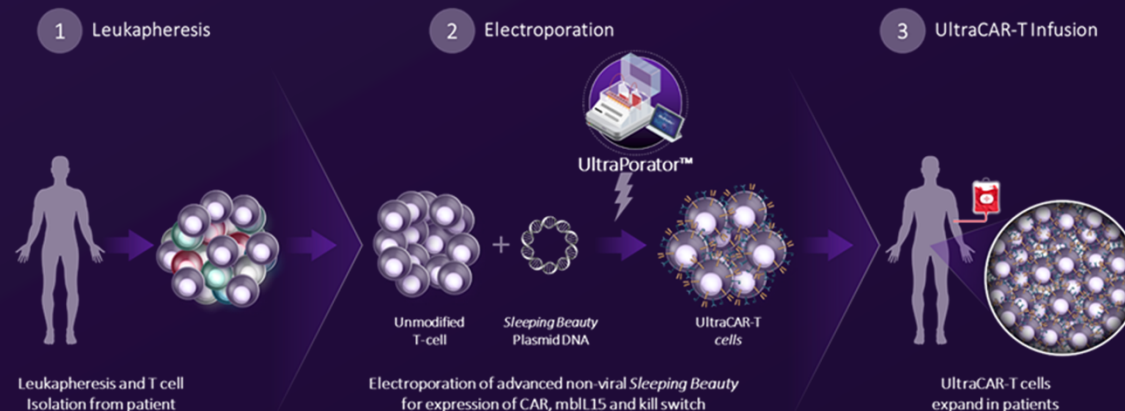


Modified from Piché A, et al., World J Obstet Gynecol. 2016

¹Suh H, et al., Chemo Open Access (2017)

PRGN-3005: MULTIGENIC DESIGN & OVERNIGHT MANUFACTURING

- Non-viral system to simultaneously express MUC16 CAR, mblL15 and kill switch
- Overnight, decentralized manufacturing process



FIRST-IN-HUMAN, TWO-ARM, DOSE ESCALATION STUDY EVALUATING SAFETY AND EFFICACY OF PRGN-3005

ELIGIBILITY

- Advanced stage ovarian, fallopian or primary peritoneal cancer
- Measurable by RECISTv1.1
- CA125>ULN
- No stratification based on biomarker (MUC16) expression

Arm 1, IP infusion (No Lymphodepletion)



Arm 2 IV infusion (No Lymphodepletion)



SAFETY MONITORING

- Standard battery for adverse events
- CRS, Neurotoxicity

DISEASE RESPONSE

- RECIST and irRECIST

CORRELATIVES

- PRGN-3005 persistence/expansion
- Immune phenotype
- Expression of biomarkers, including MUC16

STUDY OBJECTIVES

Primary

- Evaluate the safety and determine the maximum tolerated dose (MTD) of PRGN-3005 delivered via intraperitoneal (IP) or intravenous (IV) infusion

Secondary

- To evaluate *in vivo* persistence and anti-tumor activity of PRGN-3005

PRGN-3005 Phase 1 IP Cohort: Baseline Patient Characteristics and Safety Profile

PATIENT CHARACTERISTICS

	N=10
Median age, years	60
Disease	
▪ Ovarian high grade serous carcinoma	10 (100%)
▪ Ascites	3 (30%)
▪ Locally advanced	6 (60%)
▪ Distant metastases	4 (40%)
Prior lines of chemotherapy	
▪ 2-3	1 (9%)
▪ 4-5	2 (18%)
▪ 6-9	7 (64%)

- Advanced, platinum resistant ovarian cancer patients
- Heavily pretreated patients with aggressive disease
- High target tumor burden

SAFETY

CAR-T Cell Toxicity (N=10)

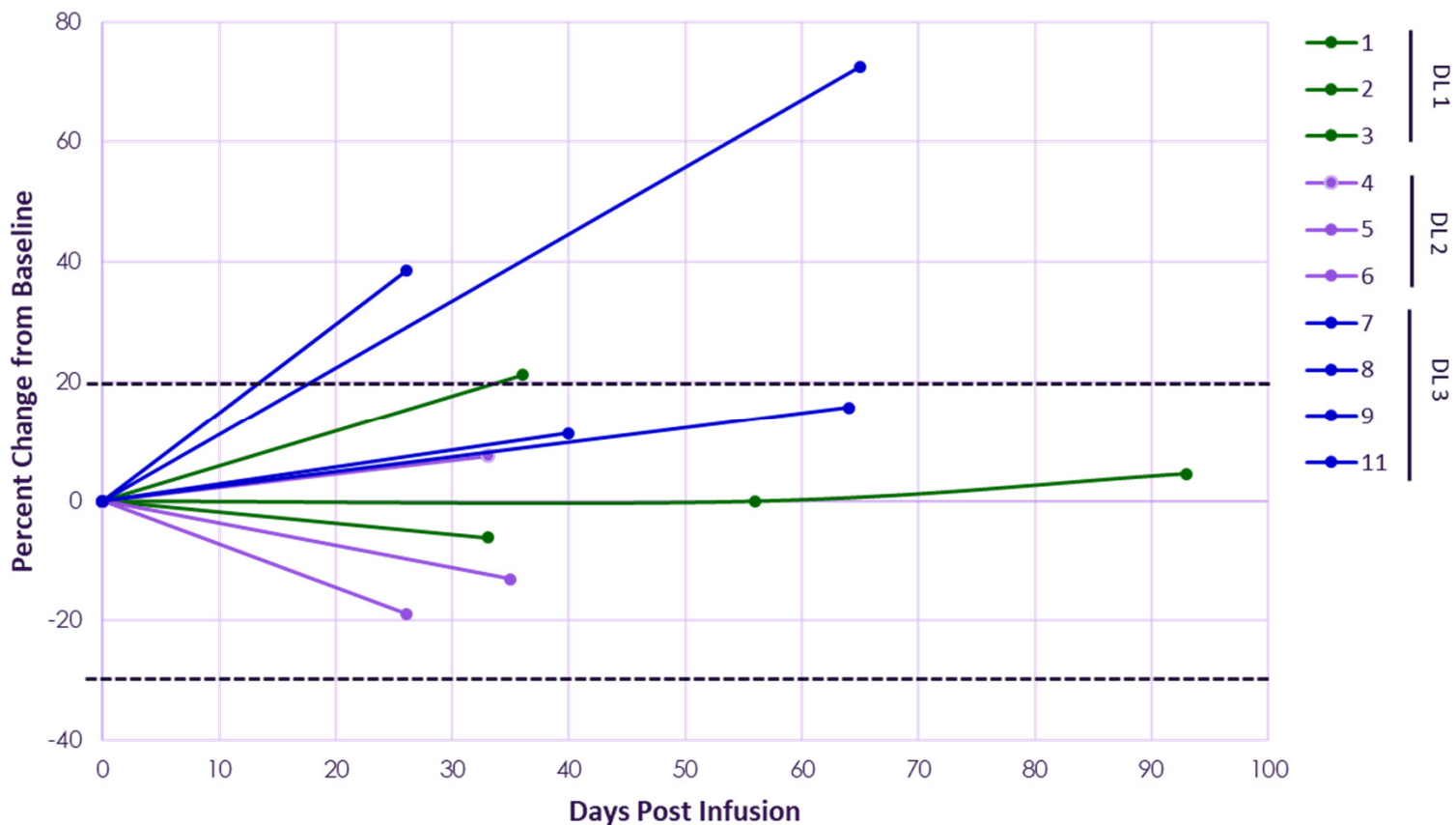
CRS (ASTCT guidelines)	Neurotoxicity (CARTOX-10)
▪ CRS, any grade: 0% (0/10)	▪ Neurotoxicity, any grade: 0% (0/10)
▪ Use of tocilizumab: 0% (0/10)	

- Excellent safety profile across the Dose Levels tested in IP Arm
- No incidences of CRS
- No neurotoxicity

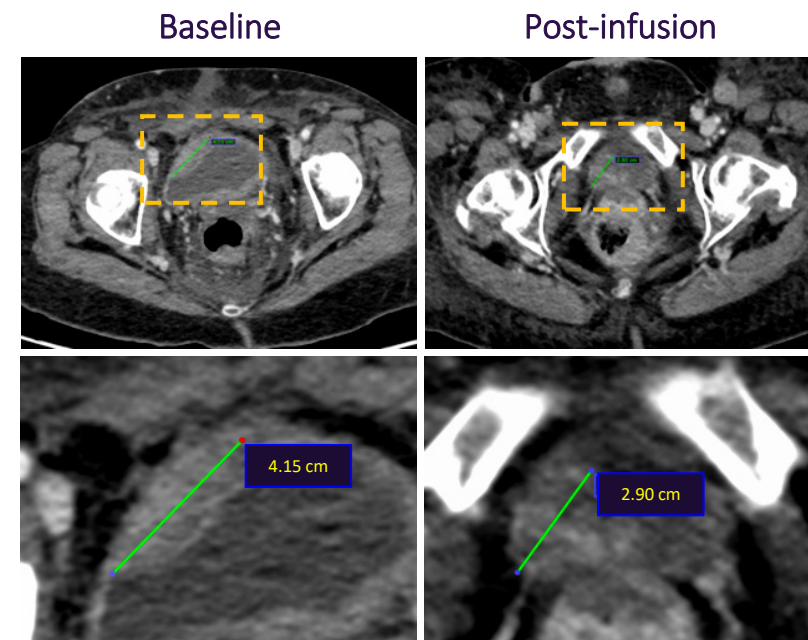
UltraCAR-T DOSES ADMINISTERED

Dose Level (DL)	Subjects	Dose Range (UltraCAR-T Cells/kg)	Total UltraCAR-T Dose Administered
DL1	N=3	>3x10 ⁴ to ≤1x10 ⁵	6 – 7.6 x10 ⁶ cells
DL2	N=3	>1x10 ⁵ to ≤ 3x10 ⁵	12 – 21 x10 ⁶ cells
DL3	N=4	>3x10 ⁵ to ≤ 5x10 ⁶	33 – 321 x10 ⁶ cells

CHANGE IN SUM OF DIAMETERS OF TARGET LESIONS



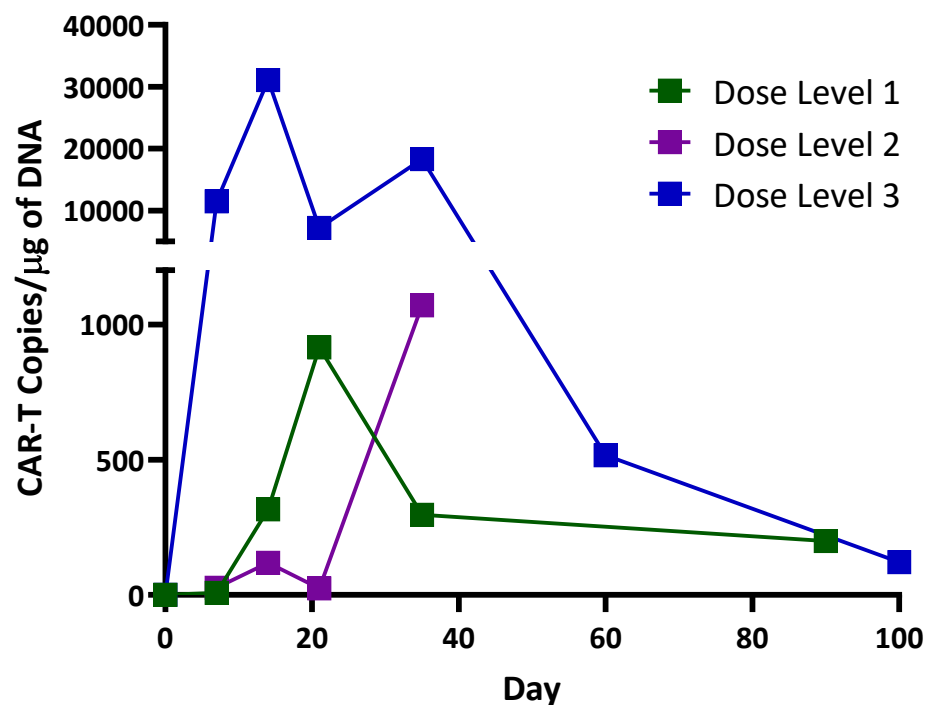
RESPONSES IN INDIVIDUAL TARGET LESIONS



- Patient administered low dose (Dose Level 2) PRGN-3005 via IP administration without lymphodepletion
- Example of observed decrease in size of target lesions, including solid lesions such as the bladder (above)

PRGN-3005 Phase 1 IP Cohort: Excellent Dose-dependent UltraCAR-T Expansion and Persistence

PRGN-3005 EXPANSION IN BLOOD



Limit of quantification: 50 CAR-T copies/μg
N=1-4 subjects at each time point

UltraCAR-T DOSES ADMINISTERED

Dose Level (DL)	Subjects	Dose Range (UltraCAR-T Cells/kg)	Total UltraCAR-T Dose Administered
DL1	N=3	>3x10 ⁴ to ≤1x10 ⁵	6 – 7.6 x10 ⁶ cells
DL2	N=3	>1x10 ⁵ to ≤ 3x10 ⁵	12 – 21 x10 ⁶ cells
DL3	N=4	>3x10 ⁵ to ≤ 5x10 ⁶	33 – 321 x10 ⁶ cells

- IP administration of UltraCAR-T resulted in expansion in the peripheral blood
- Dose-dependent expansion observed

PRGN-3005 UltraCAR-T: The Road Ahead



Complete dose escalation in Phase 1 Intraperitoneal (IP) Arm



Complete dose escalation in Phase 1 Intravenous (IV) Arm



Incorporate lymphodepletion prior to PRGN-3005 infusion (FDA clearance received)



Opportunity to evaluate repeat dosing based on the excellent safety profile of PRGN-3005

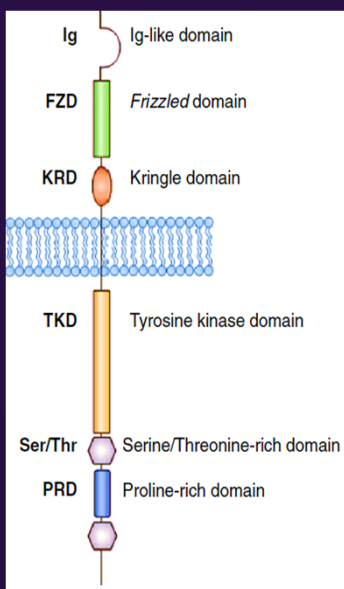
PRGN-3007 UltraCAR-T®

Helen Sabzevari, PhD
President and CEO, Precigen

PRGN-3007 UltraCAR-T: ROR1 CAR-T Cells Expressing mbIL15 and Kill Switch with Intrinsic PD-1 Blockade

ROR1: AN ATTRACTIVE TARGET FOR HEMATOLOGICAL & SOLID TUMORS

- ROR1 expression contributes to tumor cell growth and survival
- ROR1 is overexpressed in chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), and acute lymphoblastic leukemia (ALL)^{1,2}
- ROR1 is overexpressed in triple negative breast cancer (TNBC), pancreatic cancer, ovarian cancer, and lung adenocarcinomas^{1,2}
- Minimal expression detected on normal adult tissues

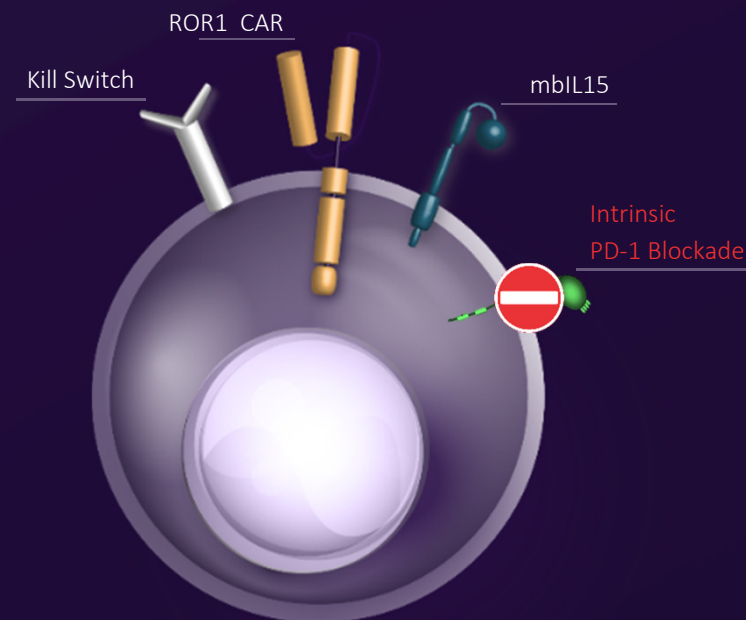


ROR1

Borcherding N, et al, 2014. *Protein & cell* 5:496-502

PRGN-3007: ROR1 CAR-T WITH INTRINSIC PD-1 INHIBITION

- ROR1 CAR to target various hematologic and solid tumors
- mbIL15 to improve *in vivo* expansion and persistence
- Kill switch to improve safety profile
- Intrinsic downregulation of PD-1 on UltraCAR-T cells to avoid systemic PD-1 blockade

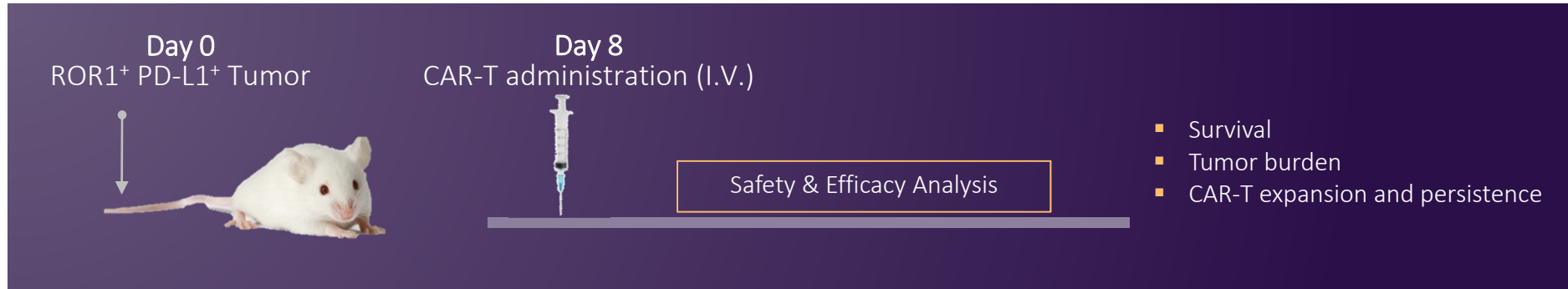


PRGN-3007 UltraCAR-T

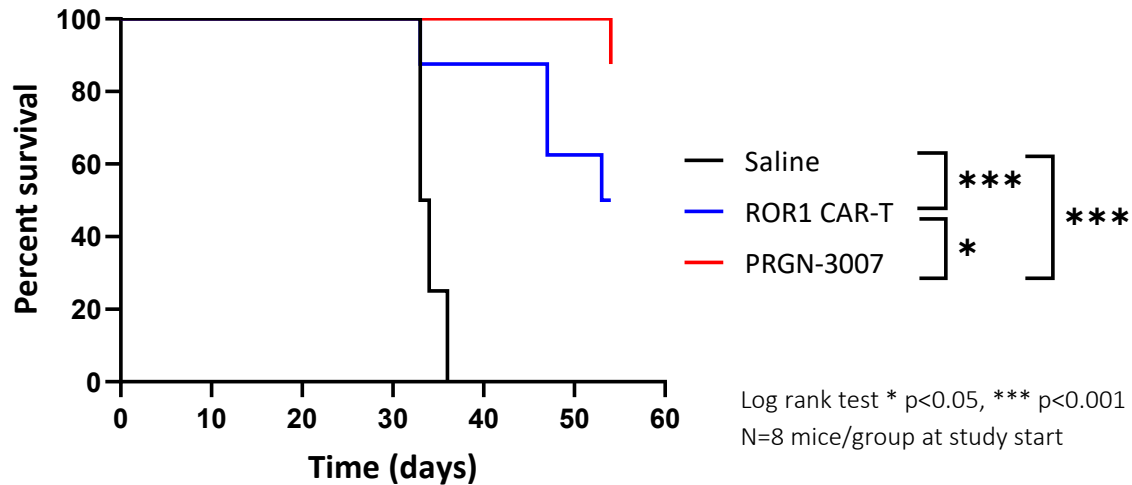
¹Balakrishnan et al. *Clin Cancer Res* 2017;23:3061-3071

²Zhang et al, 2012. <http://dx.doi.org/10.1016/j.ajpath.2012.08.024>

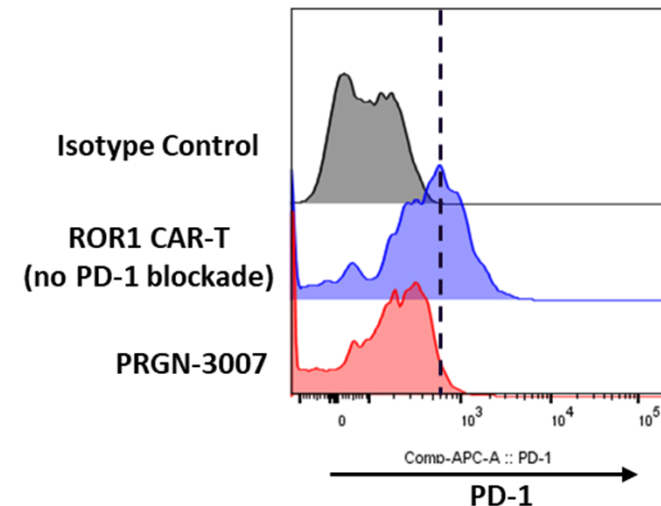
PRGN-3007 Showed Significant Downregulation of PD-1, Durable Persistence and Significant Improvement in Survival in ROR1⁺ PD-L1⁺ *In Vivo* Xenograft Model



SIGNIFICANT IMPROVEMENT IN SURVIVAL *IN VIVO*



SIGNIFICANT DOWNREGULATION OF PD-1 ON PRGN-3007 UltraCAR-T CELLS *IN VIVO*



IND Application Approved to Initiate Phase 1/1b Study of PRGN-3007 in ROR1⁺ Hematological and Solid Tumors

FIRST-IN-HUMAN DOSE ESCALATION STUDY EVALUATING SAFETY AND EFFICACY OF PRGN-3007

ELIGIBILITY

- Hematologic malignancies:
 - CLL
 - MCL
 - ALL
- Solid tumors:
 - TNBC
 - ROR1 expression confirmed

Arm 1, Hematological Malignancies



Arm 2 Solid Tumors



- SAFETY MONITORING
 - Incidence of AE, SAE, DLT
 - CRS, Neurotoxicity
- DISEASE RESPONSE
- CORRELATIVES
 - PRGN-3007 persistence/expansion
 - Immune phenotype
 - Expression of biomarkers

STUDY OBJECTIVES

Primary

- Phase 1: Dose escalation to determine the maximum tolerated dose (MTD) of PRGN-3007 in patients with advanced hematologic malignancies and solid tumors
- Phase 1b: To evaluate the safety of PRGN-3007 administered at the MTD in patients with advanced hematologic malignancies and solid tumors

Secondary

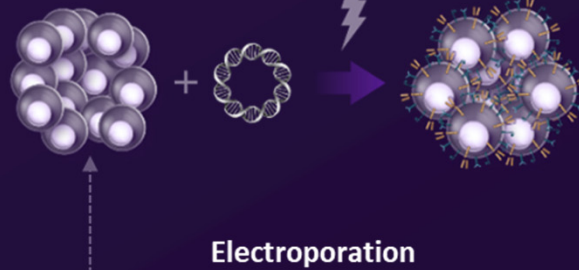
- To evaluate disease response of PRGN-3007 infusion
- To evaluate expansion and persistence of PRGN-3007
- Phase 1/1b study in collaboration with the H. Lee Moffitt Cancer Center

UltraCAR-T Library : Precigen's Vision is to Transform the Personalized Cell Therapy Landscape for Cancer Patients

Non-viral UltraCAR Library

Indication	Antigen			Indication	Antigen		
	1	2	3		1	2	3
Pancreatic				AML			
Ovarian				CLL			
Lung				ALL			
Bladder				MM			
Others				Others			

- Select one or more UltraCAR vectors from the off-the-shelf library based on a patient's tumor
- Repeat dosing if needed



**Immune Monitoring
After UltraCAR-T Administration**

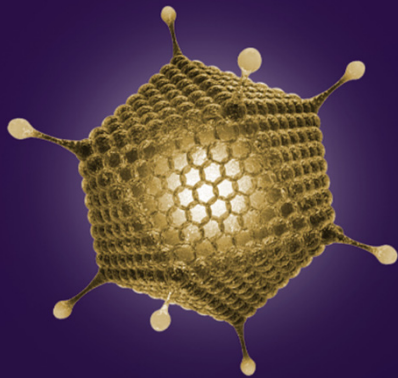
Repeat dosing if needed

AdenoVerse™ Immunotherapy Platform

Helen Sabzevari, PhD

President and CEO, Precigen

PRECIGEN'S GORILLA ADENOVECTORS SHOW SUPERIOR PERFORMANCE CHARACTERISTICS



- Large genetic payload capacity
- Off-the-shelf availability
- Ability for repeat administration
- Durable antigen-specific immune response
- Non-replicating adenoviruses
- Highly productive manufacturing process

LIMITATIONS OF COMPETING APPROACHES

VACCINES

- Limited antigen coverage
- DNA vaccines may have relatively poor immunogenicity
- Pre-existing immunity to human Ad5 may limit efficacy¹

TCR-T CELLS

- Applicable in only a small subset of patients due to HLA polymorphism
- Target only a single antigen epitope
- Long and expensive manufacturing process
- Potential for the mispairing of endogenous and exogenous TCR chains



PRGN-2012 AdenoVerse™ Immunotherapy

Clint T. Allen, MD

Principal Investigator with the Section on Translational Tumor Immunology at the NIH



RRP IS CAUSED BY HPV6 OR HPV11 INFECTION

- A rare disease in which benign tumors called papillomas grow in the respiratory tract
- Symptoms include hoarse voice, difficulty sleeping and swallowing, chronic coughing, or breathing problems
- Affects both children and adults

DISEASE SNAPSHOT



HIGH UNMET NEED

No current therapeutic treatment



20K Active Cases in US⁶

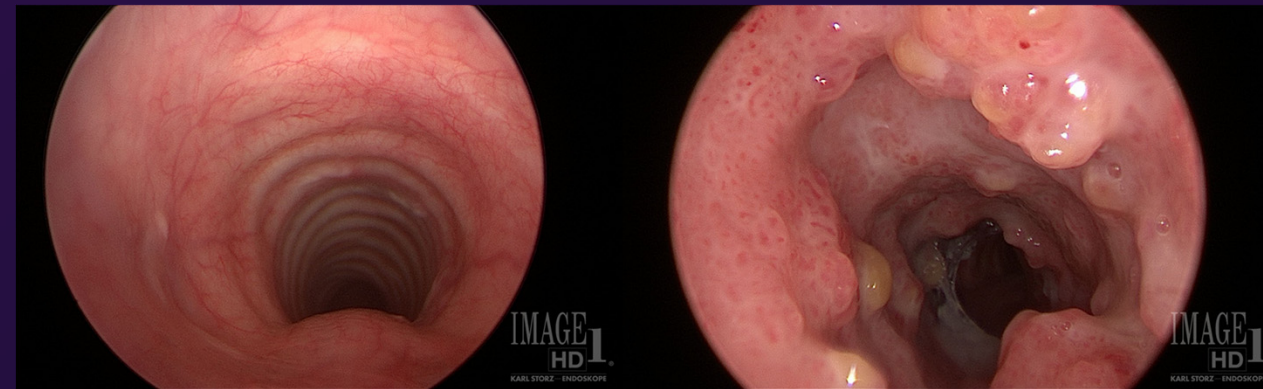
4 PER 100K

Incidence of RRP in children¹⁻⁴

2-3 PER 100K

Incidence of RRP in adults⁵

- Tracheal involvement and airway obstruction occurs in ~25% of cases



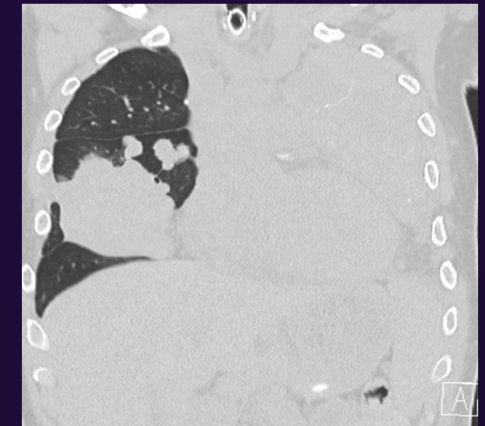
Normal trachea

RRP Patient

- RRP can lead to pulmonary papillomatosis in ~5% of cases



Normal lungs



RRP Patient

¹Derkey and Wiatrak 2008, National Organization for Rare Disorders 2019

²Armstrong, Derkey et al. 1999

³Hermann, Pontes et al. 2012

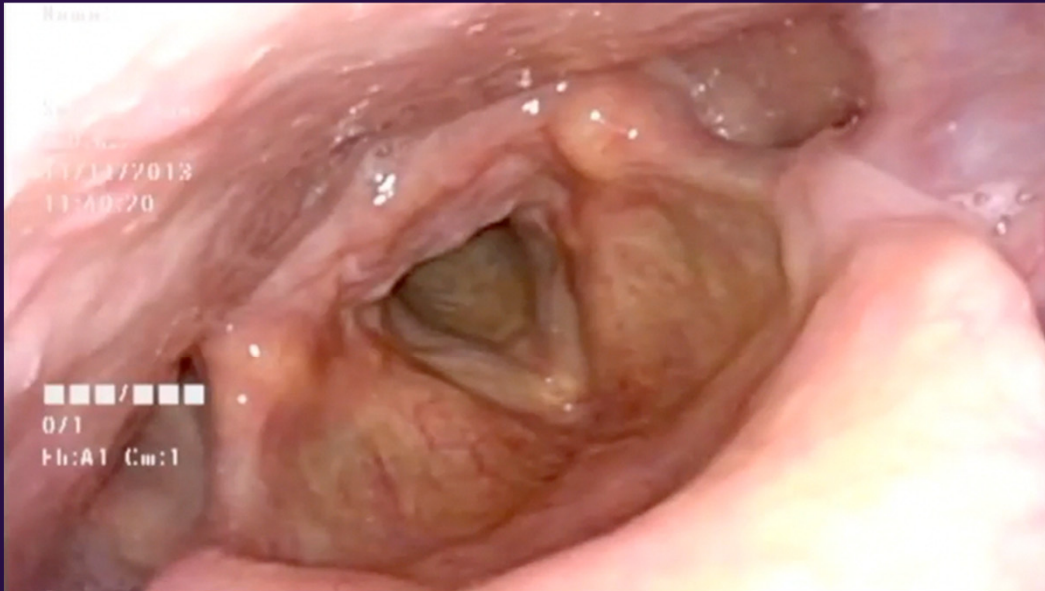
⁴Seedat 2020

⁵National Organization for Rare Disorders 2019

⁶RRP Foundation: <http://www.rrof.org/whatisRRP.html>

⁷Rodriguez-Garcia A. et al., Front. Immunol., 2020

Healthy Individual



RRP Patient



CURRENT TREATMENT PARADIGM

- Repeat surgery is the only standard-of-care treatment for RRP
- Patients can require hundreds of lifetime surgeries

BEVACIZUMAB

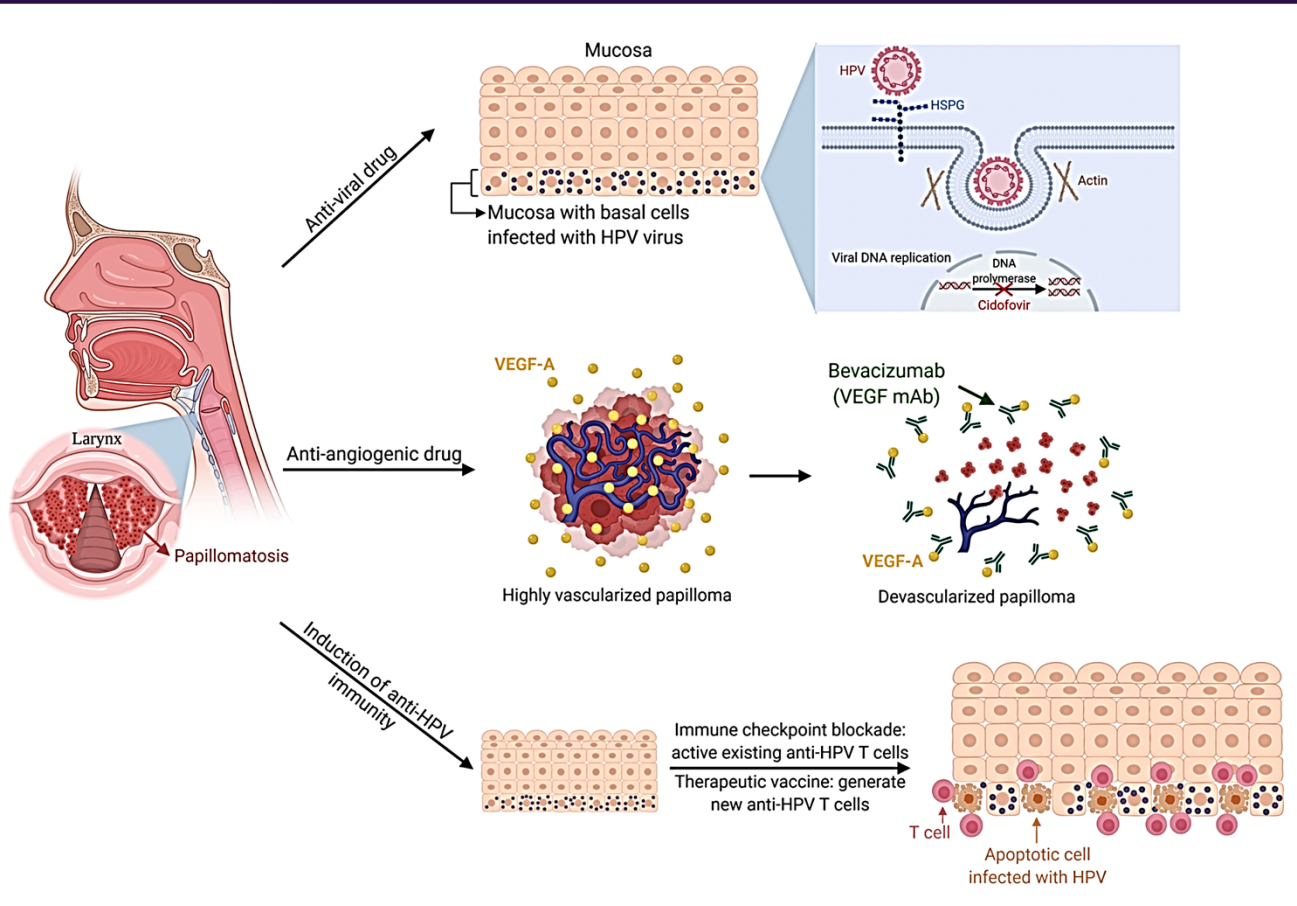
- Used off-label in the US
- Renal toxicity
- RRP rebounds after withdrawal

CHECKPOINT BLOCKADE

- Immune checkpoint blockade can activate immunity, but it does not seem to be unleashing the activity of HPV-specific T cells in most patients

PREVENTATIVE VACCINE

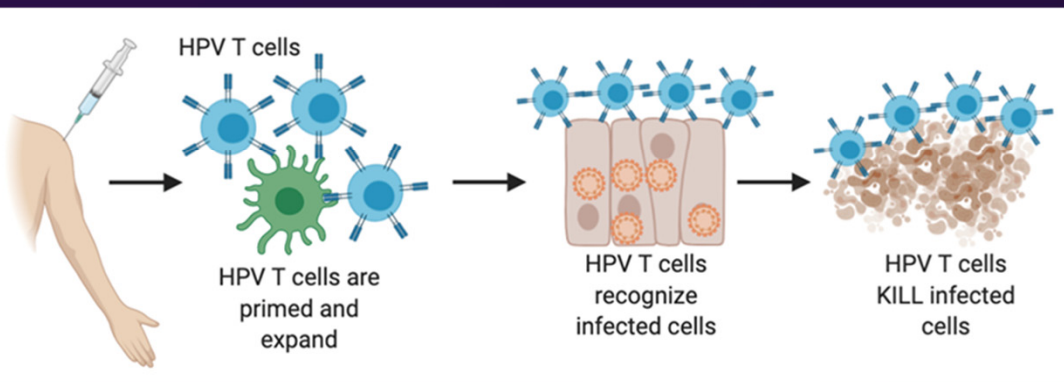
- Cannot cure RRP



RATIONALE FOR HPV6/11 THERAPEUTIC VACCINE

- Immune-mediated clearance of HPV is the only way to potentially cure RRP
- T cells are the only immune cell that can specifically detect and kill HPV infected cells
- Lack of HPV-specific T cells in RRP patients

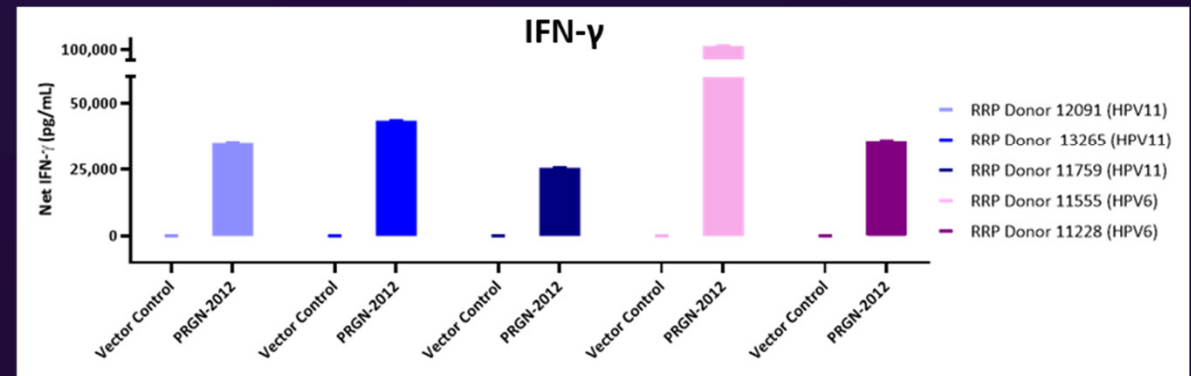
A THERAPEUTIC VACCINE DESIGNED TO INDUCE HPV-SPECIFIC T CELLS MAY CURE RRP



PRGN-2012 ANTIGEN DESIGN TO TARGET HPV6/11

- Gorilla adenoviral vector with ability for repeat injections
- Antigen designed to induce a robust T cell mediated immune response against HPV6/11
- Orphan Drug Designation (ODD) granted by the FDA

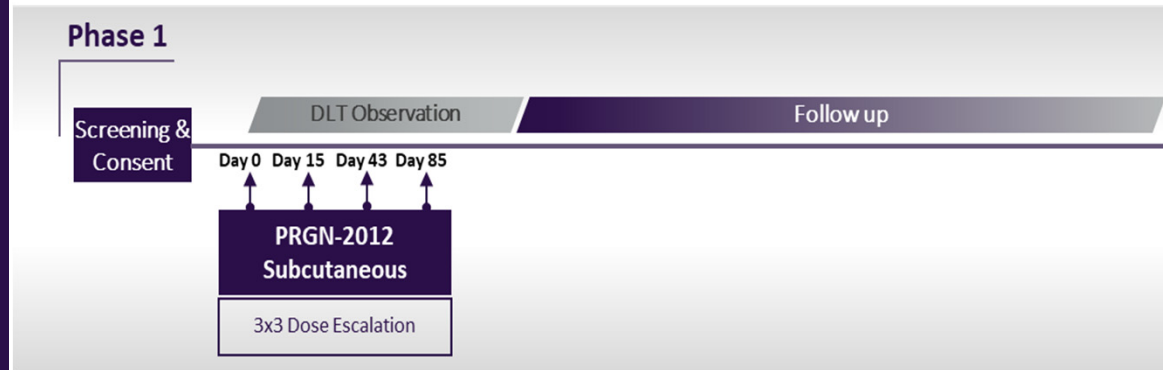
PRGN-2012 INDUCES ROBUST HPV6 AND HPV11-SPECIFIC T CELL RESPONSE IN RRP PATIENT SAMPLES *IN VITRO*



FIRST-IN-HUMAN STUDY EVALUATING SAFETY AND EFFICACY OF PRGN-2012

ELIGIBILITY

- Age ≥18 years
- Clinical diagnosis of RRP
- ECOG of 0-1



SAFETY MONITORING

- Physical exam, vitals, clinical labs

DISEASE ASSESSMENT

- Disease assessment (Derkey staging, airway evaluation)
- VHI-10 – vocal handicap index

CORRELATIVES

- HPV-specific T cell immune response
- Anti-PRGN-2012 neutralizing Abs

STUDY OBJECTIVES

Primary

- Determine the safety and tolerability and recommended Phase II adjuvant dosing (RP2D) of PRGN-2012

Secondary

- Recurrence free interval after treatment
- Frequency of clinically indicated surgery for RRP pre- and post-treatment

- Phase I study in collaboration with the National Cancer Institute

PRGN-2012 Phase I Study: Patient Characteristics and Neutralizing Antibody Response

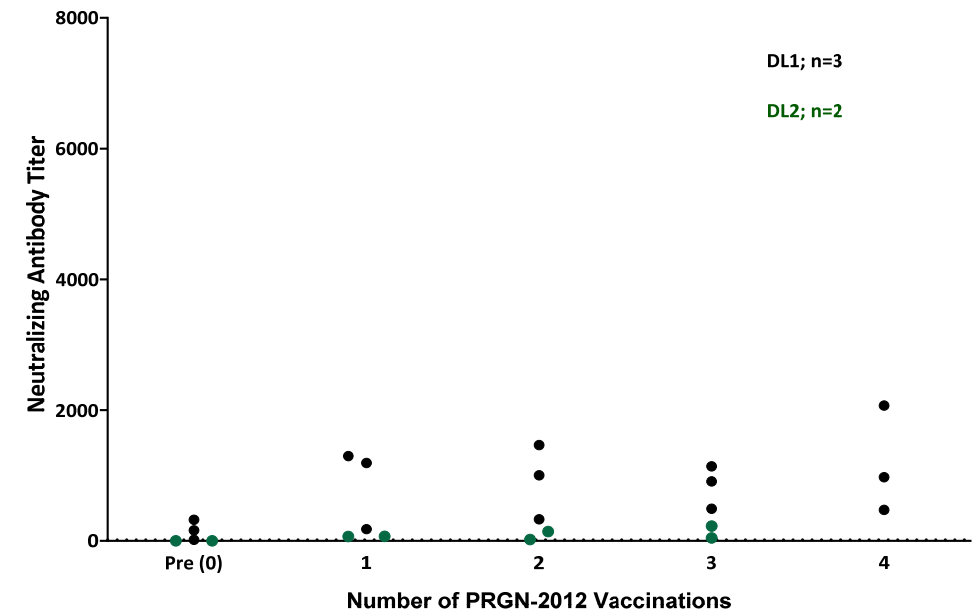
PATIENT CHARACTERISTICS

	N=14
Median age (range), years	50 (30-73)
Male	9 (64%)
Female	5 (36%)
Age at diagnosis (years)	
▪ Range	1-68
▪ Juvenile onset	2 (14%)
▪ Adult onset	12 (86%)
▪ Years since initial diagnosis	Mean 15 (range 1-43)
Baseline disease	
▪ Lifetime surgeries	Mean 51 (range 9 - 800+)
▪ Surgeries in last 2 months	Mean 5.5 (range 2-9)
▪ Tracheal disease	6 (43%)
▪ Pulmonary disease	2 (14%)

PRGN-2012 DOSING SCHEDULE

Dose Level (DL)	Subjects	Dose
DL1	N=3	1x10 ¹¹ viral particles (vp)
DL2	N=11	5x10 ¹¹ viral particles (vp)

NEUTRALIZING ANTIBODY RESPONSE



DL1: Dose Level 1; DL2: Dose Level 2

SAFETY SUMMARY

PRGN-2012 Treatment-Related Adverse Events (N=13)

Event (CTCAE v5.0)	Grade 1	Grade 2
Injection site reaction	11/13 (85%)	-
Chills	8/13 (62%)	-
Fatigue	8/13 (62%)	2/13 (15%)
Fever	8/13 (62%)	-
Pain (at injection site)	4/13 (31%)	-
Myalgia	3/13 (23%)	2/13 (15%)
Nausea	2/13 (15%)	-
Sinus tachycardia	1/13 (8%)	-
Vomiting	1/13 (8%)	-
Malaise	1/13 (8%)	-
Lethargy	1/13 (8%)	-
Diarrhea	1/13 (8%)	-
Dyspnea	1/13 (8%)	-
Pruritis	1/13 (8%)	-
Night sweats	1/13 (8%)	-

Data indicates the number and percent of subjects experiencing the event for the 13 subjects receiving at least one dose prior to the data cut-off.

- PRGN-2012 administrations were well-tolerated
- Most intense local and systemic side effects typically occurred with first vaccination
- Subsequent vaccinations had less intense side effects

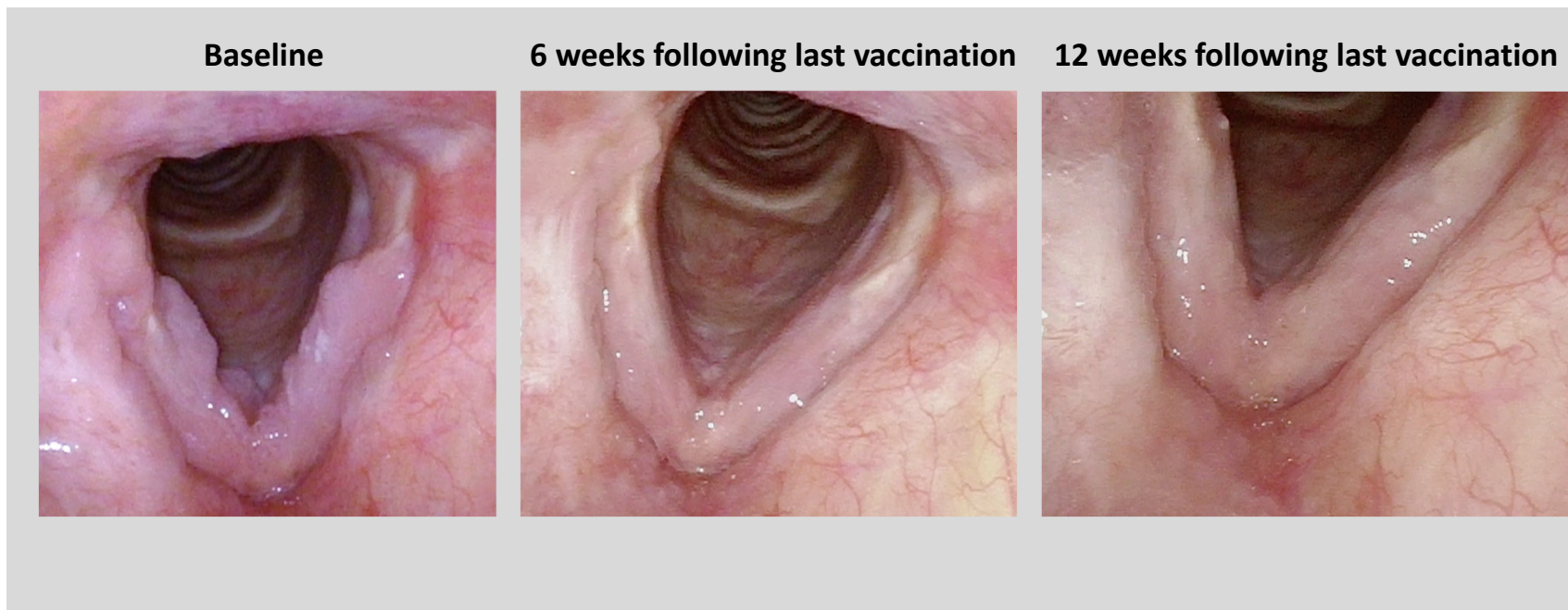


PATIENT BASELINE CHARACTERISTICS

- ~60 year old male
- Required surgery every 6 weeks for 3 years before enrollment
- Patient received 4 vaccinations of PRGN-2012 at 1×10^{11} vp/dose (Dose Level 1)

RESPONSE

- Patient did not require surgery at initial follow-up visit at 6 weeks
- A surgery was performed at the 12-week follow-up

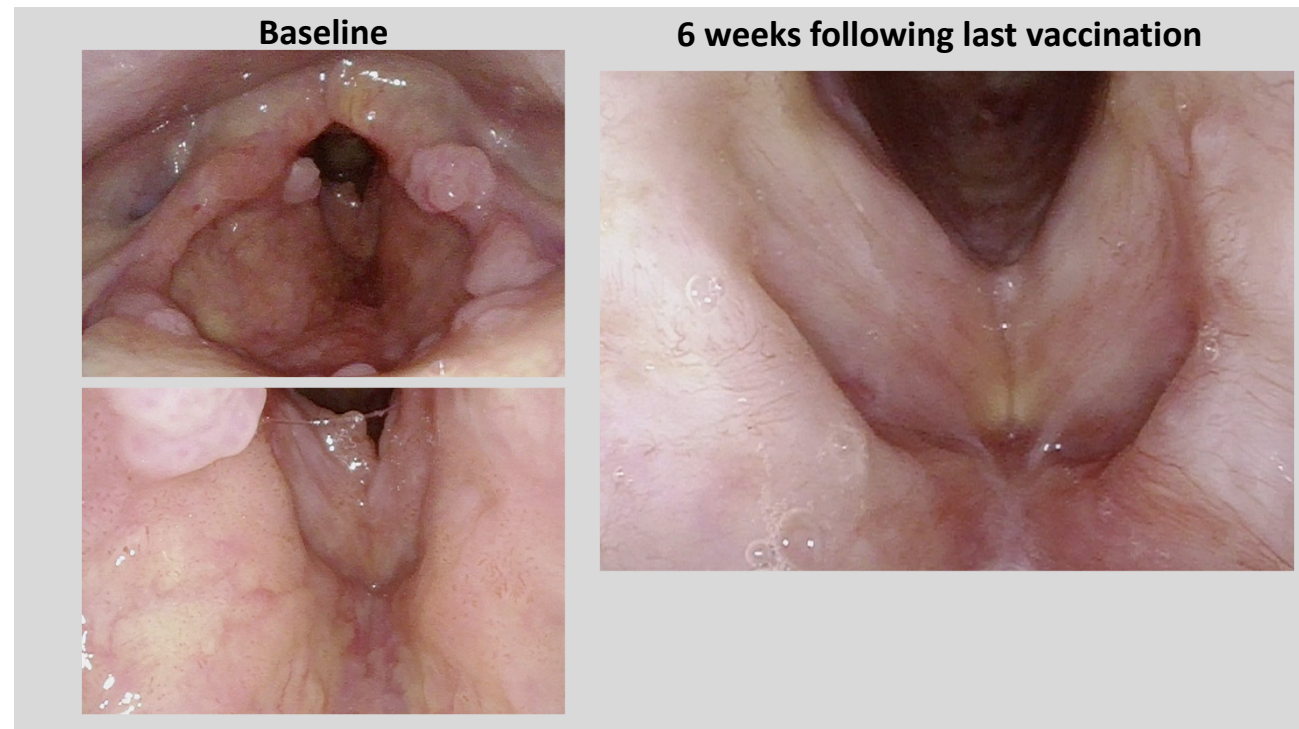


PATIENT BASELINE CHARACTERISTICS

- ~30 year old male
- Required surgery once every 6 weeks for 2.5 years prior to enrollment
- Patient received 4 vaccinations of PRGN-2012 at 5×10^{11} vp/dose (Dose Level 2)

RESPONSE

- Patient did not require surgery at initial follow-up visit at 6 weeks after treatment completion
- 12 weeks since the last surgery (6 weeks after treatment completion)



PATIENT BASELINE CHARACTERISTICS

- ~60 year old male
- Required surgery once every 2-3 months prior to enrollment
- Patient has received 3 vaccinations of PRGN-2012 at 5×10^{11} vp/dose (Dose Level 2)

RESPONSE

- Patient is disease-free
- Patient has not required any surgery for 4 months (16 weeks)

Baseline



16 weeks following last surgery



BASELINE



16 WEEKS FOLLOWING LAST SURGERY



PRGN-2012: Summary

Repeated administrations of PRGN-2012 were well-tolerated with no DLTs or serious adverse events

Neutralizing antibody data support repeated administrations of gorilla adenovirus-based AdenoVerse therapies

Preliminary data shows very encouraging response in RRP patients, including fewer surgical interventions following PRGN-2012 treatment

Phase I correlative analyses will provide mechanistic data to support safety and efficacy analyses

Phase Ib expansion cohort is enrolling patients



PRGN-2009 AdenoVerse™ Immunotherapy

NCI Clinical Data

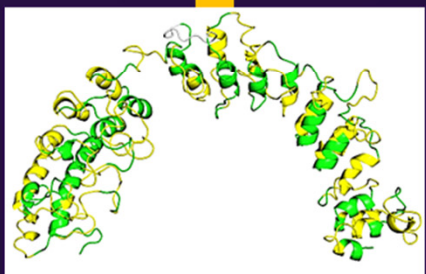
James L. Gulley, MD, PhD, FACP

Head, Immunotherapy Section, GMB, CCR, NCI, NIH



PRGN-2009: MULTI-EPI TOPE ANTIGEN DESIGN TO TARGET HPV16/18

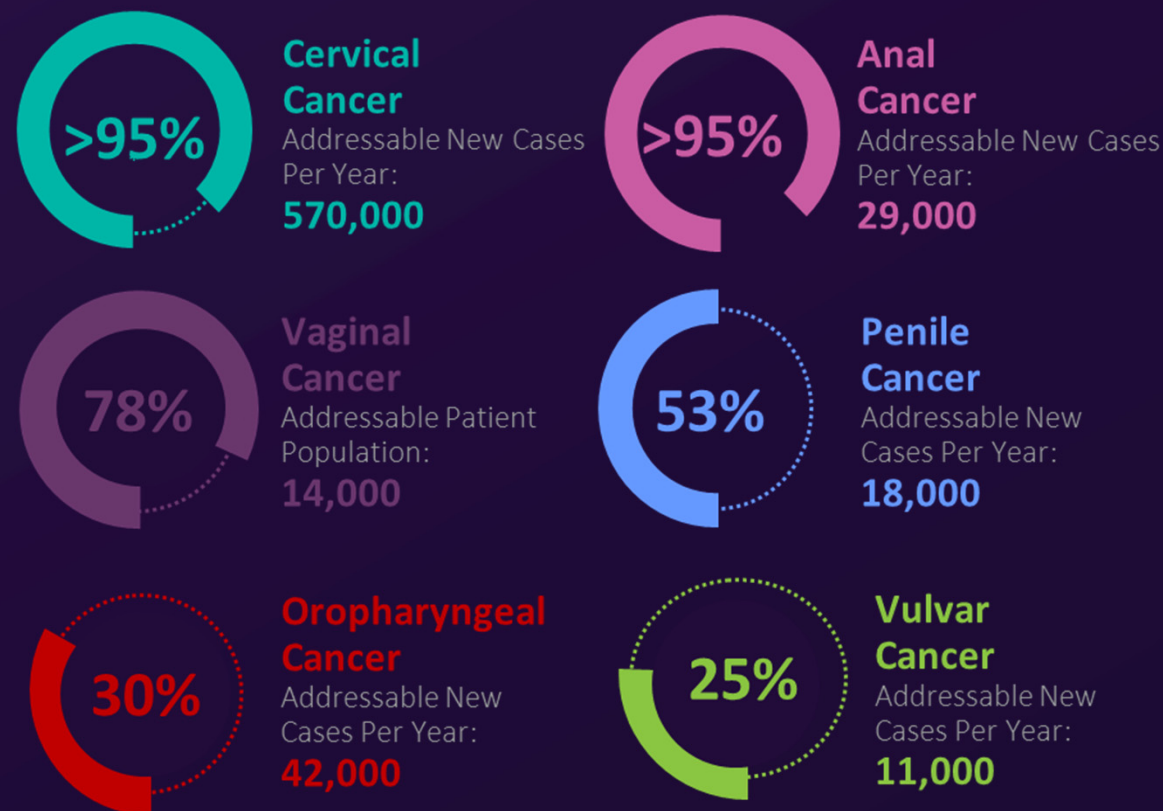
- Gorilla adenoviral vector with ability for repeat injections
- Multi-epitope antigen design to induce a robust immune response against HPV16/18



Multi-epitope antigen design

HPV-ASSOCIATED CANCERS

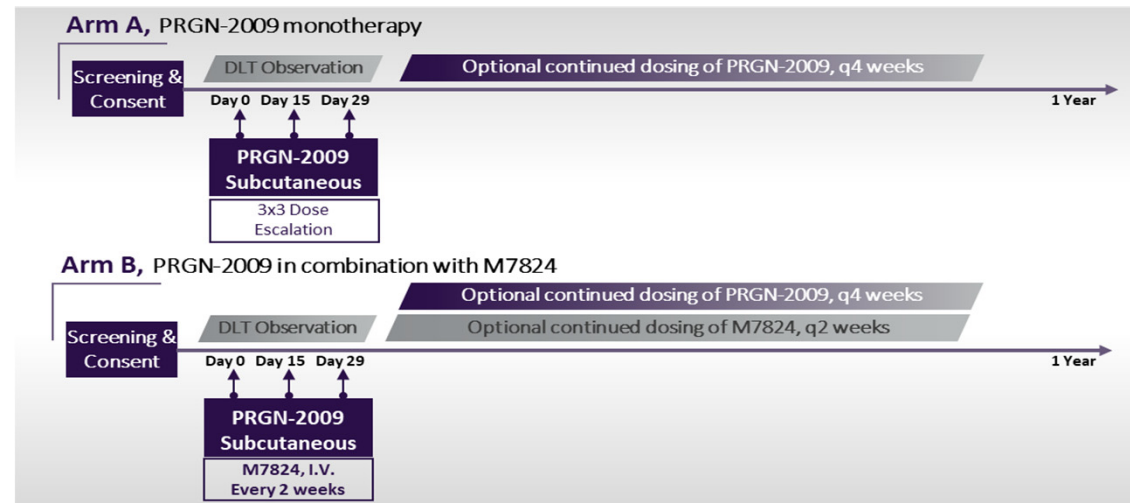
- HPV infections account for 5% of all cancers¹
- Globally 690,000 new cancer cases attributable to HPV infections per year²



FIRST-IN-HUMAN, STUDY EVALUATING SAFETY AND EFFICACY OF PRGN-2009 AS MONOTHERAPY & COMBINATION THERAPY

ELIGIBILITY

- Age ≥18 years
- R/M HPV-associated cancers; disease progression following SOC
- ≥1 measurable (RECIST 1.1) lesion



SAFETY MONITORING

- Physical exam, vitals, clinical labs
- ECG

DISEASE RESPONSE

- RECIST v1.1

CORRELATIVES

- HPV-specific T-cell immune response
- Anti-PRGN-2009 neutralizing Abs

STUDY OBJECTIVES

Primary

- Evaluate safety and recommended Phase II dose of PRGN-2009

Secondary

- Objective Response Rate (ORR) (RECIST 1.1), Duration of Response (DOR), Progression Free Survival (PFS), and Overall Survival (OS)

- Phase I/II study in collaboration with the National Cancer Institute; PI C. “Harris” Floudas MD, DMSc, MS

PRGN-2009 Phase I Monotherapy Arm: Patient Characteristics, Safety Summary and Neutralizing Antibody Response

PATIENT CHARACTERISTICS

Patient Information	Arm 1A (n=6)
Median age (range)	61 (43-70)
Female, n (%)	6 (100)
Tumor Types, n (%)	
Cervical	3 (50)
Anal	2 (33)
Vaginal	1 (17)
Prior systemic therapies (median, range)	2.5 (1-3)
Prior anti-PD-(L)1	6 (100)
PRGN-2009 doses (median, range)	5 (3-16)

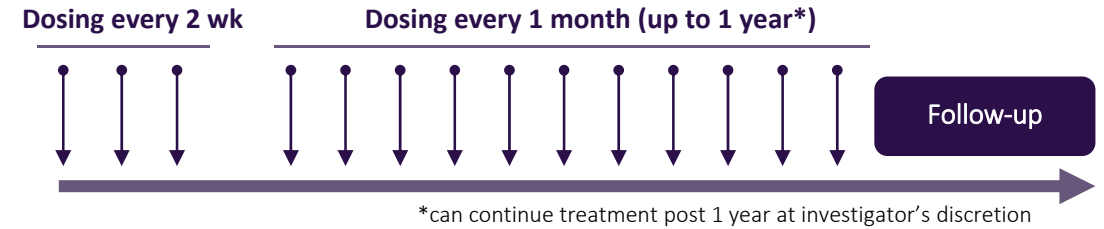
SAFETY SUMMARY

Treatment-related AEs	Arm 1A n (%)
Flu-like symptoms, G1-2	2 (33)
Injection site reactions, G1-2	5 (83)
Fatigue, G1-2	2 (33)
Rash, maculopapular, G1-2	1 (17)

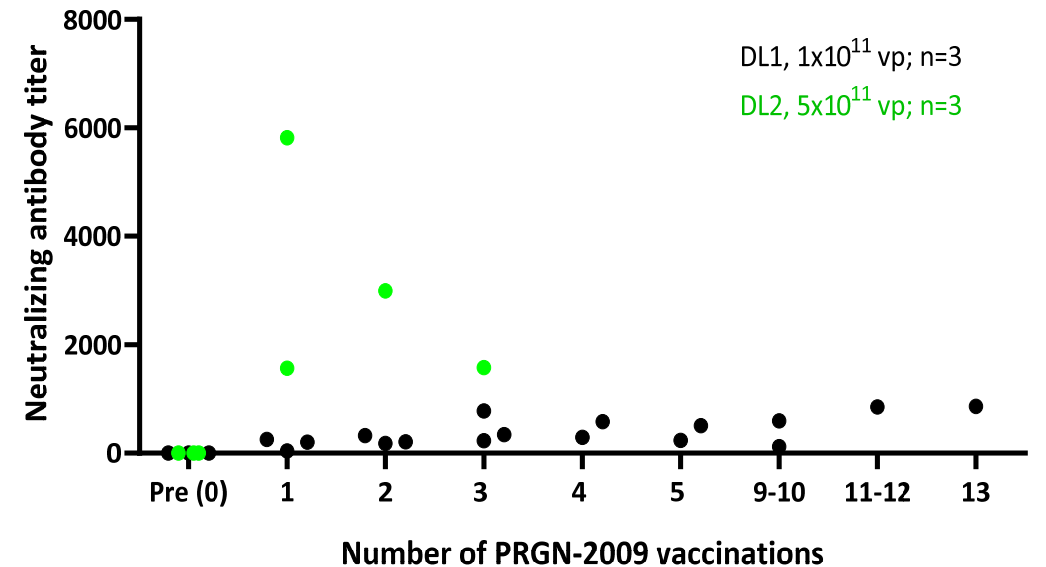
G1-2: Grade 1-2

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PRGN-2009 DOSING SCHEDULE



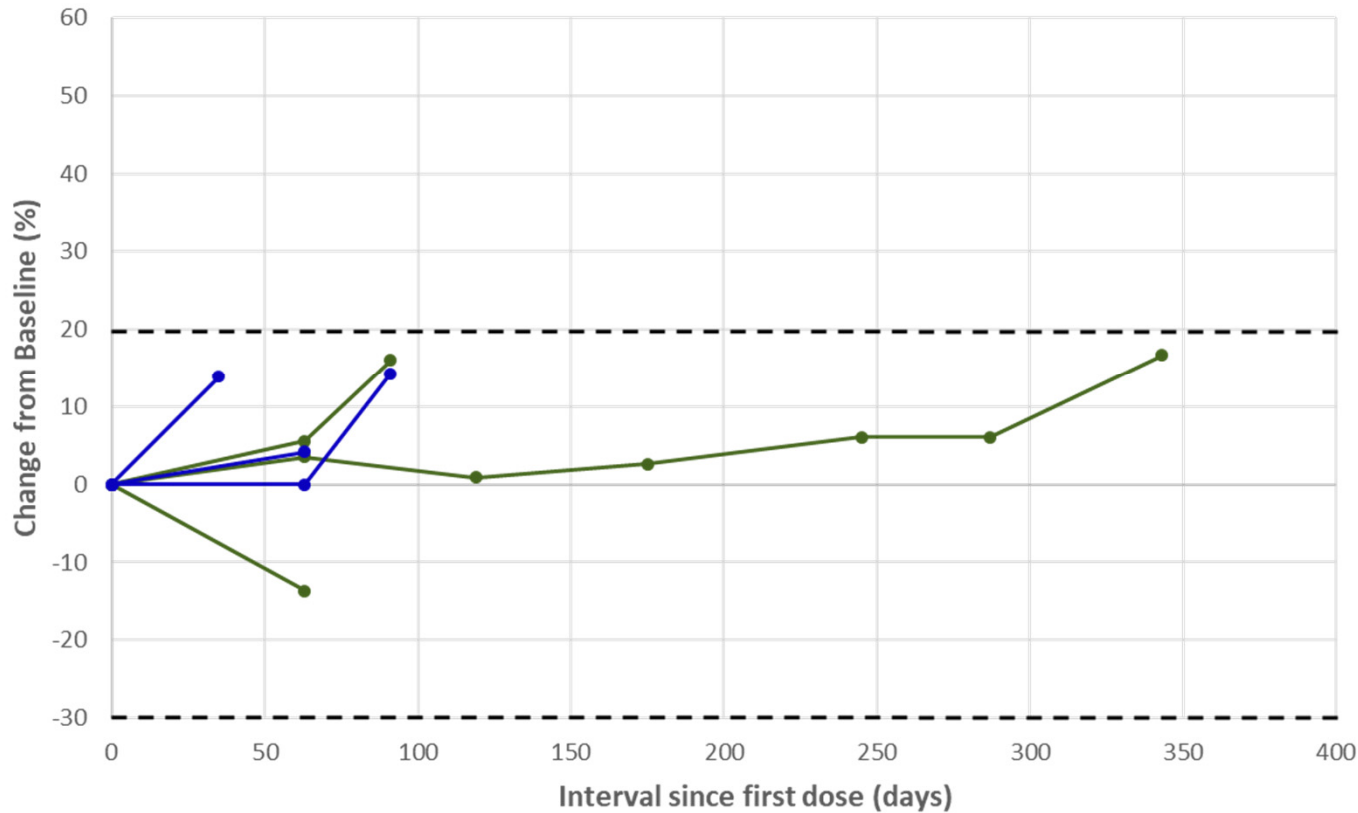
NEUTRALIZING ANTIBODY RESPONSE



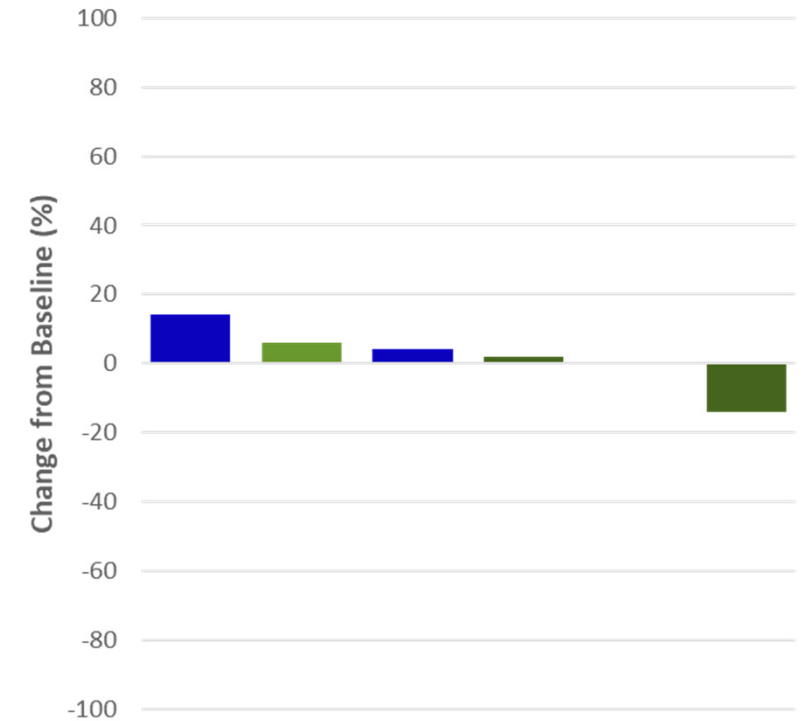
DL1: Dose Level 1; DL2: Dose Level 2

PRGN-2009 Phase I Monotherapy Arm: Change in Tumor Burden Following PRGN-2009 Treatments

LONGITUDINAL CHANGE IN SUM OF LONGEST DIAMETER OF TARGET LESIONS



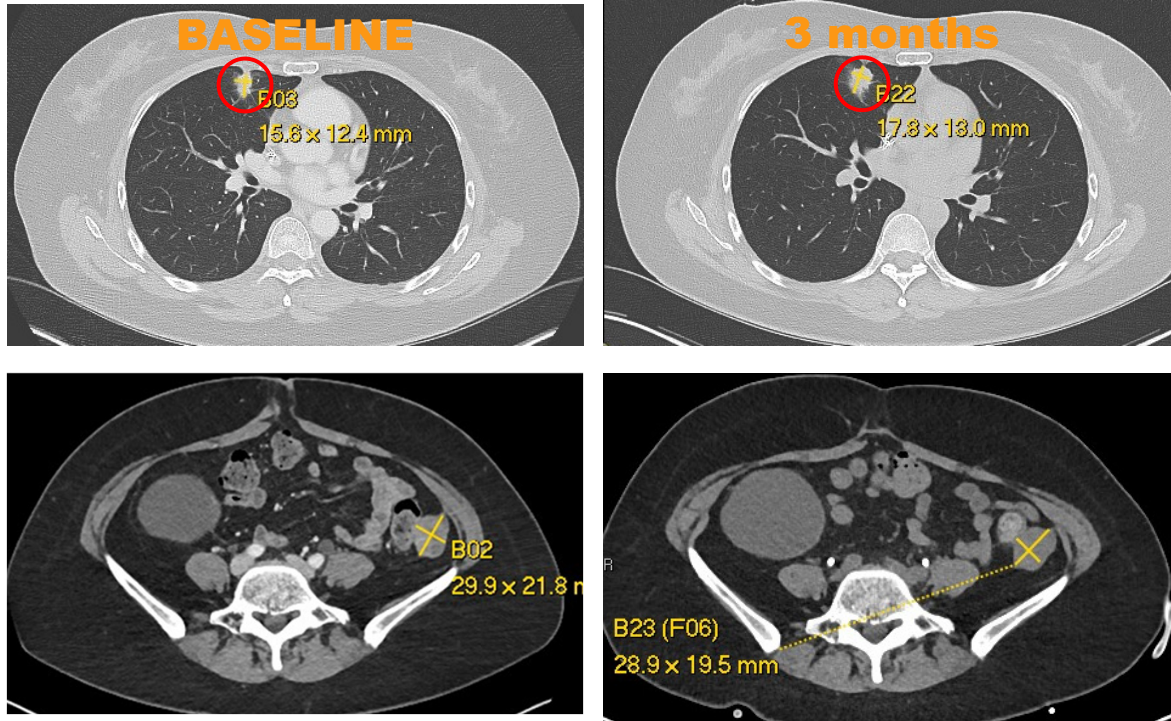
MAXIMUM CHANGE IN SUM OF LONGEST DIAMETER OF TARGET LESIONS



PRGN-2009 1x10¹¹ vp, n=3
PRGN-2009 5x10¹¹ vp, n=3

Case Study Phase I Monotherapy Arm: Subject with Durable Stable Disease (> 1 Year) has Received 16 PRGN-2009 Vaccinations

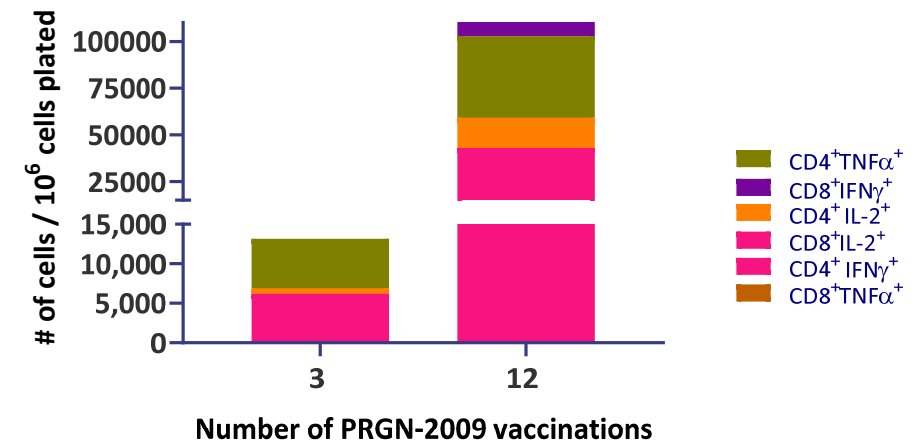
TUMOR LESION RESPONSE



PATIENT BASELINE CHARACTERISTICS

- Cervical cancer patient
- PRGN-2009 monotherapy at Dose Level 1 (1×10^{11} vp)
- Has received 16 PRGN-2009 vaccinations
- Continues to receive monthly PRGN-2009 vaccination
- Durable Stable Disease (SD) since the initial re-staging

HPV-SPECIFIC T CELL RESPONSE

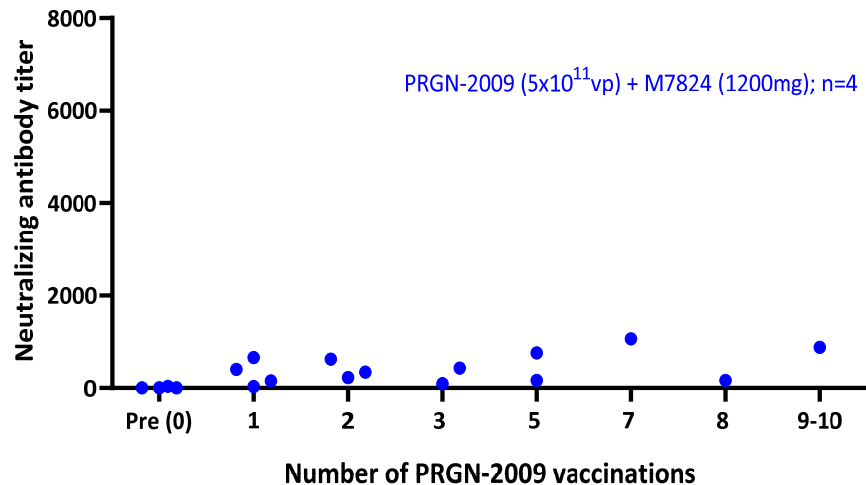


PRGN-2009 Phase I Combination Arm: Patient Characteristics, Safety Summary and Neutralizing Antibody Response

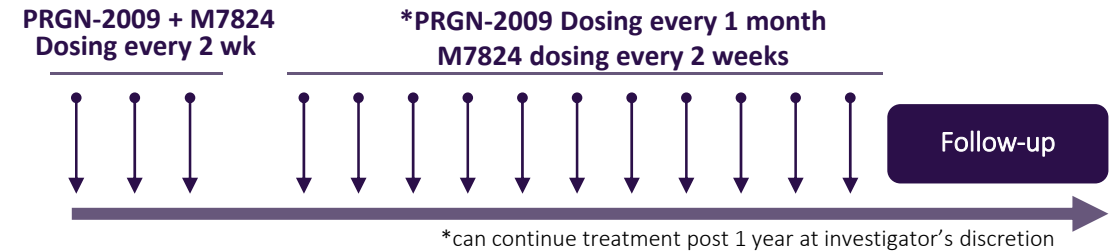
PATIENT CHARACTERISTICS

Patient Information	Arm 1B (n=6)
Median age (range)	61 (64-80)
Female, n (%)	2 (33)
Tumor Types, n (%)	
▪ OPSCC	4 (67)
▪ Cervical	2 (33)
Prior systemic therapies (median, range)	3 (1-4)
Prior anti-PD-(L)1	6 (100)
PRGN-2009 doses (median, range)	5 (1-10)

NEUTRALIZING ANTIBODY RESPONSE



PRGN-2009 DOSING SCHEDULE



SAFETY SUMMARY

Treatment-related AEs	Arm 1B n (%)
Flu-like symptoms, G1-2	3 (50)
Injection site reactions, G1-2	4 (67)
Fatigue, G1-2	1 (17)
Rash, maculopapular, G1-2	1 (17)
Keratoacanthoma, G1-2	2 (33) *M7824-related
Anemia, G3-4	1 (17) *M7824-related
Duodenal Hemorrhage, G3-4	2 (33) *M7824-related

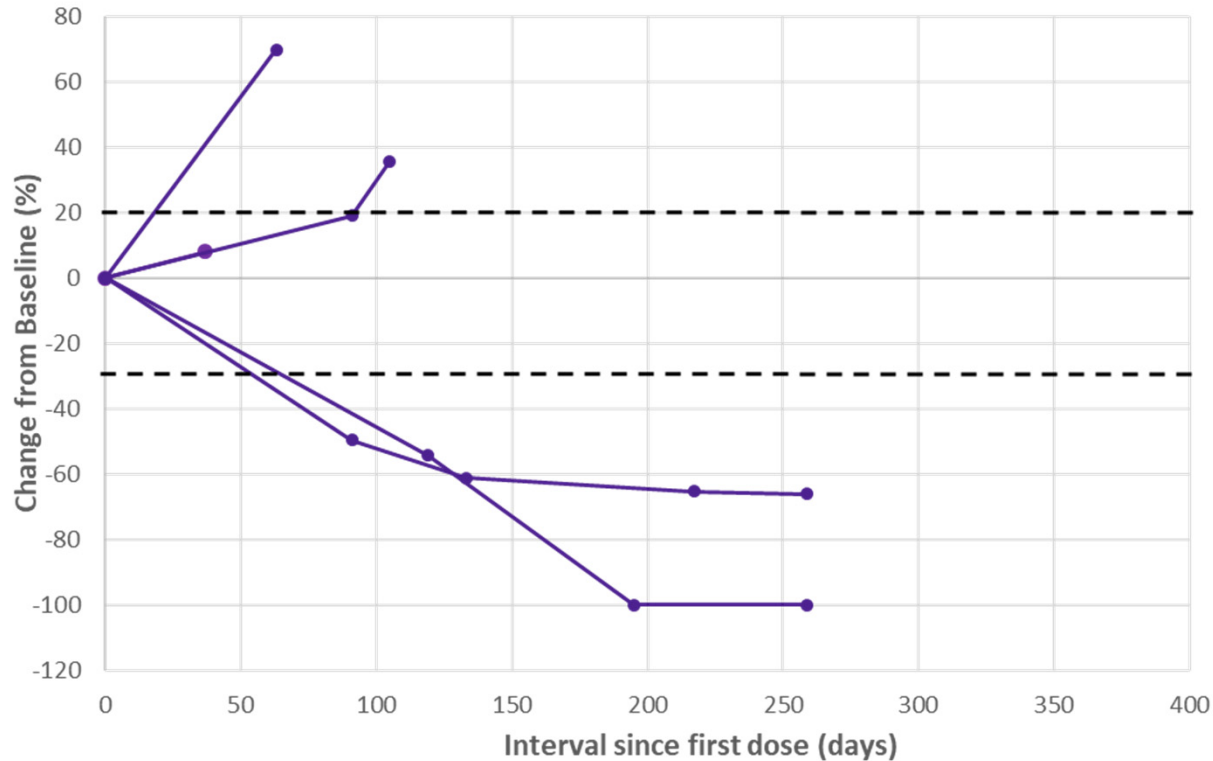
Additional AEs : In one patient(all Grade 1-2): diarrhea, headache, hemoglobinuria, hyperglycemia, fever, anorexia, epistaxis, dysgeusia, lymphocyte count decreased.

One patient died due to a duodenal hemorrhage (related to M7824) following refusal of core standard medical management (blood transfusion).

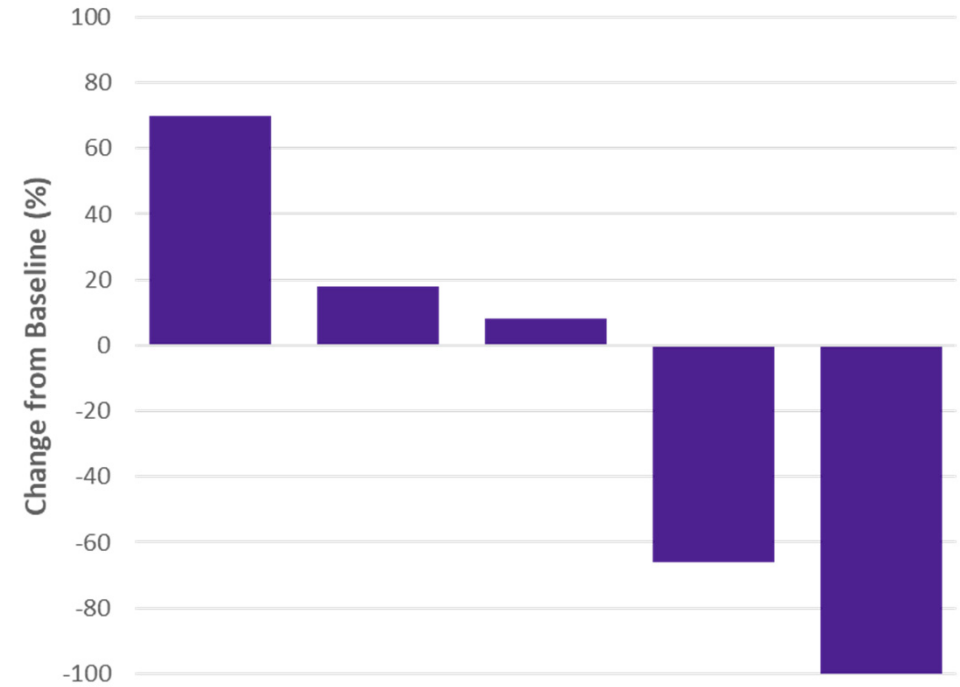
G1-2: Grade 1-2; G3-4: Grade 3-4

PRGN-2009 Phase I Combination Arm: Change in Tumor Burden Following Combination Treatments

LONGITUDINAL CHANGE IN SUM OF LONGEST DIAMETER OF TARGET LESIONS

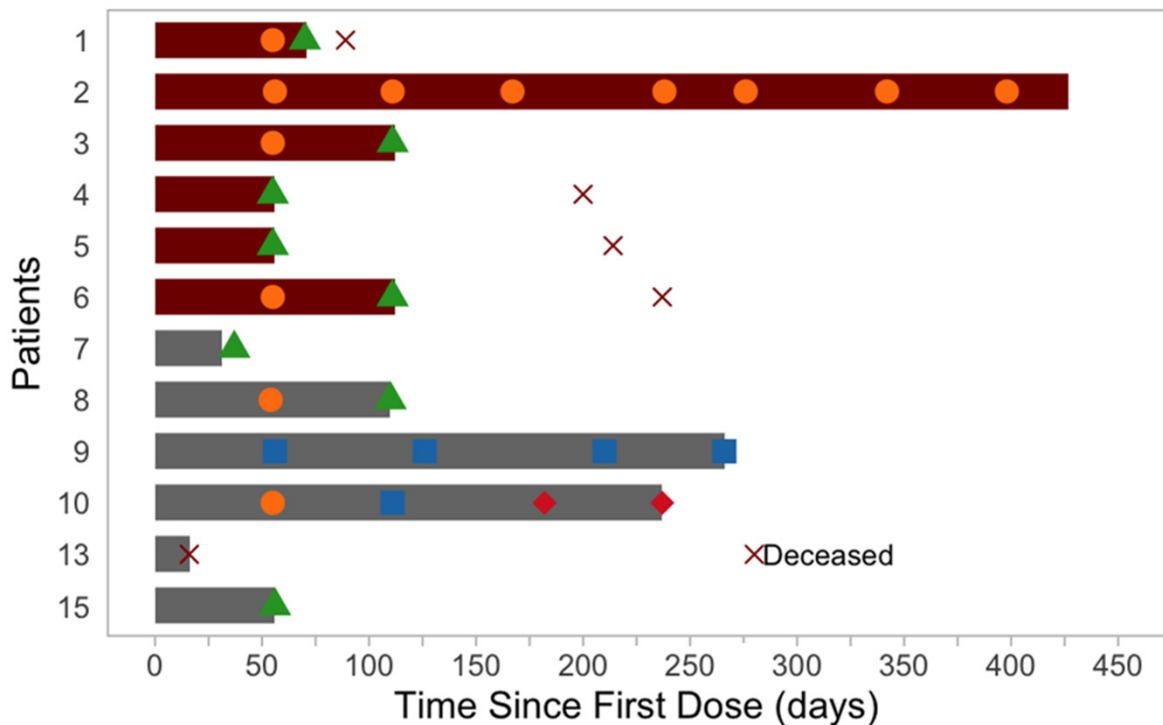


MAXIMUM CHANGE IN SUM OF LONGEST DIAMETER OF TARGET LESIONS



PRGN-2009 5x10¹¹ vp + M7824, n=5

SUMMARY OF RESPONSES



Arm 1A: PRGN-2009 Monotherapy
 Arm 1B: PRGN-2009 in Combination with M7824

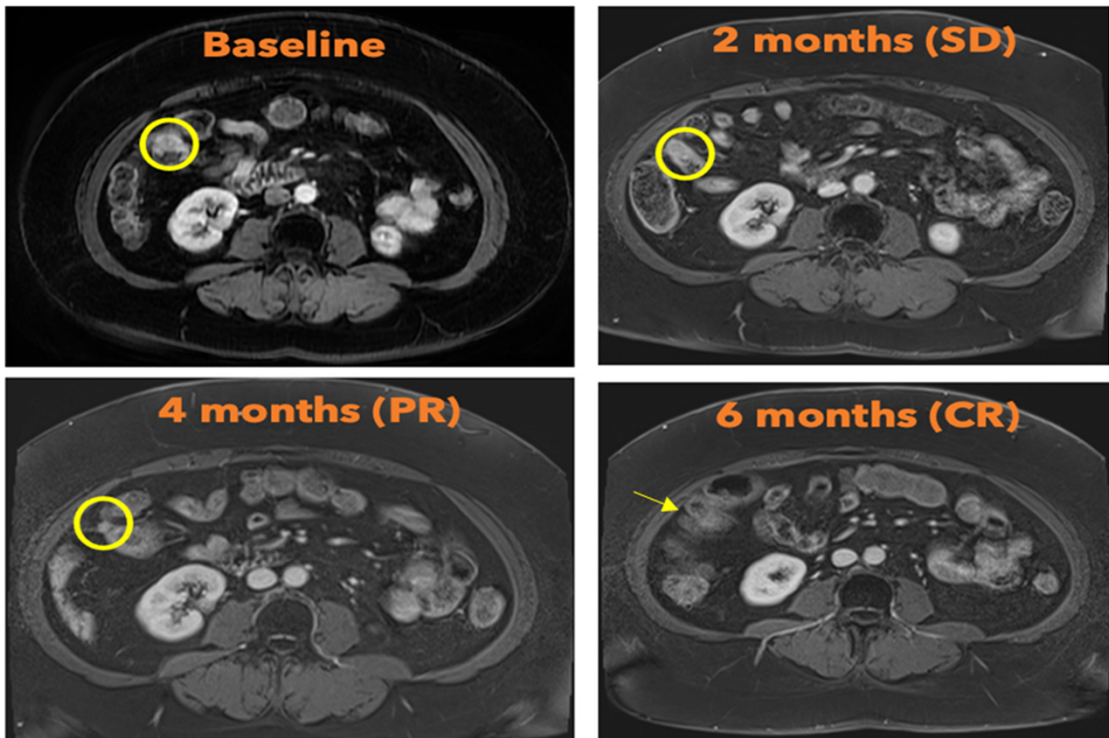
CR: Complete Response
 PR: Partial Response
 SD: Stable Disease
 PD: Progressive Disease

BEST OVERALL RESPONSE (RECIST v1.1 CRITERIA)

	PRGN-2009 Monotherapy (Arm 1A)	PRGN-2009 Combination (Arm 1B)
Disease Control Rate (DCR) at first restaging	50% (3/6)	60% (3/5)
Objective Response Rate (ORR)	0% (0/6)	40% (2/5)

40% Objective Response Rate (ORR) in patients treated in the PRGN-2009 Combination Arm 1B

TUMOR LESION RESPONSE

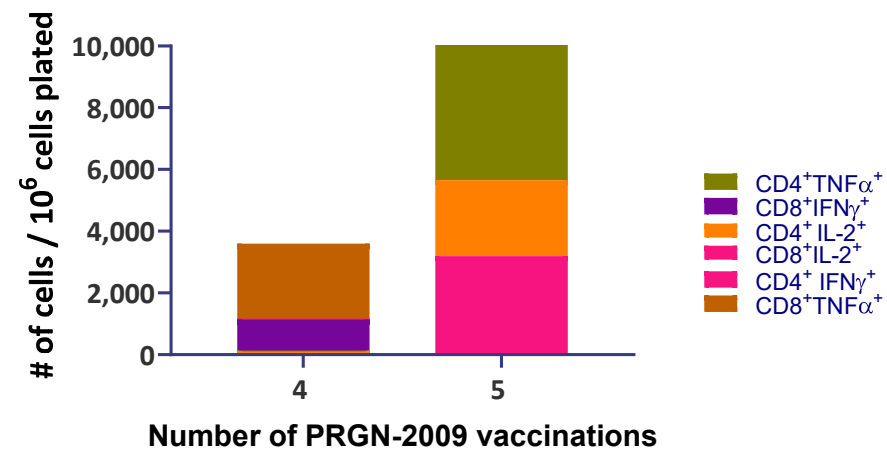


CR: Complete Response
 PR: Partial Response
 SD: Stable Disease

PATIENT BASELINE CHARACTERISTICS

- Cervical cancer patient
- PRGN-2009 at 5×10^{11} vp in combination with M7824
- Off-study due to toxicity related to M7824
- PR at initial re-staging
- CR at approx. 6 months following treatment start

HPV-SPECIFIC T CELL RESPONSE



PRGN-2009: Summary

Repeated administrations of PRGN-2009 were well-tolerated as monotherapy and combination therapy (No DLTs)

Increase in HPV16 and/or HPV18 specific immune response with administrations of PRGN-2009

Neutralizing antibody data support repeated administrations of gorilla adenovirus based AdenoVerse therapies

Objective Response Rate (ORR) of 40% and Disease Control Rate (DCR) of 60% observed in the Combination Arm

Phase II study in newly diagnosed OPSCC patients is ongoing

Summary & Road Ahead

Helen Sabzevari, PhD
President and CEO, Precigen

UltraCAR-T Platform is Designed to Address Major Limitations of Current T Cell Therapies

UltraCAR-T	PRODUCT	PLATFORM	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
	PRGN-3005	UltraCAR-T	Ovarian Cancer	█				
	PRGN-3006	UltraCAR-T	AML, MDS	█				
	PRGN-3007	UltraCAR-T	ROR1+ Hematological & Solid Tumors	█				

UltraCAR-T OVERNIGHT, DECENTRALIZED MANUFACTURING PROCESS PROMISES A MORE EFFECTIVE WAY TO TREAT PATIENTS

SUMMARY

- Excellent **safety profile** in both hematological and solid malignancies
- **Validation of overnight, decentralized manufacturing**
- Excellent *in vivo* **expansion** and long-term **persistence** of UltraCAR-T in both hematological and solid malignancies
- Encouraging **objective responses** with PRGN-3006 in Lymphodepletion Cohort in r/r AML
- Incorporation of intrinsic checkpoint inhibition in the **next generation UltraCAR-T**

ROAD AHEAD

- **Expansion** of clinical trials
- Potential to pursue **rapid regulatory development** path for PRGN-3006
- Opportunity to evaluate **repeat dosing**
- Initiate dosing in **PRGN-3007 trial** for hematological and solid malignancies
- Continue to **innovate UltraCAR-T platform** to build non-viral library to transform the personalized cell therapy landscape for cancer patients



ADENOVERSE	PRODUCT	PLATFORM	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
	PRGN-2009	AdenoVerse	HPV+ Solid Tumors					
	PRGN-2012	AdenoVerse	Recurrent Respiratory Papillomatosis (RRP)					

ABILITY FOR REPEAT ADMINISTRATION TO GENERATE STRONG IMMUNE RESPONSES REPRESENTS AN ATTRACTIVE OPPORTUNITY FOR AdenoVerse IMMUNOTHERAPY PLATFORM

SUMMARY

- Excellent **safety profile** in both cancer and infectious disease settings
- Patient data strongly support **repeat administrations**
- Increase in **antigen-specific immune response** with repeat administrations
- Robust **clinical activity** with PRGN-2009 in combination with checkpoint inhibitor
- Very encouraging preliminary **clinical responses in RRP**, including **reduction/elimination in surgical interventions** following PRGN-2012 treatment



ROAD AHEAD

- **Completion** of ongoing clinical trials
- Potential to pursue **rapid regulatory development** path for PRGN-2012
- **Attractive opportunity** for combination of PRGN-2009 with checkpoint inhibitors in multiple HPV-associated cancers
- Continue to **innovate AdenoVerse platform** to advance additional therapies for cancer and infectious disease patients

Q&A



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