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This presentation and the accompanying verbal remarks contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, such as statements regarding data and results from clinical trials and potential implications therefrom, commercialization plans and timelines, including product availability and shipments, potential regulatory pathways and approval requests and submissions, FDA and other regulatory agency meetings, timelines and potential results therefrom, global expansion efforts, strategic collaborations and expected results therefrom, the regulatory review process and timing thereof, market and prevalence data, potential benefits to patients, potential treatment outcomes for patients, the described mechanism of action and results and contributions therefrom, information regarding potential benefit to patients, information regarding ongoing pre-clinical studies and clinical trials, potential future uses and applications of ANKTIVA and use in cancer vaccines and across multiple tumor types, methods, ImmunityBio's financial condition, and ImmunityBio's approved product and investigational agents as compared to existing treatment options, among others. Statements in this presentation that are not statements of historical fact are considered forward-looking statements, which are usually identified by the use of words such as "anticipates," "believes," "continues," "goal," "could," "estimates," "scheduled," "expects," "intends," "may," "plans," "potential," "predicts," "indicate," "projects," "seeks," "should," "will," "strategy," and variations of such words or similar expressions. Statements of past performance, efforts, or results of our preclinical and clinical trials, about which inferences or assumptions may be made, can also be forward-looking statements and are not indicative of future performance or results. Forward-looking statements are neither forecasts, promises nor guarantees, and are based on the current beliefs of ImmunityBio's management as well as assumptions made by and information currently available to ImmunityBio. Such information may be limited or incomplete, and ImmunityBio's statements should not be read to indicate that it has conducted a thorough inquiry into, or review of, all potentially available relevant information. Such statements reflect the current views of ImmunityBio with respect to future events and are subject to known and unknown risks, including business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about ImmunityBio, including, without limitation, (i) the risks and uncertainties associated with commercial launch execution, success and timing, (ii) risks and uncertainties related to the regulatory submission, review and approval process, (iii) the ability of ImmunityBio to continue its planned preclinical and clinical development of its development programs through itself and/or its investigators, and the timing and success of any such continued preclinical and clinical development, patient enrollment and planned regulatory submissions, (iv) potential delays in product availability and regulatory approvals, (v) risks and uncertainties associated with third party collaborations and agreements, (vi) whether ImmunityBio's and/or its collaborators' investigational agents will receive regulatory approval in the U.S. and/or other regions, (vii) ImmunityBio's ability to retain and hire key personnel, (viii) ImmunityBio's ability to obtain additional financing to fund its operations and complete the development and commercialization of its various product candidates, (ix) potential product shortages or manufacturing disruptions that may impact the availability and timing of product, (x) ImmunityBio's ability to successfully commercialize its approved product and product candidates and uncertainties around regulatory reviews and approvals, (xi) ImmunityBio's ability to scale its manufacturing and commercial supply operations for its approved product and future approved products, and (xii) ImmunityBio's ability to obtain, maintain, protect and enforce patent protection and other proprietary rights for its product candidates and technologies. More details about these and other risks that may impact ImmunityBio's business are described under the heading "Risk Factors" in the Company's Form 10-K filed with the U.S. Securities and Exchange Commission ("SEC") on March 3, 2025 and in subsequent filings made by ImmunityBio with the SEC, which are available on the SEC's website at www.sec.gov. ImmunityBio cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date hereof. ImmunityBio does not undertake any duty to update any forward-looking statement or other information in this press release, except to the extent required by law.

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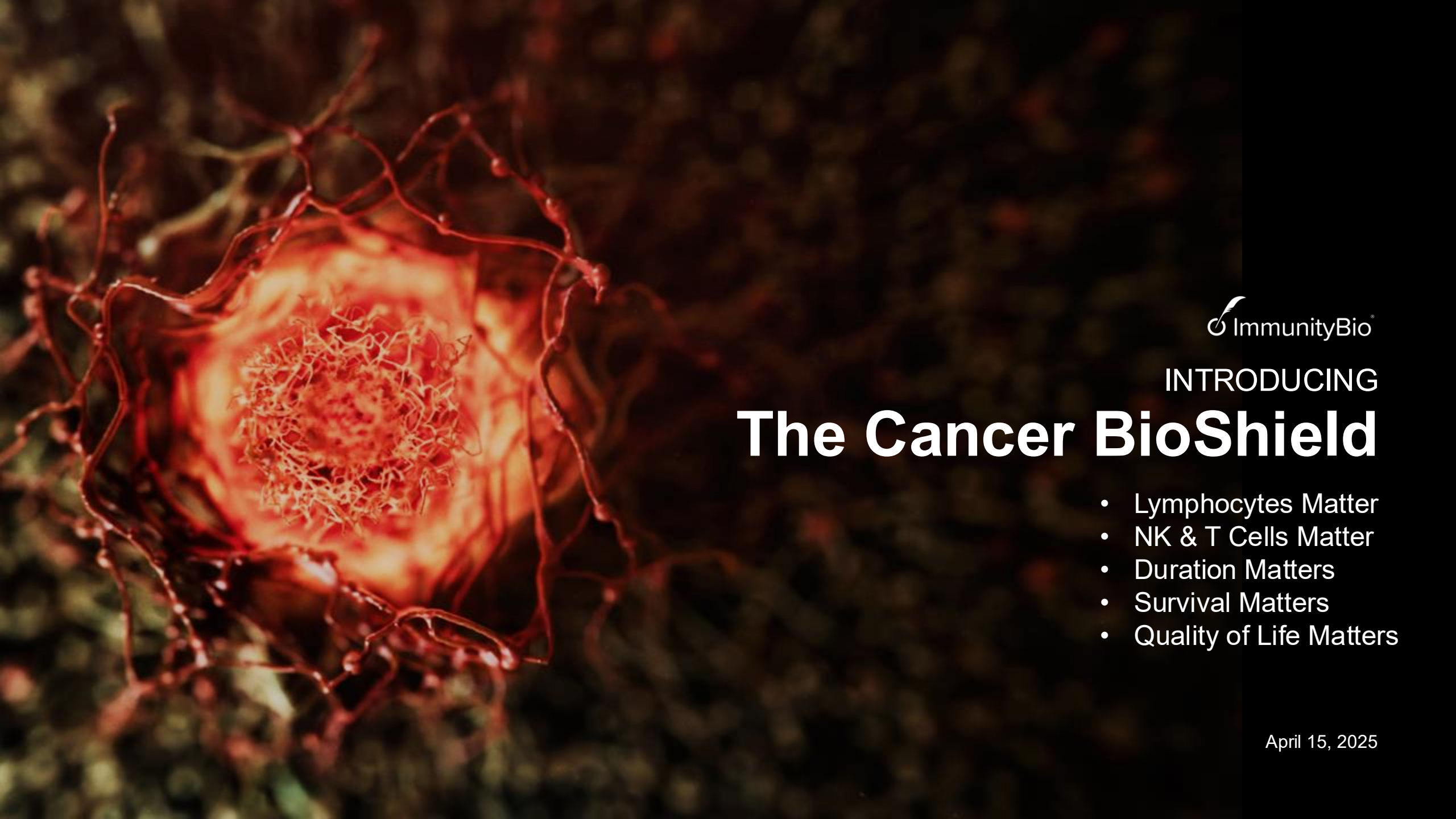


ImmunityBio

INTRODUCING

The Cancer BioShield

- Lymphocytes Matter
- NK & T Cells Matter
- Duration Matters
- Survival Matters
- Quality of Life Matters

April 15, 2025

ImmunityBio Leadership Team

Patrick Soon-Shiong, M.D. FACS
Executive Chairman,
Global Chief Medical
& Scientific Officer

Rich Adcock
President & Chief
Executive Officer

Leonard S. Sender, M.D.
Chief Medical Officer
Liquid Tumors & Cell Therapy

Sandeep Reddy, M.D.
Chief Medical Officer
Solid Tumors & Diagnostics

Enrique Diloné, Ph.D.
Chief Technology Officer

Charles G. Garlisi, Ph.D.
Senior Vice President,
Regulatory Affairs

Sarah Singleton
Chief Communications
Officer & Head of Patient
Advocacy

Bruce Brown, M.D.
Senior Vice President
Medical Affairs

Elizabeth Gabitzsch
Senior Vice President,
Product Development &
Vaccine Programs

David Sachs
Chief Financial Officer

Regan Lauer
Chief Accounting Officer

Manju Saxena, Ph.D.
Senior Vice President of
Product Development, Cell
Therapy Program

Jason Liljestrom, Esq.
General Counsel

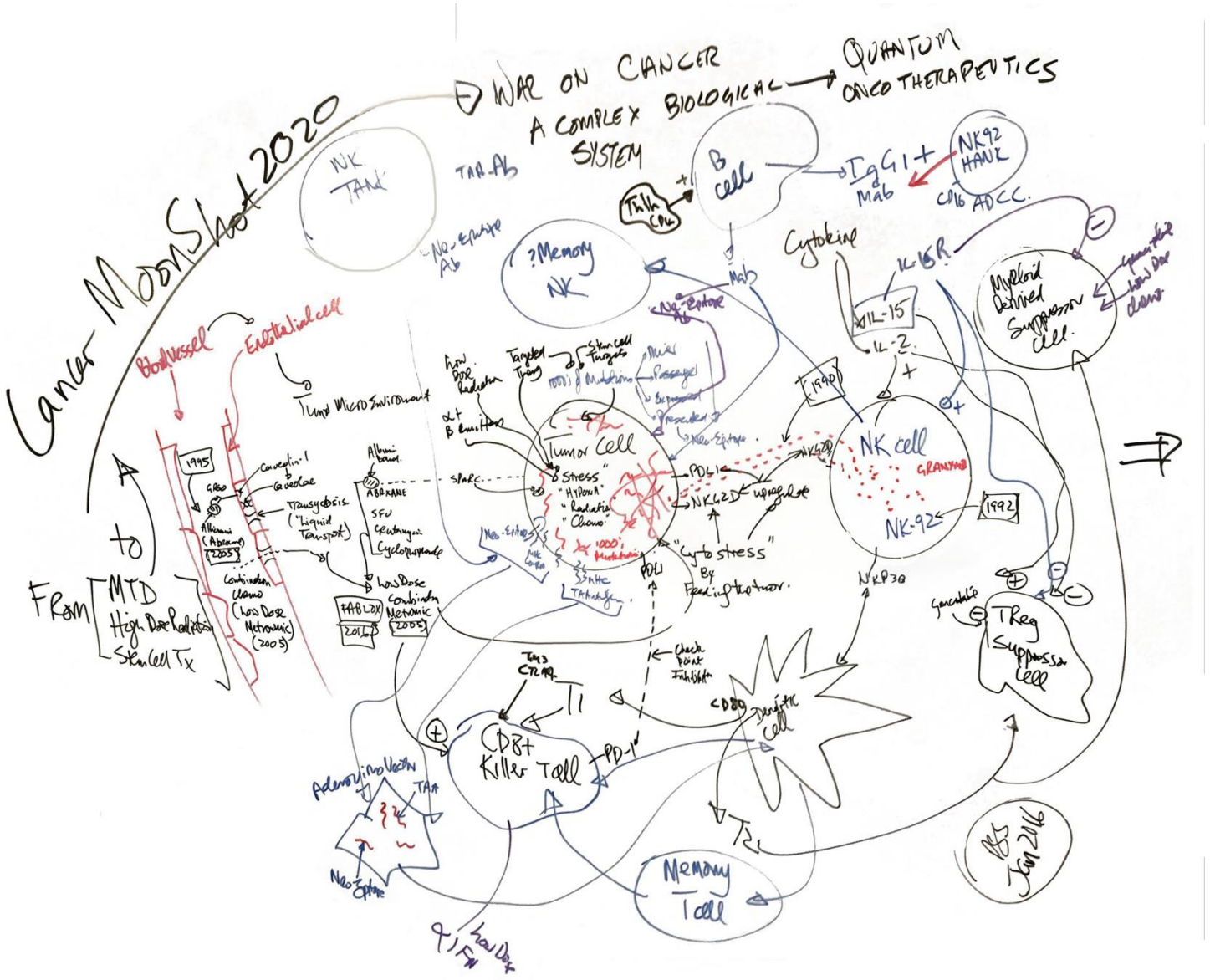
Barry Simon, M.D.
Chief Corporate Affairs
Officer

The Natural Killer Cell

Video Link:
https://vimeo.com/1076098743

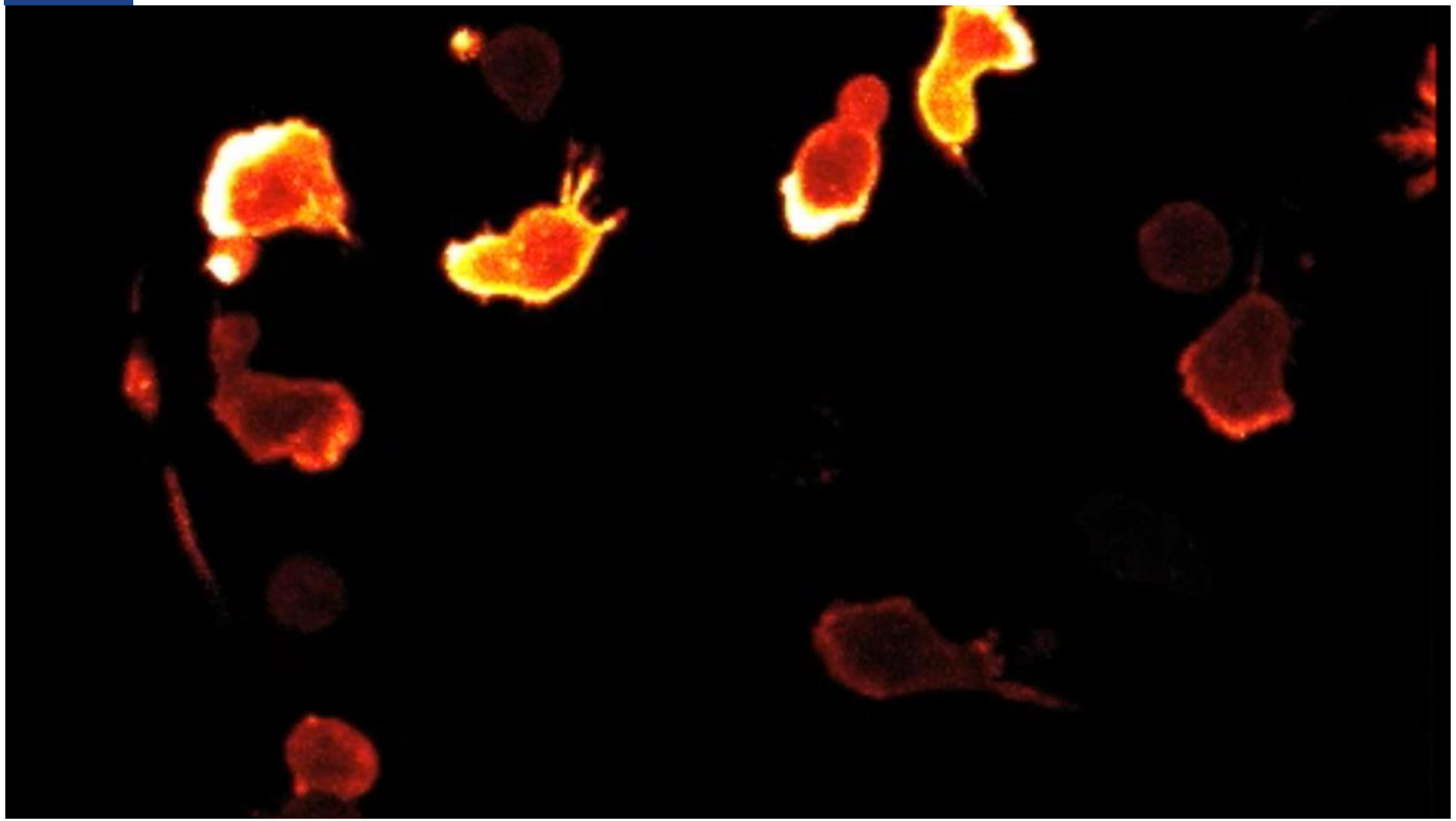
Evolved over millions of years early in vertebrate evolution to protect mammals from infection and cancer

2016: “Cancer MoonShot 2020”



Lymphocytes (T Cells and NK Cells)

Video



Video Link: https://vimeo.com/1076098772

2016: NANT Cancer Vaccine Intellectual Property

(12) **United States Patent**
Soon-Shiong et al.

(10) **Patent No.: US 11,071,774 B2**
(45) **Date of Patent: *Jul. 27, 2021**

(54) **NANT CANCER VACCINE**

(71) Applicants: **NANT HOLDINGS IP, LLC**, Culver City, CA (US); **NANTCELL, INC.**, Culver City, CA (US)

(72) Inventors: **Patrick Soon-Shiong**, Culver City, CA (US); **Kayvan Niazi**, Culver City, CA (US); **Shahrooz Rabizadeh**, Culver City, CA (US); **Hans G. Klingemann**, Culver City, CA (US); **Laurent H. Boissel**, Culver City, CA (US)

(73) Assignees: **NantCell, Inc.**, Culver City, CA (US); **Nant Holdings IP, LLC**, Culver City, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **16/783,734**

(22) Filed: **Feb. 6, 2020**

(65) **Prior Publication Data**

US 2020/0171137 A1 Jun. 4, 2020

Related U.S. Application Data

(63) Continuation of application No. 16/312,246, filed as application No. PCT/US2017/040297 on Jun. 30, 2017.

(60) Provisional application No. 62/357,324, filed on Jun. 30, 2016, provisional application No. 62/371,665, filed on Aug. 5, 2016, provisional application No. 62/393,528, filed on Sep. 12, 2016, provisional application No. 62/404,753, filed on Oct. 5, 2016, provisional application No. 62/463,037, filed on Feb. 24, 2017, provisional application No. 62/474,034, filed on Mar. 20, 2017, provisional application No. 62/473,207, filed on Mar. 17, 2017.

(51) **Int. Cl.**

A61K 39/00	(2006.01)
A61P 35/00	(2006.01)
C07K 16/28	(2006.01)
A61K 38/20	(2006.01)

(52) **U.S. Cl.**

CPC .. ***A61K 39/001106*** (2018.08); ***A61K 38/2013*** (2013.01); ***A61K 38/2046*** (2013.01); ***A61K 38/2086*** (2013.01); ***A61K 39/00117*** (2018.08); ***A61K 39/001152*** (2018.08); ***A61K 39/001164*** (2018.08); ***A61K 39/001182*** (2018.08); ***C07K 16/2827*** (2013.01); *A61K 2039/507* (2013.01); *A61K 2039/523* (2013.01); *C07K 2317/76* (2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

7,758,891	B2	7/2010	Desai et al.	
7,771,751	B2	8/2010	Desai et al.	
7,780,984	B2	8/2010	Desai et al.	
7,981,445	B2	7/2011	De et al.	
8,034,375	B2	10/2011	Desai et al.	
9,492,499	B2	11/2016	Jaynes et al.	
9,683,048	B2	6/2017	Freeman et al.	
2012/0059670	A1	3/2012	Sanborn et al.	
2012/0066001	A1	3/2012	Sanborn et al.	
2014/0012843	A1	1/2014	Soon-Shiong	
2014/0114675	A1	4/2014	Soon-Shiong	
2015/0032468	A1	1/2015	Soon-Shiong	
2015/0125463	A1	5/2015	Cogswell et al.	
2015/0231241	A1	8/2015	Chang et al.	
2016/0095942	A1	4/2016	Markovic et al.	
2018/0222982	A1 *	8/2018	Dranoff	A61K 39/00
2019/0381156	A1	12/2019	Soon-Shiong et al.	

FOREIGN PATENT DOCUMENTS

CA	3 027 911	A1	1/2018
CN	109789190	A	5/2019
JP	2019-524692	A	9/2019
KR	10-2019-0031492	A	3/2019
MX	2018015796	A	5/2019
TW	201803598	A	2/2018
WO	2011/139345	A2	11/2011
WO	2013/062505	A1	5/2013
WO	2013/192339	A1	12/2013
WO	2014/059036	A1	4/2014
WO	2014/163684	A1	10/2014
WO	2014/193982	A1	12/2014
WO	2014/210611	A1	12/2014
WO	2015/095811	A2	6/2015
WO	2015/184439	A1	12/2015
WO	2016/057554	A1	4/2016

(Continued)

OTHER PUBLICATIONS

Eureka Alert! Public Release (Jan. 14, 2016) (https://www.eurekalert.org/pub_releases/2016-01/muos-mlf011416.php).*
Rx Times (Apr. 11, 2016) (http://rxtimes.com/altor-bioscience-corporation-partners-with-the-national-cancer-institute-to-further-develop-altors-alt-803-and-alt-801-cancer-immunotherapeutics/).*
Bristol Myers Squibb Press Release (Aug. 20, 2014) (https://news.bms.com/press-release/rd-news/bristol-myers-squibb-and-celgene-enter-clinical-collaboration-agreement-evalua).*
Mancheril et al (Hosp. Pharm. 2014, 49:804-808).*

(Continued)

Primary Examiner — Laura B Goddard
(74) *Attorney, Agent, or Firm* — Martin Fessenmaier; Umberg Zipser LLP

(57) **ABSTRACT**

Cancer is treated using coordinated treatment regimens that uses various compounds and compositions that drive a tumor from the escape phase of cancer immunoediting to the elimination and equilibrium phase of cancer immunoediting.

16 Claims, 28 Drawing Sheets

(12) **INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)**

(19) **World Intellectual Property Organization**
International Bureau

(43) **International Publication Date**
04 **January** 2018 (04.01.2018)

W!P O | PCT

(10) **International Publication Number**
WO 2018/005973 A1

(51) **International Patent Classification:**
A61K 38/38 (2006.01) *A61K 31/69* (2006.01)
A61K 39/395 (2006.01) *A61K 39/00* (2006.01)
A61K 31/4184 (2006.01)

(21) **International Application Number:**
PCT/US20 17/040297

(22) **International Filing Date:**
30 June 2017 (30.06.2017)

(25) **Filing Language:** English

(26) **Publication Langi:age:** English

(30) **Priority Data:**

62/357,324	30 June 2016 (30.06.2016)	US
62/371,665	05 August 2016 (05.08.2016)	US
62/393,528	12 September 2016 (12.09.2016)	US
62/404,753	05 October 2016 (05.10.2016)	US
62/463,037	24 February 2017 (24.02.2017)	US
62/473,207	17 March 2017 (17.03.2017)	US
62/474,034	20 March 2017 (20.03.2017)	US

(71) **Applicants: NANT HOLDINGS IP, LLC** [US/US]; 9920 Jefferson Boulevard, Culver City, California 90232 (US). **NANTCELL, INC.** [US/US]; 9920 Jefferson Boulevard, Culver City, California 90232 (US).

(72) **Inventors: SOON-SHIONG, Patrick;** 9920 Jefferson Boulevard, Culver City, California 90232 (US). **NIAZI, Kayvan;** 9920 Jefferson Boulevard, Culver City, California 90232 (US). **RABIZADEH, Shahrooz;** 9920 Jefferson Boulevard, Culver City, California 90232 (US).

(74) **Agent: FESSENMAIER, Martin;** Umberg Zipser LLP, 1920 Main Street, Suite 750, Irvine, California 92614 (US).

(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available):* AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available):* ARIPO (BW, GH,

(54) **Title:** NANT CANCER VACCINE

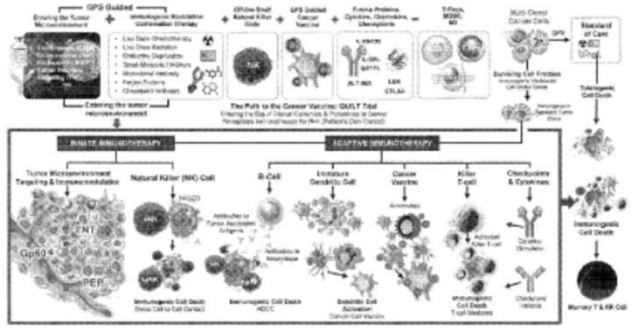


Figure 2

(57) **Abstract:** Cancer is treated using coordinated treatment regimens that uses various compounds and compositions that drive a tumor from the escape phase of cancer immunoediting to the elimination and equilibrium phase of cancer immunoediting.

WO 2018/005973 A1

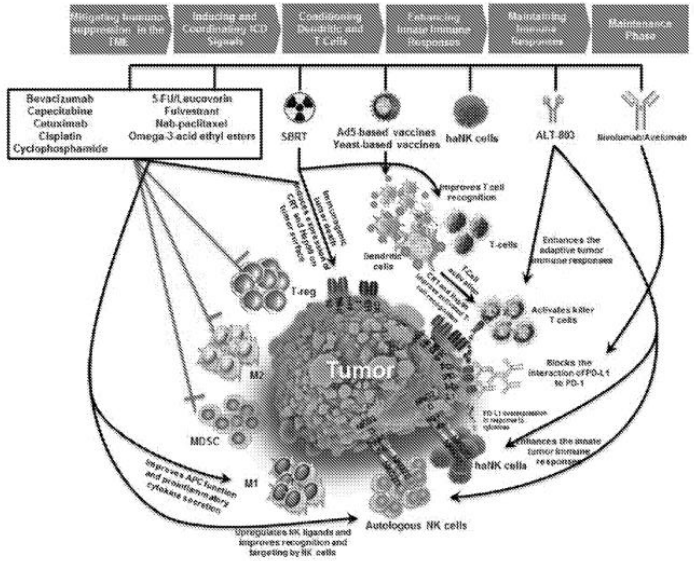


Figure 5

Video

Physicians Journey – Following the Science of the Immune System (7:30)

Video Link: https://vimeo.com/1076098806

ImmunityBio

10:15am – 11:00am

Bladder Cancer

April 15, 2025

NMIBC CIS +/- Papillary

FDA Approved April 2024

FDA Approved April 2024: Anktiva + TICE BCG

Intravesical NAI + BCG Elicits Median DFS of 25.3 Months & Cystectomy Avoidance of 82% at 36-Months in BCG-Unresponsive Papillary Disease

NAI (ANKTIVA) + BCG:

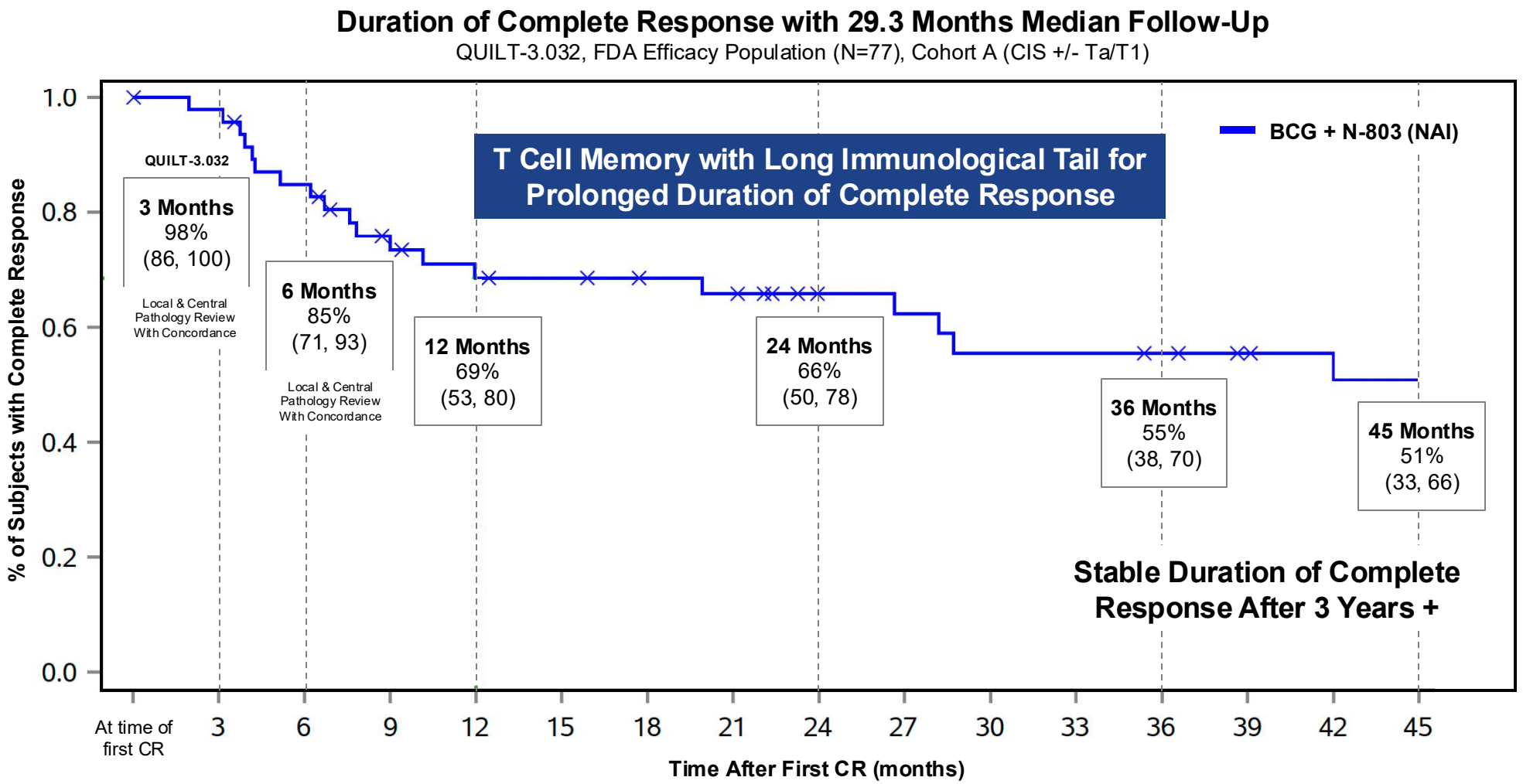
Papillary N=80

- In BCG-unresponsive high-grade papillary disease, NAI + BCG results in cystectomy avoidance of 92% at 12 months & 82% at 36 months
- Disease Specific Overall Survival Rate at 36-Months 96%

Cystectomy avoidance rate of 82% at 36 months is the highest percentage of bladder sparing and longest duration available to date in BCG Unresponsive NMIBC Papillary Disease

QUILT-3.032 Cohort B: NMIBC Papillary	NAI + BCG Efficacy, N=80
Disease-Free Survival (DFS)	
12 Months (Primary Endpoint)	**58% (46.6, 68.2)**
24 Months	**52% (40.3, 62.7)**
Median Disease-Free Survival, Months (95% CI)	**25.3 Months (9.8 - 40.1)**
Cystectomy Avoidance Rate	
Cystectomy Free Rate at 12 Months	**92%**
Cystectomy Free Rate at 24 Months	**88%**
Cystectomy Free Rate at 36 Months	**82%**
Disease Specific Overall Survival %	
12 Months	**99%**
24 Months	**96%**
36 Months	**96%**
July 2024 data cutoff by KM, N=80	

QUILT-3.032 FDA Label Population Duration of CR Follow Up 51% Ongoing Complete Response at 45+ Months



NMIBC PAPILLARY

Supplemental BLA Submitted Q1 2025

NEJM Published 2022

Intravesical NAI + BCG Elicits Median DFS of 25.3 Months & Cystectomy Avoidance of 82% at 36-Months in BCG-Unresponsive Papillary Disease

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Cystectomy Free Rate at 36 Months	**82%**
Disease Specific Overall Survival %	
12 Months	**99%**
24 Months	**96%**
36 Months	**96%**

July 2024 data cutoff by KM, N=80

Intravesical NAI + BCG is Well Tolerated in Both CIS & Papillary NMIBC with Only 3% Grade 3 TRAEs & Zero Grade 4 or 5 TRAEs

NAI (ANKTIVA) + BCG:

Cohort A: CIS +/- Papillary (N=100)
Cohort B: Papillary (N=80)

N=180

Treatment-Related Adverse Events (TRAEs) for NAI (ANKTIVA) + BCG:

- Most TRAEs were grade 1 or 2 and related to intravesical instillation consistent with BCG alone - dysuria, pollakiuria, hematuria, and micturition urgency.

TRAEs of Grade 3 occurred at a rate of only 3% (6 out of 180 NMIBC CIS & papillary subjects). There were no Grade 4 or 5 TRAES

NAI + BCG Treatment-Related Adverse Events (TRAEs) Cohorts A & B Combined (N=180)			
Participants with at Least 1 Grade 3 or Higher TRAE	**6 Subjects out of 180 = 3%**		
Treatment Related Adverse Events (%)	**Grade 3**	**Grade 4**	**Grade 5**
Bladder spasm	0	0	0
Chills	0	0	0
Fatigue	0	0	0
Micturition urgency	0	0	0
Pyrexia	0	0	0
Nocturia	0	0	0
Urinary incontinence	0	0	0
Urinary tract pain	0	0	0
Dysuria	<1%	0	0
Pollakiuria	<1%	0	0
Hematuria	<1%	0	0
Urinary tract infection	<1%	0	0
Pain in extremity	<1%	0	0
Urine flow decreased	<1%	0	0
Arthralgia	<1%	0	0
Non-infective cystitis	<1%	0	0
Myalgia	1%	0	0

NMIBC CIS +/- Papillary
VS.
NMIBC Papillary Alone

NMIBC + BCG Therapy Preserves the Bladder for Greater than 36 Months in Over 90% of Patients with Equal Safety in Both CIS and Papillary Disease

NMIBC: CIS +/- Papillary

FDA Approved 2024

BCG Unresponsive NMIBC CIS +/- Papillary (N=100)	
Cystectomy Avoidance in Responders %*	
Cystectomy-Free Rate at 12 months	**96%**
Cystectomy-Free Rate at 24 months	**90%**
Cystectomy-Free Rate at 36 months	**84%**
Disease Specific Overall Survival %* (N=100)	
12 Months	**100%**
24 Months	**99%**
36 Months	**99%**

NMIBC: Papillary Alone

Supplemental BLA Filed 2025, Awaiting Approval

BCG Unresponsive NMIBC Papillary (N=80)	
Cystectomy Avoidance Rate	
Cystectomy Free Rate at 12 Months	**92%**
Cystectomy Free Rate at 24 Months	**88%**
Cystectomy Free Rate at 36 Months	**82%**
Disease Specific Overall Survival % (N=80)	
12 Months	**99%**
24 Months	**96%**
36 Months	**96%**

FDA Approved April 2024

Bladder Sparing Efficacy

sBLA Submitted Awaiting Approval

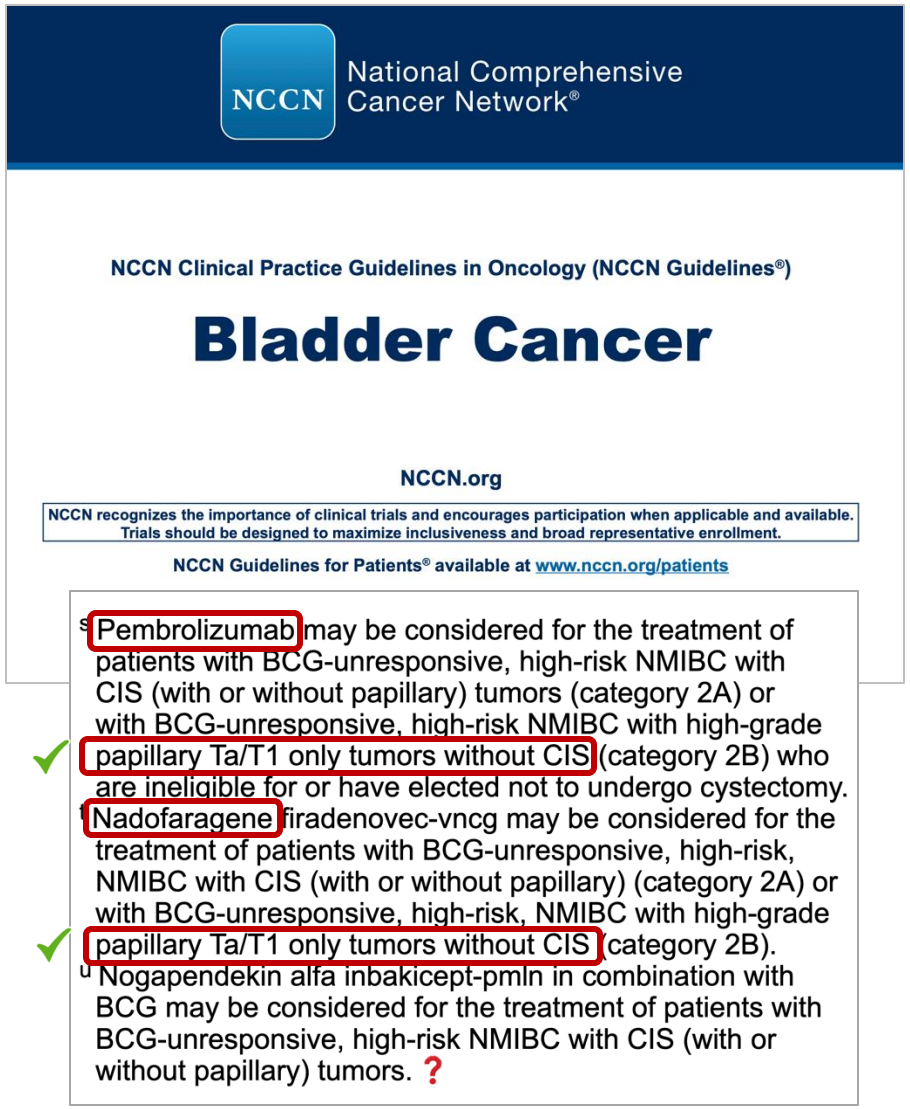
NMIBC: CIS +/- Papillary
NMIBC: Papillary Alone

Supplemental BLA Filed 2025, Awaiting Approval

NMIBC CIS + NAI + BCG Treatment-Related Adverse Events (TRAEs) Cohorts A & B Combined (N=180)			
Participants with at Least 1 Grade 3 or Higher TRAE	**Only 6 Subjects Out of 180 = 3%**		
Treatment Related Adverse Events (%)	**Grade 3**	**Grade 4**	**Grade 5**
Bladder spasm	0	0	0
Chills	0	0	0
Fatigue	0	0	0
Micturition urgency	0	0	0
Pyrexia	0	0	0
Nocturia	0	0	0
Urinary incontinence	0	0	0
Urinary tract pain	0	0	0
Dysuria	<1%	0	0
Pollakiuria	<1%	0	0
Hematuria	<1%	0	0
Urinary tract infection	<1%	0	0
Pain in extremity	<1%	0	0
Urine flow decreased	<1%	0	0
Arthralgia	<1%	0	0
Non-infective cystitis	<1%	0	0
Myalgia	1%	0	0

Combined Safety (CIS + Papillary)

NCCN Inconsistent Policy



National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Bladder Cancer

NCCN.org

NCCN recognizes the importance of clinical trials and encourages participation when applicable and available. Trials should be designed to maximize inclusiveness and broad representative enrollment.

NCCN Guidelines for Patients® available at www.nccn.org/patients

s Pembrolizumab may be considered for the treatment of patients with BCG-unresponsive, high-risk NMIBC with CIS (with or without papillary) tumors (category 2A) or with BCG-unresponsive, high-risk NMIBC with high-grade papillary Ta/T1 only tumors without CIS (category 2B) who are ineligible for or have elected not to undergo cystectomy.

t Nadofaragene firadenovec-vncg may be considered for the treatment of patients with BCG-unresponsive, high-risk, NMIBC with CIS (with or without papillary) (category 2A) or with BCG-unresponsive, high-risk, NMIBC with high-grade papillary Ta/T1 only tumors without CIS (category 2B).

u Nogapendekin alfa inbakicept-pmln in combination with BCG may be considered for the treatment of patients with BCG-unresponsive, high-risk NMIBC with CIS (with or without papillary) tumors. ?

NCCN Guidelines Approval for BCG Unresponsive Papillary Disease Only
Nadofaragene, Pembrolizumab vs. Anktiva

NMIBC Papillary Only Indication	Nadofaragene	Pembrolizumab	Anktiva
Cystectomy Free Rate at 12 Months	86%	76%	92%
Cystectomy Free Rate at 36 Months	No Data	45%	82%
Treatment Related AE's	3.8 Grade 3s	~14% Grade 3s Immune Related AE	3% Grade 3 No Immune Related AE
FDA Approval	No	No	No
BLA Submission	No	Unknown	Supplemental Submitted
NCCN Guidelines: "Papillary only tumors without CIS"	Yes ✓	Yes ✓	No ?
Company	Ferring	Merck	ImmunityBio

NMIBC NAÏVE

Phase 1: Durable Complete Remission in CIS and Papillary NMIBC Bladder Cancer with BCG + N-803 (Anktiva)

ONCOIMMUNOLOGY
2021, VOL. 10, NO. 1, e1912885 (7 pages)
https://doi.org/10.1080/2162402X.2021.1912885

Taylor & Francis

ORIGINAL RESEARCH

OPEN ACCESS

Safety, Tolerability, and Long-Term Clinical Outcomes of an IL-15 analogue (N-803) Admixed with Bacillus Calmette-Guérin (BCG) for the Treatment of Bladder Cancer

Charles J. Rosser[a], Sergei Tikhonenkov[a], Jeffrey W. Nix[b], Owen T.M. Chan[a], Irina Ianculescu[c], Sandeep Reddy[d,c], and Patrick Soon-Shiong[d]

[a]Clinical & Translational Research Program, University of Hawaii Cancer Center,Honolulu, Hawaii; [b]Department of Urology, University of Alabama, Birmingham, Alabama; [c]ImmunityBio, Inc., Culver City, California; [d]NantHealth Inc, Culver City, California

ABSTRACT

Intravesical BCG is active against non-muscle invasive bladder cancer (NMIBC), but bladder cancer will recur and even progress in a significant number of patients. To improve the response rate, N-803, an IL-15 superagonist was administered in combination with BCG. To evaluate the safety and efficacy associated with the use of intravesical N-803 and BCG in patients with BCG-naive NMIBC. This phase 1b clinical trial used a 3 + 3 dose-escalation design. Participants were enrolled from July 2014 and July 2015, with follow-up and analyses through January 15, 2021. Eligibility criteria included histologically confirmed non-muscle invasive urothelial carcinoma of intermediate or high risk who had not received prior treatment with intravesical BCG (ie, BCG-naive). All 9 participants met the eligibility criteria, received treatment according to the protocol, and were included in all analyses. Treatment was done once weekly for 6 consecutive weeks with bladder infusion of the standard dose of BCG, 50 mg/instillation, in combination with increasing doses of N-803 (100, 200, or 400 µg N-803 per instillation). No DLTs were noted in any of the dose cohorts. All adverse events (AEs) were manageable and less than grade 3. During the 2-year follow-up, all 9 participants were disease free. Furthermore, 6 y after treatment, all 9 participants (100%) were disease free with no evidence of disease progression and an intact bladder. This phase 1b trial found the combination of intravesical N-803 and BCG to be associated with modest toxic effects, low immunogenicity, and substantial prolonged antitumoral activity; phase 2 trials are in progress.

ARTICLE HISTORY
Received 3 March 2021
Revised 31 March 2021
Accepted 31 March 2021

KEYWORDS
Non-muscle invasive bladder cancer; IL15; BCG

Dose (intravesicular instillation)	Patient	CIS Papillary	Response Assessments							
			W12	6M	9M	12M	15M	18M	21M	24M
100 µg	1	Pap T1	NR	NR	NR	NR	NR	NR	NR	NR
	2	Pap Ta	NR	NR	NR	NR	NR	ND	NR	NR
	3	Pap T1	NR	NR	NR	NR	NR	NR	NR	NR
200 µg	4	Pap T1	IC	NR	NR	NR	NR	ND	NR	NR
	5	CIS	No CR	IC	IC	CR	CR	CR	CR	CR
	6	Pap T1	NR	NR	NR	NR	NR	NR	NR	NR
400 µg	7	Pap T1	NR	NR	NR	NR	NR	NR	NR	NR
	8	CIS	CR	CR	CR	CR	CR	CR	CR	CR
	9	Pap Ta	NR	NR	NR	NR	NR	NR	NR	NR

NR = no recurrence, ND = not done, IC = Inconclusive

>9 Year Follow-Up Data Pending

Unpublished Data. Date of First CR Recorded on Nov 2014 to Sept 2015

ANKTIVA + BCG in the NMIBC BCG Naïve Setting Durable Complete Response and Disease Free ≥ 9.5 Years

QUILT-205 Trial[1, 2]

- **Complete Response and Disease Free in 9 out of 9 (100%) 2-year trial**
- 6 out of 9 were evaluable in 2023
- 2 subjects died of natural causes independent of bladder cancer
- 1 lost to follow up
- All 6 out of 6 (100%) remain in complete response (CIS) or disease free (Papillary) for >9.5 years
- **All 6 patients avoided cystectomy for >9.5 years**

As of 2024

6 out of 6 (100%) Remain Disease Free

≥ 9.5 Years

Conclusion: ANKTIVA + BCG in BCG Naïve Patients Results in Durable Complete Response with Quality of Life and Adverse Events Consistent with BCG Alone

1. Adapted From Rosser CJ, et al., Safety, Tolerability, and Long-Term Clinical Outcomes of an IL-15 analogue (N-803) Admixed with Bacillus Calmette-Guérin (BCG) for the Treatment of Bladder Cancer. Oncoimmunology. 2021 May 2. Data on File

QUILT-2.005: Randomized Control Pivotal Trial of BCG versus BCG + ANKTIVA in BCG Naïve NMIBC CIS & Papillary: FDA Request Interim Analysis

Oct 2019, the FDA requested a interim analysis of QUILT-2.005 to confirm contribution of effect of ANKTIVA

Efficacy Results in CIS (QUILT-2.005) Phase 1 and Phase 2 (Unplanned Interim Analysis, as Requested by the Agency) October 2019

3.1. Efficacy in Patients with BCG-Naïve NMIBC

3.1.1. Phase 1b BCG-Naïve NMIBC (QUILT-2.005)

Appendix 4 show the study design and summary of patient response data during the 24 months of the first phase of QUILT 2.005 (refer to IND 121,976, sequence 0039, dated 14 May 2019, for the full QUILT-2.005 Phase 1b Clinical Study Report).

3.1.2. Phase 2 BCG-Naïve CIS (QUILT-2.005)

While efficacy data collection is ongoing, preliminary response data for patients with CIS is shown in Appendix 5. The preliminary evaluation was an unplanned interim analysis in response to FDA's request during review of ImmunityBio's Preliminary Breakthrough Therapy Designation Advice submission (IND 121,976, sequence 0035, dated 25 March 2019) and does not include papillary data as time to recurrence analyses have not yet been conducted.

In this phase, 85% of assessable patients with CIS treated in the combination arm have a CR compared to 57% in the BCG arm at month 6. At every time point of evaluation (6, 9, 12, 15, 18, 21, and 24 months), the CR rate in the CIS population of assessable patients is markedly higher in the N-803 plus BCG combination arm compared to BCG alone. Moreover, in addition to the increased response rate seen at each time point, the durability of response is longer when N-803 is administered in combination with BCG.

The preliminary data in the BCG-naïve CIS population provides supporting evidence that N-803 enhances the immune activity of local BCG, thereby increasing overall tumor clearance.

N-803 — ImmunityBio, Inc.
Request for Breakthrough Therapy Designation – NMIBC CIS

REQUEST FOR BREAKTHROUGH THERAPY DESIGNATION

For

N-803 in Combination with Bacillus Calmette-Guérin (BCG) for the Treatment of Patients with Non-muscle Invasive Bladder Cancer (NMIBC) Carcinoma in Situ (CIS)

Product Name:	N-803 (also known as ALT-803, a recombinant human agonist interleukin-15 (IL-15) fusion complex; INN *nogapendekin alfa inbakicept*) is the "working name" of the drug under investigation. N-803 has also been referred to as IL-15N72D:IL-15RaSu/IgG1 Fc complex. A trade name for commercial distribution has not been selected.
Proposed Indication:	In combination with Bacillus Calmette-Guérin (BCG) for the treatment of patients with non-muscle invasive bladder cancer (NMIBC) carcinoma in situ (CIS).
Contact Person (Name, Address, email, telephone and fax):	Melissa Luras, Director, Regulatory Affairs Melissa.Luras@ImmunityBio.com Phone: 310-633-3123 Fax: 310-853-7408 9920 Jefferson Blvd, Culver City, CA 90232
Submitted to:	Food and Drug Administration Center for Drug Evaluation and Research Office of Hematology and Oncology Products Division of Oncology Product 1 (DOP1)
IND Number:	121,976

Submitted October 4, 2019

Complete Response Rate and Durability of Response in Evaluable Patients with CIS BCG Naïve NMIBC Receiving ANKTIVA + BCG

These data provide evidence that the addition of N-803 to BCG increases initial CR rate and the durability of response for BCG-naïve patients with CIS. Furthermore, treatment was well tolerated by all patients in the phase 1b study, and well tolerated and balanced between treatments arms in the phase 2.

Table 4: Response Data in NMIBC Patients with BCG-Naïve CIS (N-803 + BCG Arm)

Time point	Evaluable Patients (Phase 1b & 2)	Complete Response Rate	95% Confidence Interval
At any time	n = 22	86% (19 / 22)	65%, 97%
6 Months[a]	n = 22	82% (18 / 22)	60%, 95%
12 Months	n = 19	63% (12 / 19)	38%, 84%

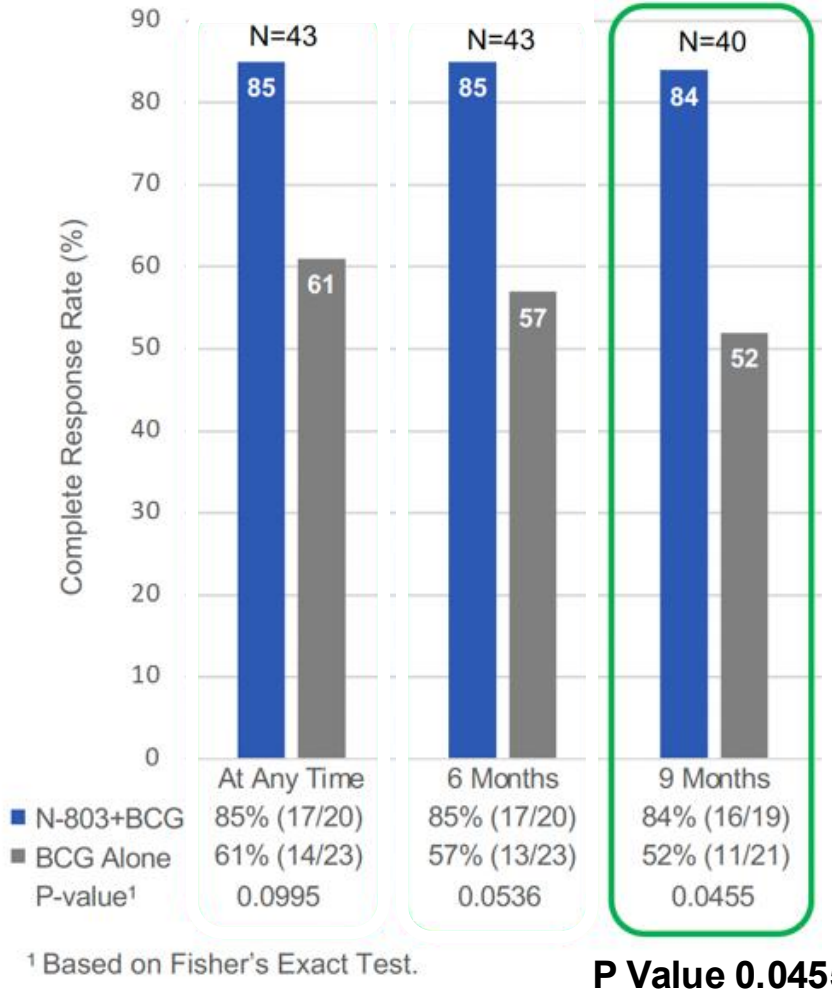
[a] Patients who had an absent or inconclusive assessment and had a CR at 3 or 9 months are assigned CR at 6 months.

BCG Naïve Papillary and CIS NMIBC, QUILT-2.005 Randomized Phase 3, Enrolling

- Interim analysis of randomized trial requested by the FDA demonstrates significance difference between BCG alone vs. BCG + Anktiva

- At nine months:
  - BCG alone: CR 52%
  - BCG + Anktiva: CR 84%
  - P-Value 0.0455

- Randomized trial enrolling to date in USA, India, South Africa



P Value 0.0455

85% CR Consistent Across Time with Anktiva + BCG

- Any Time: 85%
- 6 Months: 85%
- 9 Months: 84%

Recombinant BCG

Addressing Alternative Source of BCG

Discussion with FDA for Regulatory Guidance for Market Access - January 2025

ImmunityBio, Serum Institute of India Agree on an Exclusive Arrangement for Global Supply of Bacillus Calmette-Guerin (BCG) Across All Cancer Types

Thursday, May 2, 2024

- Collaboration will result in BCG manufacture at large scale for use in combination with ANKTIVA®, ImmunityBio's recently approved treatment for non-muscle invasive bladder cancer (NMIBC)

Potential Increased Tolerability Compared to TICE BCG with Increased Immunogenicity

ONCOIMMUNOLOGY
2020, VOL. 9, NO. 01, e1748981 (8 pages)
https://doi.org/10.1080/2162402X.2020.1748981

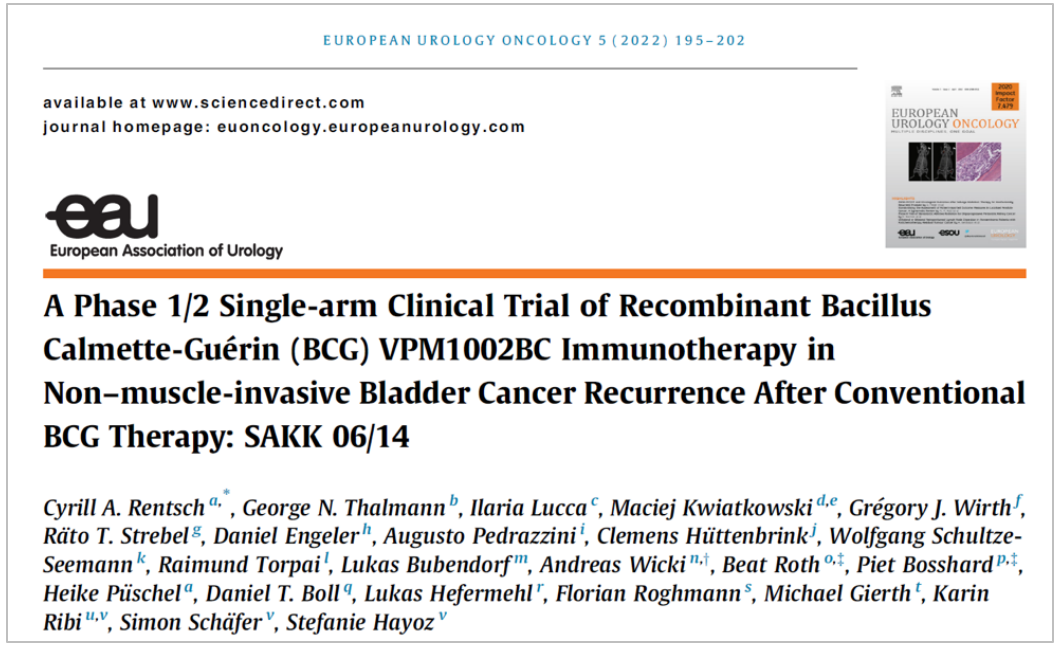
Taylor & Francis
Taylor & Francis Group

BRIEF REPORT

OPEN ACCESS Check for updates

Results of the phase I open label clinical trial SAKK 06/14 assessing safety of intravesical instillation of VPM1002BC, a recombinant mycobacterium Bacillus Calmette Guérin (BCG), in patients with non-muscle invasive bladder cancer and previous failure of conventional BCG therapy

Cyrill A. Rentsch[a], Piet Bosshard[a,b*], Grégoire Mayor[c], Malte Rieken[a], Heike Püschel[a], Grégory Wirth[c], Richard Cathomas[d], Gerald P. Parzmair[e], Leander Grode[e], Bernd Eisele[e], Hitt Sharma[f], Manish Gupta[f], Sunil Gairola[f], Umesh Shaligram[f], Daniel Goldenberger[g], François Spertini[h], Régine Audran[h], Milica Enoiu[i], Simona Berardi[i], Stefanie Hayoz[j], and Andreas Wicki[j] for the Swiss Group for Clinical Cancer Research (SAKK)



EUROPEAN UROLOGY ONCOLOGY 5 (2022) 195–202

available at www.sciencedirect.com
journal homepage: euoncology.europeanurology.com

European Association of Urology

A Phase 1/2 Single-arm Clinical Trial of Recombinant Bacillus Calmette-Guérin (BCG) VPM1002BC Immunotherapy in Non–muscle-invasive Bladder Cancer Recurrence After Conventional BCG Therapy: SAKK 06/14

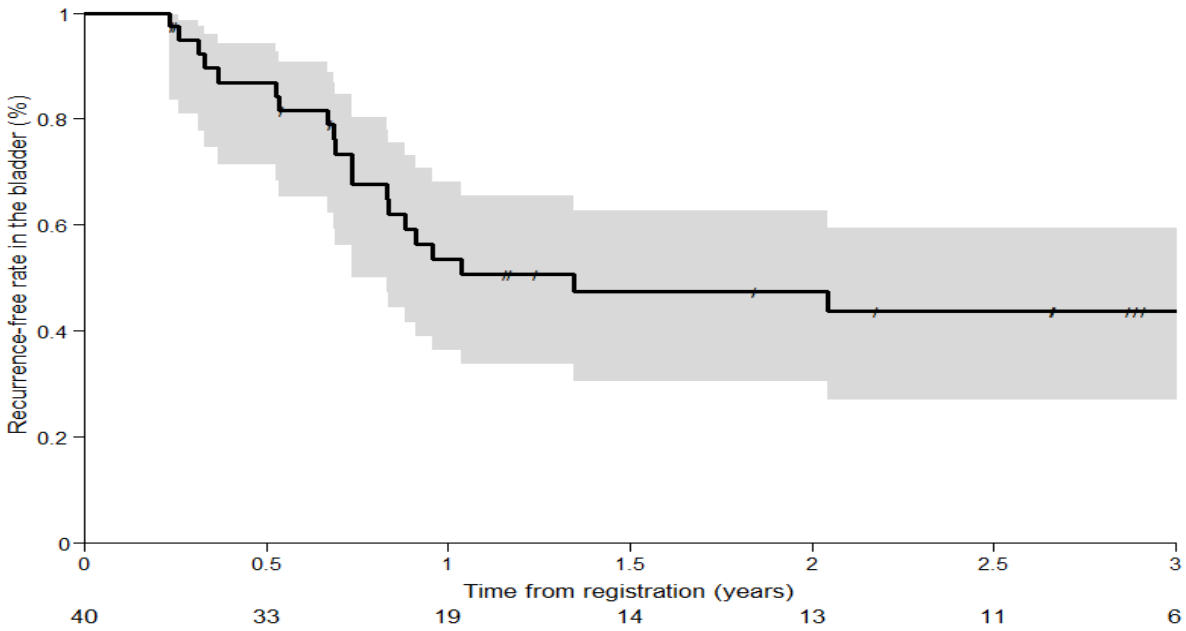
Cyrill A. Rentsch[a,], George N. Thalmann[b], Ilaria Lucca[c], Maciej Kwiatkowski[d,e], Grégory J. Wirth[f], Räto T. Strebel[g], Daniel Engeler[h], Augusto Pedrazzini[i], Clemens Hüttenbrink[j], Wolfgang Schultze-Seemann[k], Raimund Torpai[l], Lukas Bubendorf[m], Andreas Wicki[n,†], Beat Roth[o,‡], Piet Bosshard[p,‡], Heike Püschel[a], Daniel T. Boll[q], Lukas Hefermehl[r], Florian Roghmann[s], Michael Gierth[t], Karin Ribi[u,v], Simon Schäfer[v], Stefanie Hayoz[v]*

Recombinant BCG:

- VPM1002BC is a modified mycobacterium Bacillus Calmette Guérin (BCG) for the treatment of non-muscle invasive bladder cancer (NMIBC). The genetic modifications are expected to result in better immunogenicity and less side effects.
- VPM1002BC is a live, recombinant Mycobacterium bovis BCG. It was generated to direct phagosomal antigens to the major histocompatibility complex pathway and enhance the induction of CD4+ and CD8+ T cell-mediated immune responses

Recombinant BCG Effective and Tolerable in NMIBC

Recurrence Free Rate in the Bladder (60w)



Time After Trial Registration	Recurrence Free Rate in the Bladder
60w	49.3% [32.1%, 64.4%]
2y	47.4% [30.4%, 62.6%]
3y	43.7% [26.9%, 59.4%]
4y	**42.5% [26.2%, 57.8%]**

Feb 19, 2025: Addressing the BCG Shortage

FDA Authorizes ImmunityBio to Provide Recombinant BCG (rBCG) to Urologists to Address TICE® BCG Shortage

February 19, 2025

- Next-generation recombinant Bacillus Calmette-Guérin (rBCG) has undergone Phase 2 clinical trials in Europe in non-muscle invasive bladder cancer (NMIBC)
- Supplies of rBCG are now available, with shipments set to begin immediately via an FDA Expanded Access Program
- Multiple U.S. patents issued and allowed on combination of BCG plus ANKTIVA®
- Thousands of vials of rBCG available to end shortage of TICE® BCG

CULVER CITY, Calif.--(BUSINESS WIRE)--Feb. 19, 2025-- ImmunityBio, Inc. (NASDAQ: IBRX), a leading immunotherapy company, today announced the U.S. Food and Drug Administration (FDA) has authorized an expanded access program (EAP) that will bring a vital alternative source of BCG, a standard-of-care medicine in bladder cancer, to patients in the U.S.

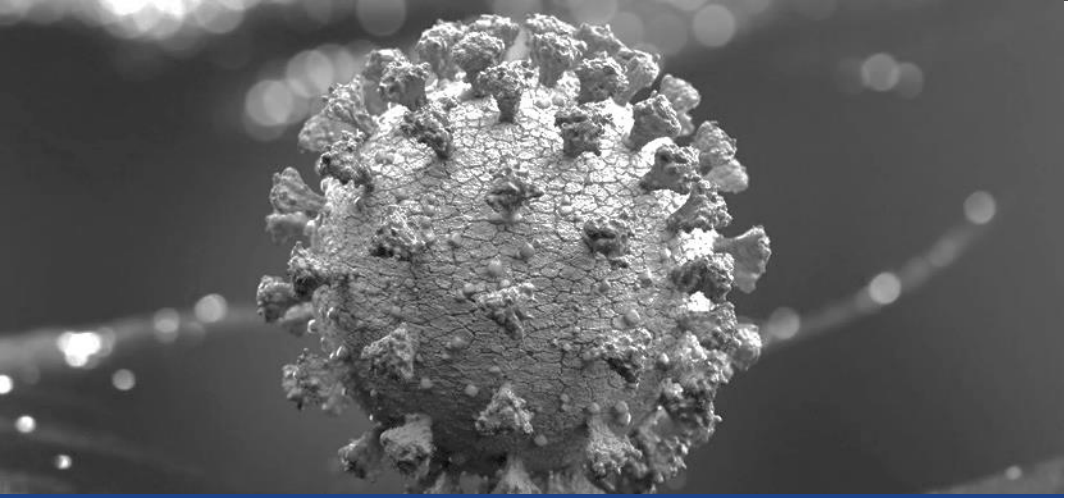
March 13, 2025: Addressing the BCG Shortage

ImmunityBio Announces First Dosing of Recombinant BCG (rBCG) in the U.S. and 60 Sites in the Process of Launching

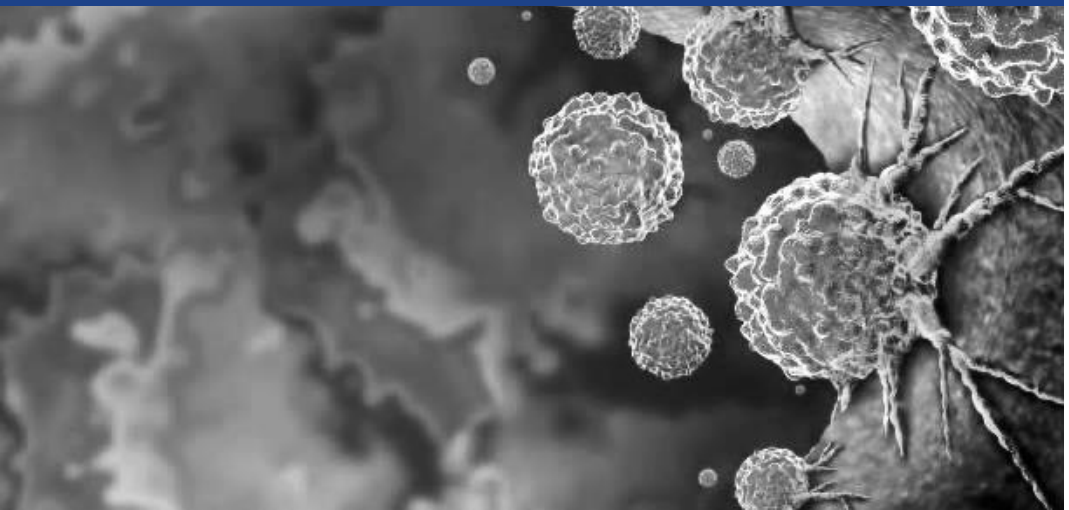
Mar 13, 2025

- U.S. Urology Partners is one of the first providers to offer patients ImmunityBio's recombinant Bacillus Calmette-Guérin (rBCG)
- The FDA recently authorized ImmunityBio's EAP for rBCG to address U.S. shortages and provide an alternative source of BCG, a critical standard-of-care in bladder cancer
- Multiple urology centers across the U.S. are in the process of activating their sites to administer rBCG

CULVER CITY, Calif., March 13, 2025 – ImmunityBio, Inc. (NASDAQ: IBRX), a leading immunotherapy company, today announced U.S. Urology Partners, one of the nation's largest independent providers of urology and related specialty services, is one of the first providers to participate in ImmunityBio's Expanded Access Program (EAP) for recombinant Bacillus Calmette-Guérin (rBCG) to address the current shortage of TICE® BCG in the U.S.



ImmunityBio®



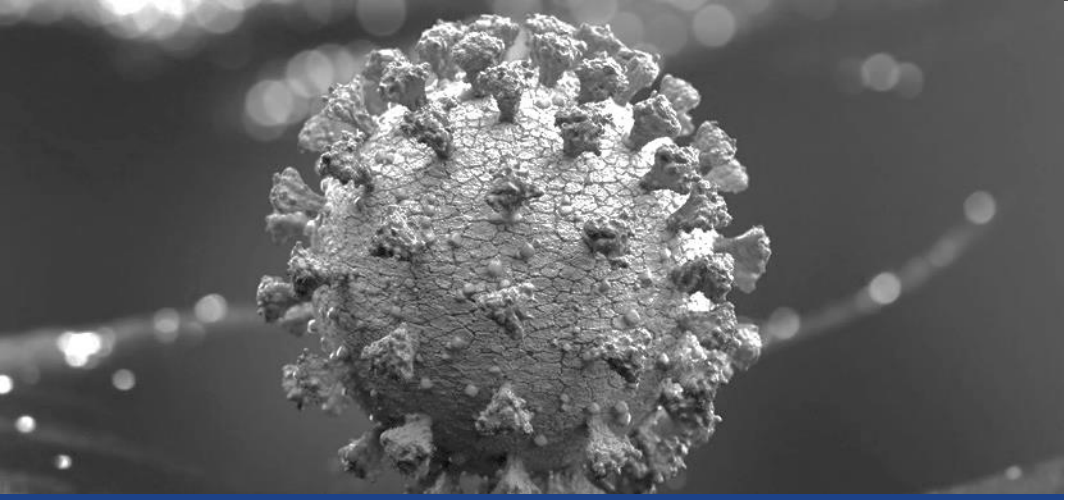
Fireside Chat

Clinical Experience with ANKTIVA & Recombinant BCG

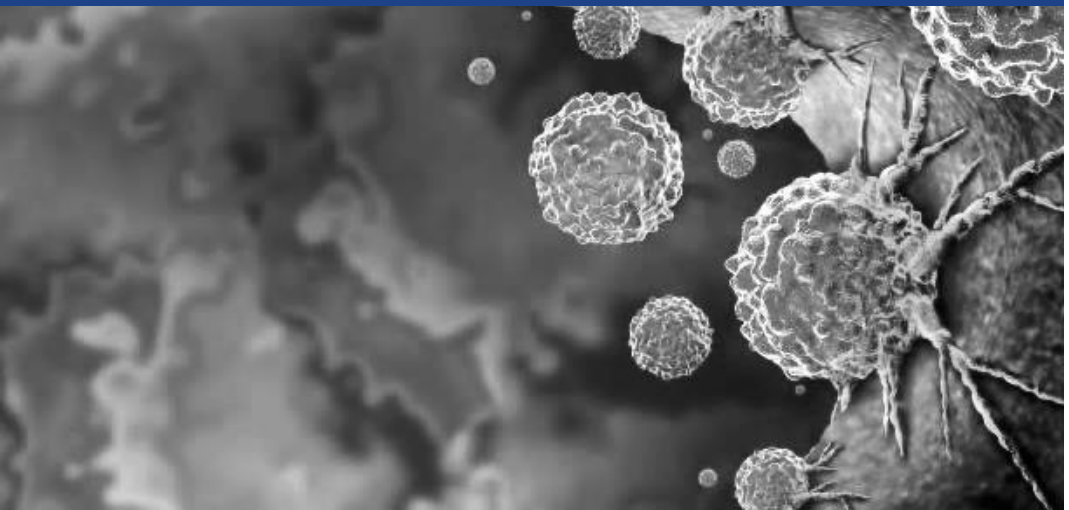
Dr. Chris Pieczonka
Chief Executive Officer,
Associated Medical Professionals of New York &
Corporate Director of Clinical Research of US Urology Partners

Dr. Patrick Soon-Shiong
Executive Chairman
Global Chief Medical & Scientific Officer
ImmunityBio

Dr. Bobby Reddy
Chief Medical Officer
ImmunityBio



ImmunityBio®



Commercial Launch Discussion

Rich Adcock
Chief Executive Officer
ImmunityBio

Dr. Chris Pieczonka
Chief Executive Officer,
Associated Medical Professionals
of New York & Corporate Director
of Clinical Research of US Urology
Partners

Matthew Hilman
Vice President
US Commercial Urology
ImmunityBio

Duration Matters, NK & T Cells Matter, Quality of Life Matters

Video Link: https://vimeo.com/1076099178

ANKTIVA Best-in-Class Duration of Response in BCG Unresponsive NMIBC-CIS Representing Overall Cost-Benefit Value

Nadofaragene	Pembrolizumab	ANKTIVA
DURATION 9.7 Months	DURATION 16.2 Months	DURATION 47+* Months & Ongoing
		Median Not Reached

DURATION is the key efficacy element to avoidance of cystectomy and represents overall cost-benefit value

Data from Individual Registration Trials and Package Inserts with No Direct Comparisons of Trials
Data from each respective FDA Approved product label

* N=77, FDA Label

ANKTIVA Launch First 6 Months Since Approval

1. ANKTIVA Approval April 2024

2. Anktiva Launched May 2024

3. NCCN Guidelines Approval May 2024

4. J-Code 9028, Effective Jan 2025

5. Global Submissions:
   - UK Nov 2024:
   - EU Dec 2024:

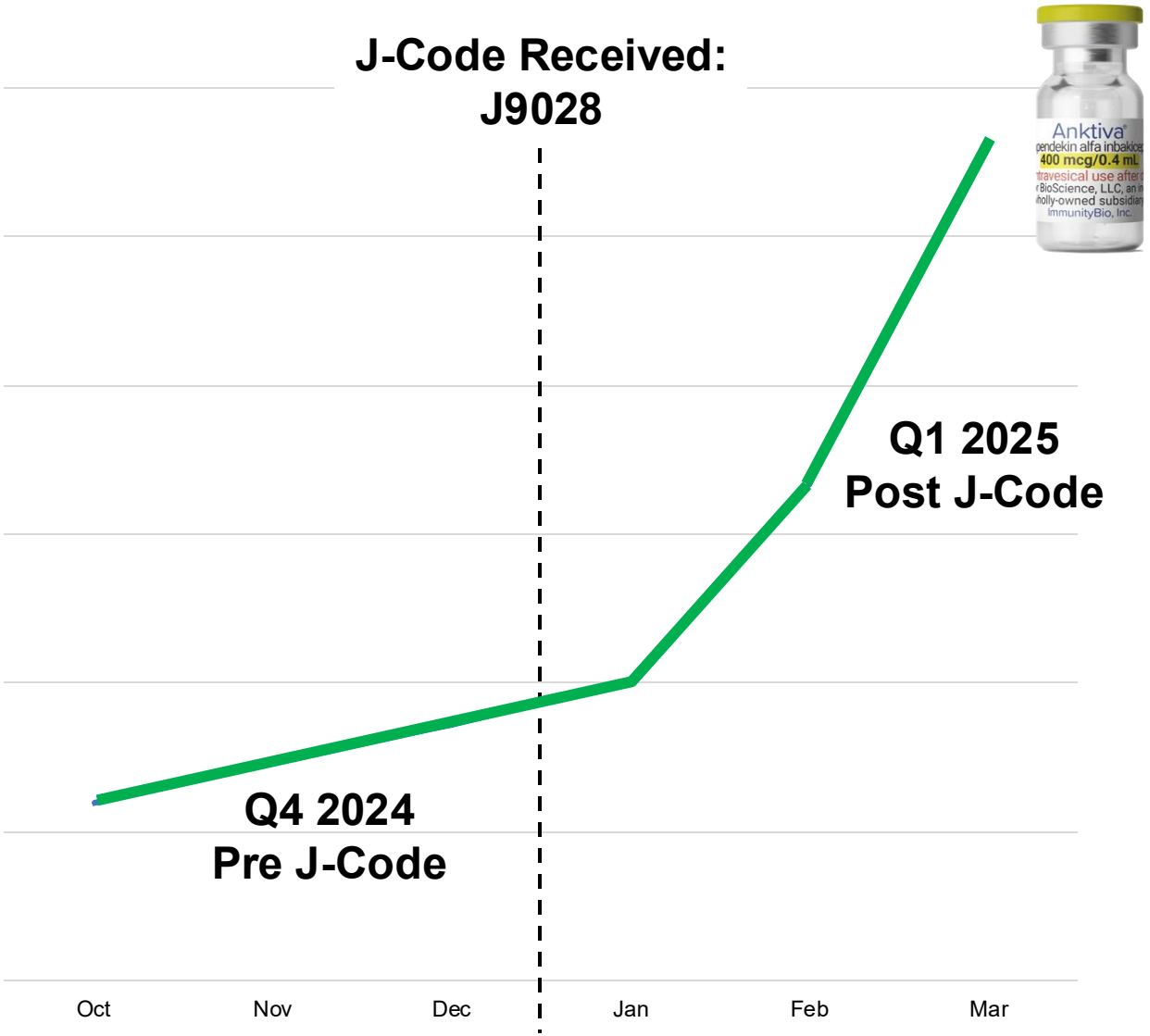
Market Access: 240 Million Medical Lives Covered as of November 2024

Florida Blue
VA | U.S. Department of Veterans Affairs
CVS caremark
cigna healthcare
EXPRESS SCRIPTS®
KAISER PERMANENTE®
United Healthcare
CENTENE® Corporation
Horizon
HIGHMARK
Humana
HCSC Health Care Service Corporation
ucare
Anthem
of Tennessee
Independence
Optum
Blue Cross Blue Shield of Michigan
Elevance Health
EmblemHealth
BlueCross BlueShield of North Dakota
aetna® COVENTRY®
Blue Cross Blue Shield of Hawai'i
BlueCross BlueShield of North Carolina
BlueCross BlueShield of Alabama
BlueCross BlueShield Minnesota

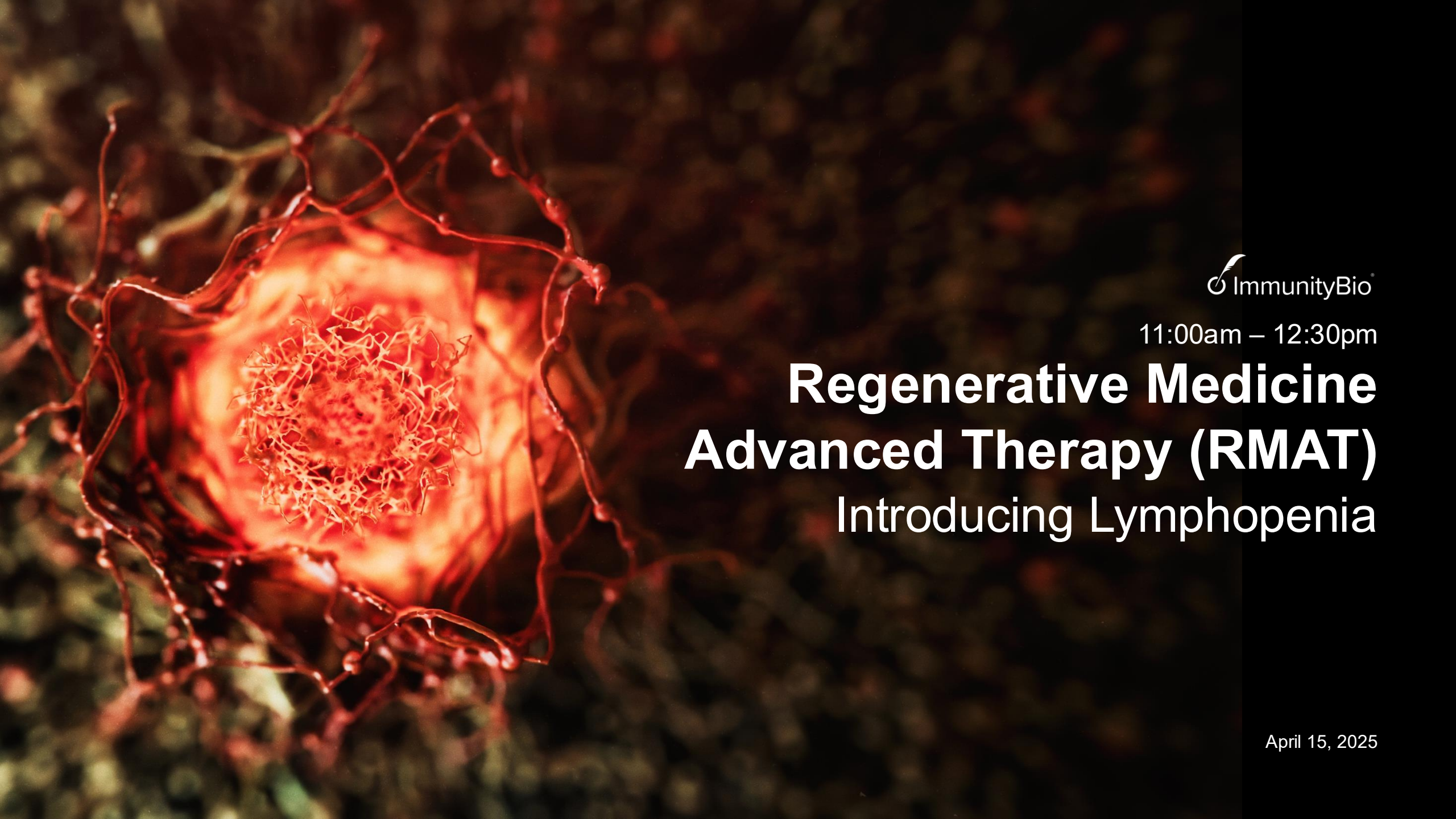
ANKTIVA
No Change in Urology Order & BCG Administration Workflow With Speed of Delivery

- ✓ One Day Delivery
- ✓ 36 Month Shelf Life
- ✓ No Special Freezers
- ✓ No Special Cleaning Agents
- ✓ No Change in BCG Workflow
- ✓ Same Order Flow as BCG

ANKTIVA Sales Growth



- With a permanent J-code (J9028) awarded in January 2025, ImmunityBio's Q1 2025 **ANKTIVA® unit sales volume grew 150%** over unit sales volume in Q4 2024
- ANKTIVA sales momentum continues to trend upward in 2025, with sales volume in **March representing a 69% increase month-over-month from February**
- For the three-month period ending March 31, 2025, ImmunityBio achieved ***estimated net product revenue of approximately $16.5 million, surpassing net product revenue of $7.2 million in the prior quarter, a 129% quarter over quarter increase***



ImmunityBio

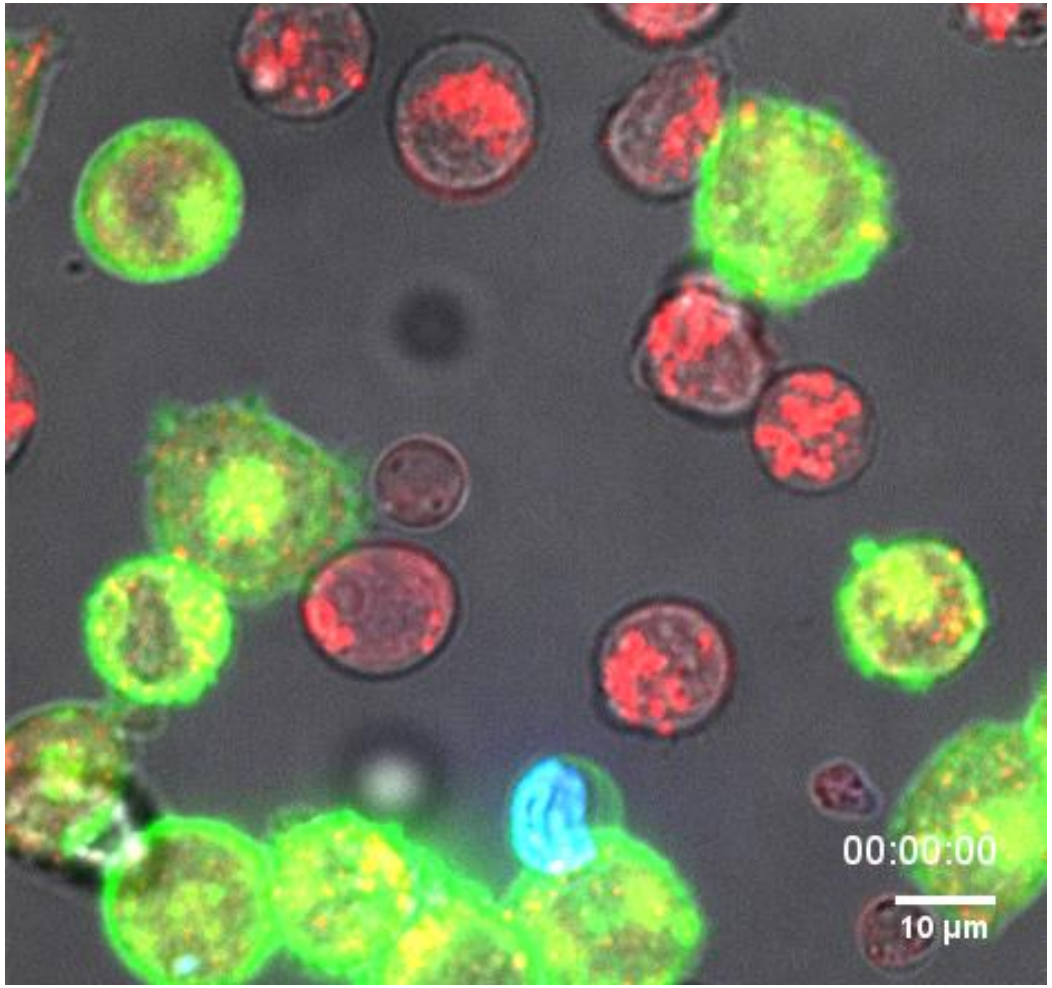
11:00am – 12:30pm

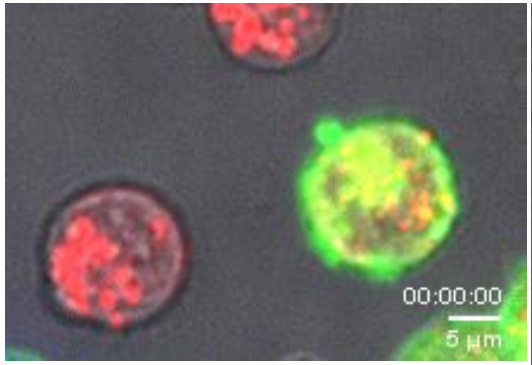
Regenerative Medicine Advanced Therapy (RMAT)

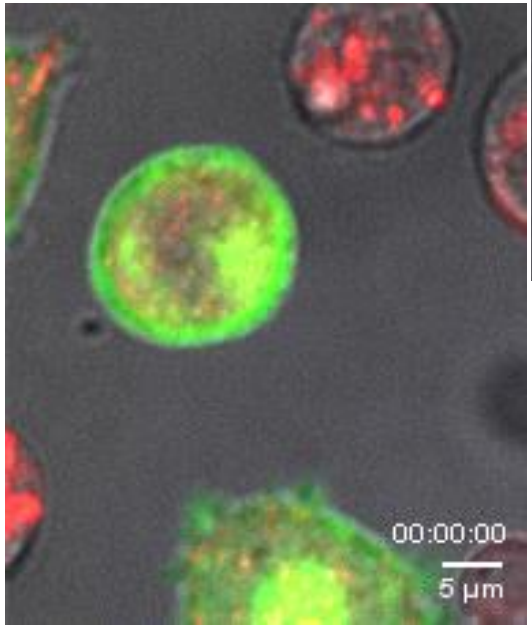
Introducing Lymphopenia

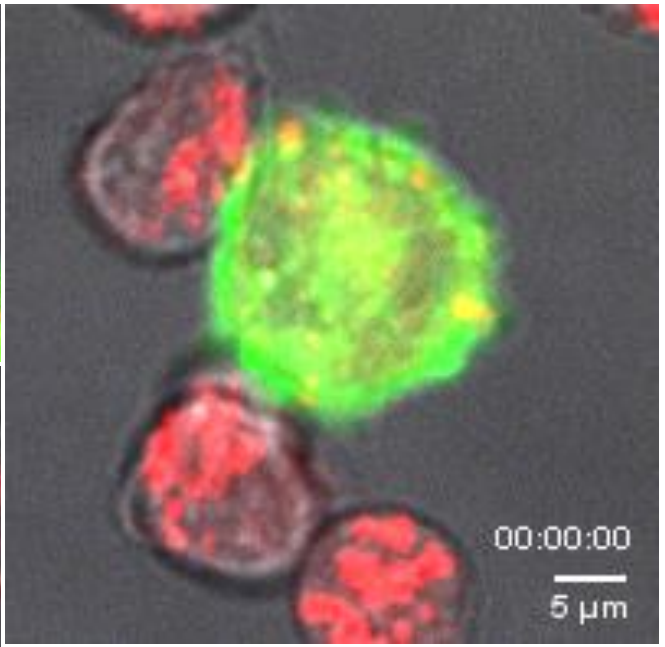
April 15, 2025

The Cancer BioShield: Lymphocytes (NK Cells & T Cells)









Red Lytic Granules in NK Cells (Cancer BioShield)

Green Live Breast Cancer Cells

Blue Dying Breast Cancer Cells

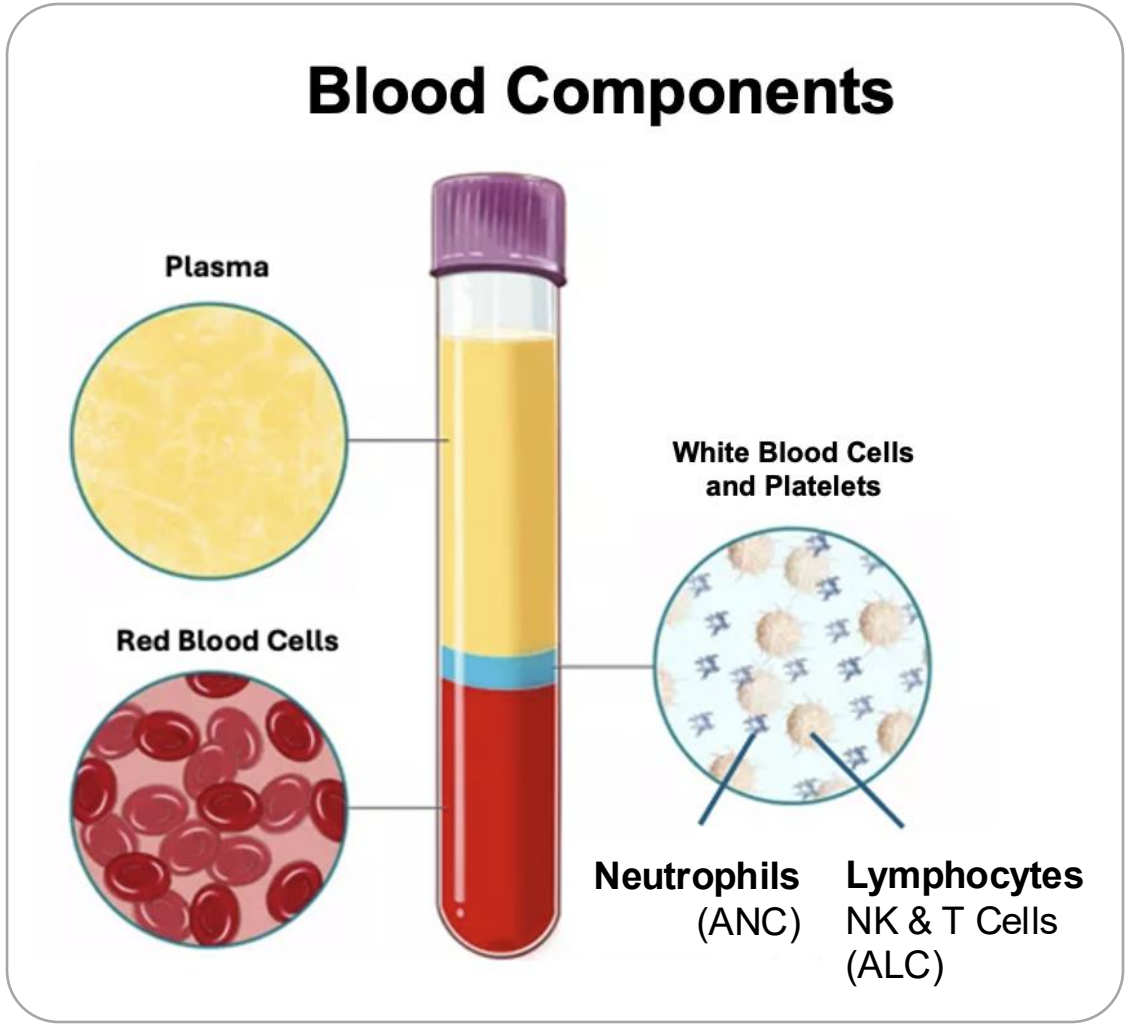
Video Link: https://vimeo.com/1076099114

Introducing Lymphopenia & Absolute Lymphocyte Count (ALC)

The Missing Link in our War Against Cancer

- No Treatment Exists to Treat Lymphopenia
- Oncologists Ignore ALC

Introducing Absolute Lymphocyte Count from a Simple CBC



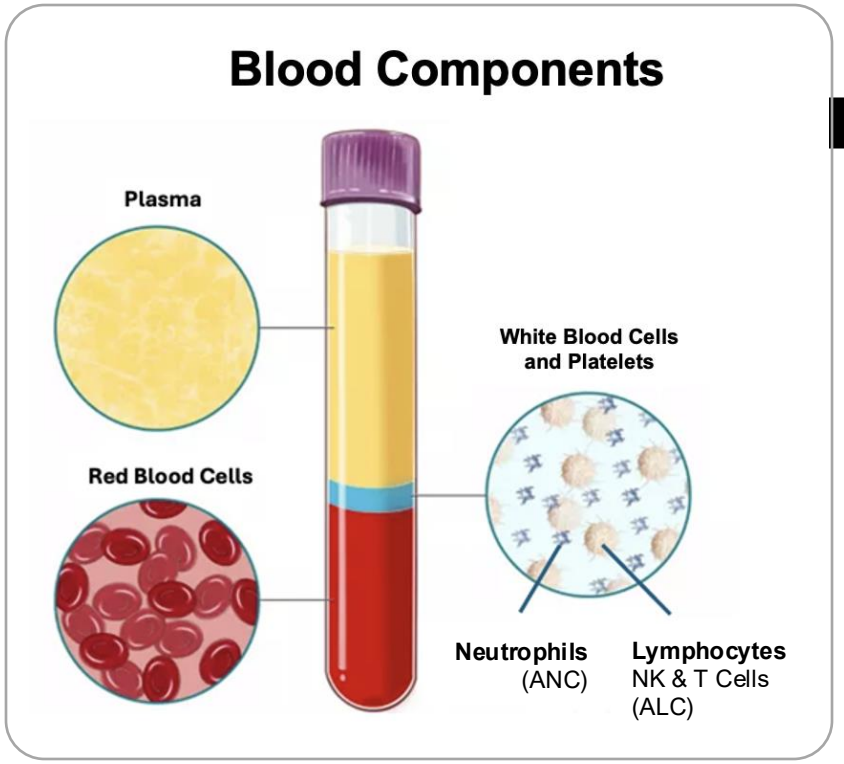
ANC: Absolute Neutrophil Count

ALC: Absolute Lymphocyte Count

ALC <1,000 Lymphocytes per Microliter = **Lymphopenia**

ALC 1,000 to 4,000 Lymphocytes per Microliter = **Normal ALC**

Introducing Absolute Lymphocyte Count (ALC) and Lymphopenia



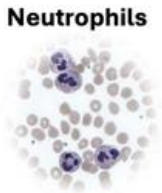
ANC: Absolute Neutrophil Count
ALC: Absolute Lymphocyte Count

Low Red Blood Count

Anemia

EPOGEN

Treats Anemia
Increases Red Blood Cell Production
1989

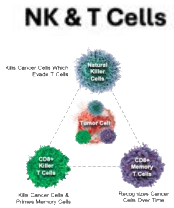


Low Neutrophil Count

Neutropenia

NEUPOGEN

Prevents Infection
Increases Neutrophil Production
1991



Low Lymphocyte Count

Lymphopenia

Loss of NK & T Cells
Which Kill Cancer &
Induce T Cell Memory

No Treatment for Over 50 Years
The Missing Link

Kills Cancer & Infected Cells

Standard of Care
Destroys the Very Cells that Kill Cancer

Lymphopenia and Low ALC Results in Reduced Overall Survival

Lymphocytes as a “New Organ” at Risk

Cancer/Radiothérapie 27 (2023) 511–518

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

Mise au point

Lymphopénie radio-induite : les lymphocytes comme nouvel organe à risque

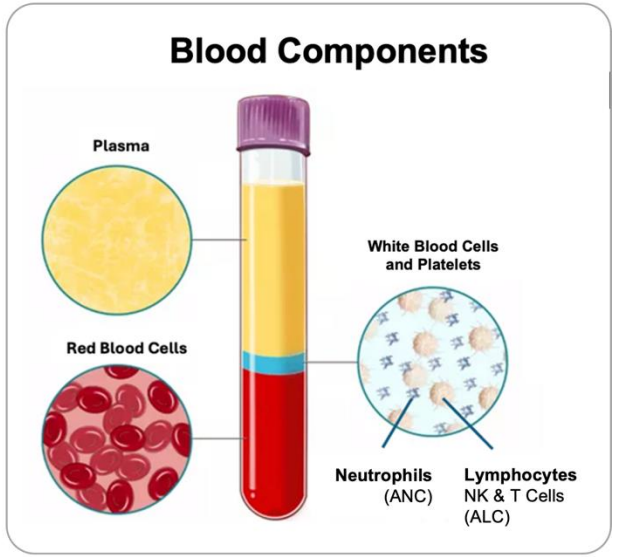
Radiation-induced lymphopenia: Lymphocytes as a new organ at risk

P.A. Laurent[a,b], É. Deutsch[a,b,*]

[a] *Service de radiothérapie oncologique, Gustave-Roussy Cancer Campus, Villejuif, France*
[b] *Inserm, U1030 Molecular Radiation Therapy and Therapeutic Innovation, Gustave-Roussy Cancer Campus, université Paris-Saclay, Villejuif, France*

S U M M A R Y

Taking the immune system into account in the fight against tumors has upset the cancer treatment paradigm in the 21st century. Combination treatment strategies associating radiotherapy with immunotherapy are being increasingly implemented in clinical practice. In this context, lymphocytes, whether lymphocytes infiltrating the tumour, circulating blood lymphocytes or lymphocytes residing within the lymph nodes, are key players in cellular and humoral anti-tumor immunity. The significant radiosensitivity of lymphocytes was demonstrated in the early 1990s. Along with the cells of the digestive mucosa, lymphocytes are thus among the most radiosensitive cell types in the body. Compared to the old practices of external radiotherapy, current intensity modulated treatments have allowed a considerable improvement in acute and late toxicity, at the cost of a significant increase in the volume irradiated at low doses. This is not without consequence on the incidence of radiation-induced lymphopenia, with prognostic implications for many tumor types. Thus, in order not to hinder the action of antitumor immunity



ANC: Absolute Neutrophil Count
ALC: Absolute Lymphocyte Count

ALC <1,000 Lymphocytes per Microliter = Lymphopenia

ALC 1,000 to 4,000 Lymphocytes per Microliter = Normal ALC

Lymphopenia Associated with Significant Lower OS (p=0.006)

2024

ARTICLE OPEN

Check for updates

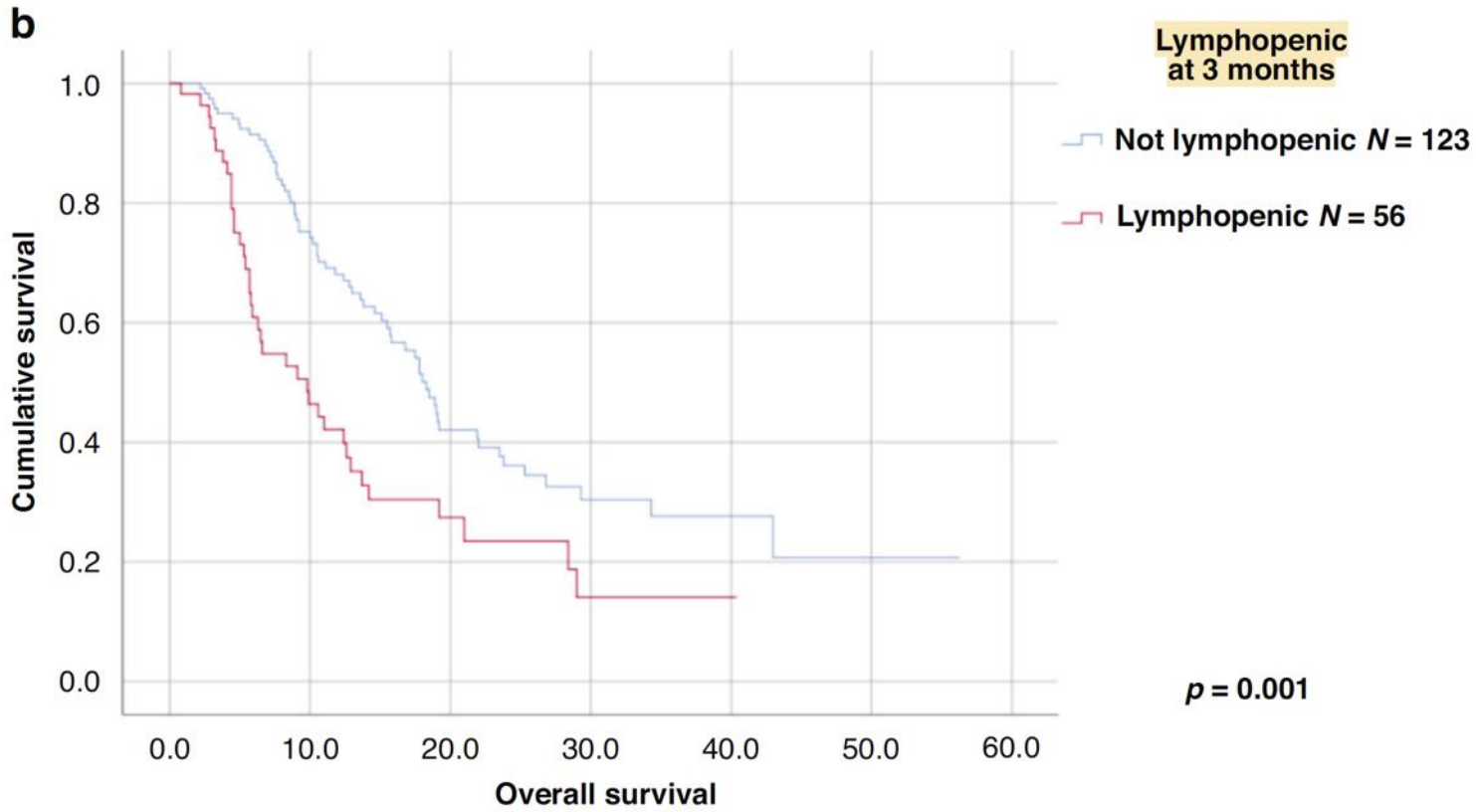
Exploring the prognostic impact of absolute lymphocyte count in patients treated with immune-checkpoint inhibitors

M. R. Conroy[1,2], H. O'Sullivan[1,2], D. C. Collins[1,2], R. M. Bambury[1,2], D. Power[1,2,3], S. Grossman[4] and S. O'Reilly[1,2,3]✉

BACKGROUND: The role of immune checkpoint inhibitors (ICI) expands but affordable and reproducible prognostic biomarkers are needed. We investigated the association between baseline and 3-month absolute lymphocyte count (ALC) and survival for patients on ICI.
METHODS: A retrospective study investigated patients who received ICI July 2014—August 2019. Survival probabilities were calculated for lymphocyte subsets. Univariate and multivariate analyses were performed to investigate risk factors for lymphopenia.
RESULTS: Among 179 patients, median age was 62 and 41% were female. The most common diagnoses were melanoma (41%) and lung cancer (40%). Median PFS was 6.5 months. 27% had baseline lymphopenia (ALC < 1×10^9cells/L) and no significant difference in PFS or OS to those with normal ALC. However, 31% had lymphopenia at 3 months and significantly shorter OS than those without (9.8 vs 18.3 months, $p < 0.001$). Those with baseline lymphopenia who recovered counts at 3 months had no difference in PFS (median NR vs 13.0 months, $p = 0.48$) or OS (22 vs 18.3 months, $p = 0.548$) to those never lymphopenic. The strongest risk factor for lymphopenia on multivariable analysis was previous radiation therapy (RT).
CONCLUSIONS: 3-month lymphopenia is a negative prognostic marker in cancer patients on ICI. Previous RT is significantly associated with lymphopenia.

BJC Reports; https://doi.org/10.1038/s44276-024-00058-6

When analysis was limited to those with lymphopenia grade 3 and 4 (<0.5×10^9cells/L), there were similar findings to all-grade lymphopenia. Those with severe lymphopenia at baseline had no significant difference in PFS compared to those without, but those with severe lymphopenia at 3 months had significantly shorter PFS than those without (3.6 vs 10.9 months, $p = 0.026$). This was further explored with a Cox regression analysis incorporating presence of severe lymphopenia as a time-dependent covariate. This found that the difference in PFS did not reach statistical significance ($p = 0.214$) but the difference in OS was significant ($p = 0.006$). This difference in OS remained significant on multivariable analysis incorporating age, sex, histologic subtype, previous RT, previous SACT, ICI type and whether the patient had an irAE.



Lymphocyte Count and Response to PD1

Ho *et al. Journal for ImmunoTherapy of Cancer* (2018) 6:84
https://doi.org/10.1186/s40425-018-0395-x

Journal for ImmunoTherapy of Cancer

RESEARCH ARTICLE Open Access

Association between pretreatment lymphocyte count and response to PD1 inhibitors in head and neck squamous cell carcinomas

Won Jin Ho, Mark Yarchoan, Alex Hopkins, Ranee Mehra, Stuart Grossman and Hyunseok Kang*

Abstract

Background: Low absolute lymphocyte count (ALC) has previously been established as a marker of poor prognosis in multiple cancer types. There is growing evidence that ALC may also be associated with response to immunotherapy. This study explores whether response to PD1 inhibitors in recurrent and/or metastatic head and neck squamous cell carcinoma (R/M HNSCC) is associated with pretreatment ALC.

Methods: Thirty-four R/M HNSCC patients who received either nivolumab or pembrolizumab between January 2014 and May 2018 at Johns Hopkins were identified retrospectively. Pretreatment blood counts in patients with and without clinical benefit from PD1 inhibitors were compared. Time-to-progression analyses were performed by dichotomizing the study cohort with the threshold of ALC 600 cells/μl, which is approximately 1.5 standard deviations away from treatment-naïve baseline mean.

Results: Patients with lower ALC appeared to have significantly less clinical benefit from anti-PD1 therapy. Those patients with pretreatment ALC < 600 cells/μl also had shorter PFS than patients with pretreatment ALC ≥ 600 cells/μl (median
PFS 60 days vs. 141 days, $p < 0.05$). These results were consistent with multivariate proportional hazards analyses demonstrating significant association with progression. These observations were further supported by an expansion cohort analysis incorporating additional fourteen R/M HNSCC patients who received other checkpoint immunotherapy regimens at our institution.

Conclusions: This study for the first time demonstrates that pretreatment ALC is significantly associated with response to PD1 inhibitors in R/M HNSCC patients.

Keywords: Head and neck squamous cell cancers, Absolute lymphocyte count, NLR, PD1 inhibitor, Immunotherapy

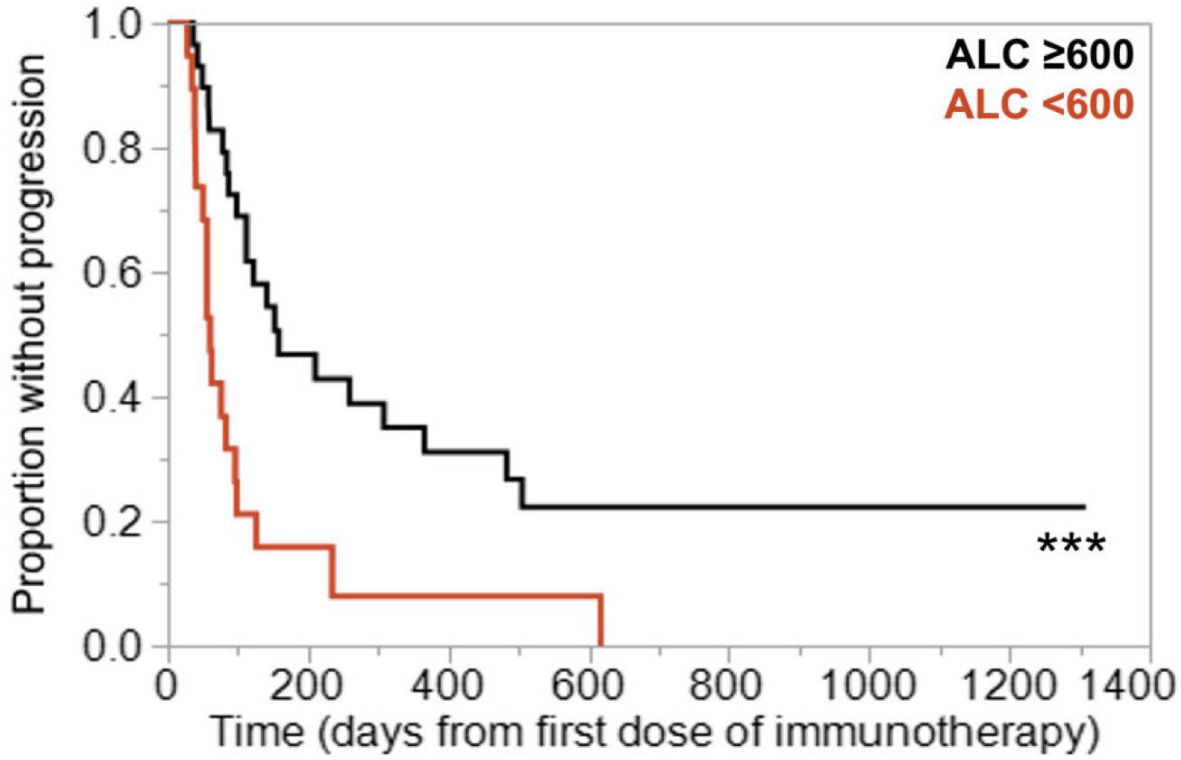


Fig. 3 An expanded cohort time-to-progression analysis was performed by including additional patients who have received other checkpoint inhibitor regimens. Patients with ALC < 600 cells/μl were associated with significantly shorter PFS. ***$P < 0.005$ by Wilcoxon test

Table 1 Different published studies exploring the impact of the global lymphopenia or NK and T cell subsets on relapse-free survival (RFS) or overall survival (OS) in patients with solid tumors

From: Lymphopenia in Cancer Patients and its Effects on Response to Immunotherapy: an opportunity for combination with Cytokines?

Tumor Type	N	Type of lymphopenia evlauated	Lymphocyte Threshold (% lymphopenia)	RFS (Cox Analysis)			OS (Cox Analysis)			References
				RR	IC 95%	P value	RR	IC 95%	P value	
Sarcoma	193	Overall Lymphopenia	<1000 (24%)	Not evaluated			1.46	1.0-2.1	0.05	[68]
Ewing Sarcoma	24	Overall Lymphopenia	<500 (33%)	Not evaluated			4.34	1.35-14.28	0.007	[75]
Renal Cell Carcinoma	424	Overall Lymphopenia	≤1300 (28.06%)	Not evaluated			1.75	1.14-2.67	0.0102	[65]
Colon Carcinoma	260	Overall Lymphopenia	<1000 (19%)	1.56	1.0-2.43	0.048	2.35	2.34-4.14	0.003	[66]
Breast Carcinoma	195	Overall Lymphopenia	<1000 (28.7%)	1.82	1.27-2.59	0.001	2.23	1.36-3.65	0.001	[89]
Non Hodgkin Lymphoma	322	Overall Lymphopenia	<1000 (25%)	1.71	1.2-2.4	0.002	1.48	1.03-2.21	0.04	[68]
Diffuse large B cell lymphoma (DLBCL)	151	Overall Lymphopenia	≤1000 (35.8%)	Not evaluated			2.38	1.29-4.34	0.005	[90]
DLBCL	221	Overall Lymphopenia	<1000 (38.9%)	2.72	1.61-4.60	<0.001	2.51	1.38-4.58	0.003	[80]
DLBCL	89	Overall Lymphopenia	<840 (23%)	3.81	1.72-8.42	0.0009	4.38	1.88-13.28	0.0012	[79]
Follicular Lymphoma	228	Overall Lymphopenia	≤1000 (28%)	Not evaluated			1.72	1.33-2.24	$<10^{-4}$	[70]
Hodgkin Lymphoma	476	Overall Lymphopenia	<600 (18.06%)	1.59	0.96-2.58	0.06	1.25	0.74-2.15	0.4	[82]
Hodgkin Lymphoma	2497	Overall Lymphopenia	<600 (11%)	1.38		0.002	Not evaluated			[81]
Multiple Myeloma	537	Overall Lymphopenia	<1400 (62%)	Not evaluated			1.71	1.53-2.35	$<10^{-4}$	[92]
ATLL	60	Overall Lymphopenia	<1000 (35.6%)	1.93		0.004	2.37		0.0003	[93]
PTCLU	69	Overall Lymphopenia	<1000 (38%)	Not evaluated			4.0	1.9-8.3	$<10^{-4}$	[71]
PTCL-NOS	118	Overall Lymphopenia	1000 (30.5%)	1.94	1.19-3.18	0.008	2.24	1.33-3.78	0.002	[72]
Breast Carcinoma	287	Overall Lymphopenia	<1000 (27%)	1.48	1.1-2.0	0.01	1.8	1.3-2.4	0.0002	[68]
Breast Carcinoma	195	Overall Lymphopenia	<1000 (28.7%)	1.82	1.27-2.59	0.001	2.23	1.36-3.65	0.001	[89]
Breast Carcinoma 1st relapse	128	Overall Lymphopenia	<1000 (44.27%)	Not evaluated			1.8	1.15-2.82	0.01	[50][b]
Breast Carcinoma 1st relapse 1st relapse	103	Overall Lymphopenia	<700 (22.3%)	Not evaluated			2.03	1.17-3.50	0.016	[21][b]
Breast Carcinoma 1st relapse 1st relapse	103	$CD4^+$ Lymphopenia	≤450 (53.4%)	Not evaluated			2.50	1.57-3.98	$<10^{-4}$	[21][b]
Breast Carcinoma >2nd relapse	101	$CD4^+$ Lymphopenia	≤450 (70.3%)	1.35	0.87-1.1	0.183	1.69	1.04-2.78	0.036	[21]
Metastatic Solid Tumors	219	$CD4^+$ Lymphopenia	≤450 (47.9%)	Not evaluated			1.5	1.1-2.1	0.017	[20]
Metastatic Solid Tumors	213	$CD4^+$ Lymphopenia	<450 (49.7%)	Not evaluated			7.7[a]	1.6-35[a]	0.007[a]	[19][a]
Non Hodgkin Lymphoma	88	$CD8^+$ Lymphopenia	<200	Not evaluated			3.30	1.21-9.0	0.01	[88]
Follicular Lymphoma	75	NK cells Lymphopenia	<150 (44%)	Not evaluated			6.73	0.76-59	0.08	[69]
DLBCL	136	NK cells Lymphopenia	≤80 (37.5%)	1.81	1.27-2.57	0.001	Not evaluated			[94]

[a] Analysis of the risk of early death; [b] Univariate analysis only

2019

Ménétrier-Caux *et al. Journal for ImmunoTherapy of Cancer* (2019) 7:85
https://doi.org/10.1186/s40425-019-0549-5

Journal for ImmunoTherapy of Cancer

REVIEW Open Access

Lymphopenia in Cancer Patients and its Effects on Response to Immunotherapy: an opportunity for combination with Cytokines?

Christine Ménétrier-Caux[1,2*], Isabelle Ray-Coquard[3], Jean-Yves Blay[1,3†] and Christophe Caux[1,2†]

Abstract

Quantitative lymphocyte alterations are frequent in patients with cancer, and strongly impact prognosis and survival. The development of cancers in immunosuppressed patients has demonstrated the contribution of different T cell populations, including $CD4^+$ cells, in the control of cancer occurrence.

Whereas absolute numbers of neutrophils, platelets and red blood cells are routinely monitored in clinic following treatments, because of possible short-term complications, absolute lymphocyte counts (ALC), their subpopulations or diversity (phenotype, TCR) are rarely analyzed and never used to choose therapy or as prognostic criteria. The recent identification of immune checkpoint inhibitors (ICPi) as powerful therapeutic agents has revitalized immunotherapy of cancer in a broader group of diseases than anticipated. The status of the immune system is now recognized as an important biomarker for response to these novel treatments. Blood ALC values, along with tumor infiltration by $CD8^+$T cells, and ICPi and ICPi-ligand expression, are likely to be a potential marker of sensitivity to anti-ICPi therapy.

In this article, we review the current knowledge on the incidence and significance of lymphopenia in cancer patients, and discuss therapeutic strategies to restore lymphocyte numbers.

Keywords: Lymphopenia, solid tumors, TCR diversity, anti-cancer immunotherapy

High Lymphocyte Count Associated with Prolonged Overall Survival (Hazard Ratio 0.035, P<0.001)

2022

scientific reports

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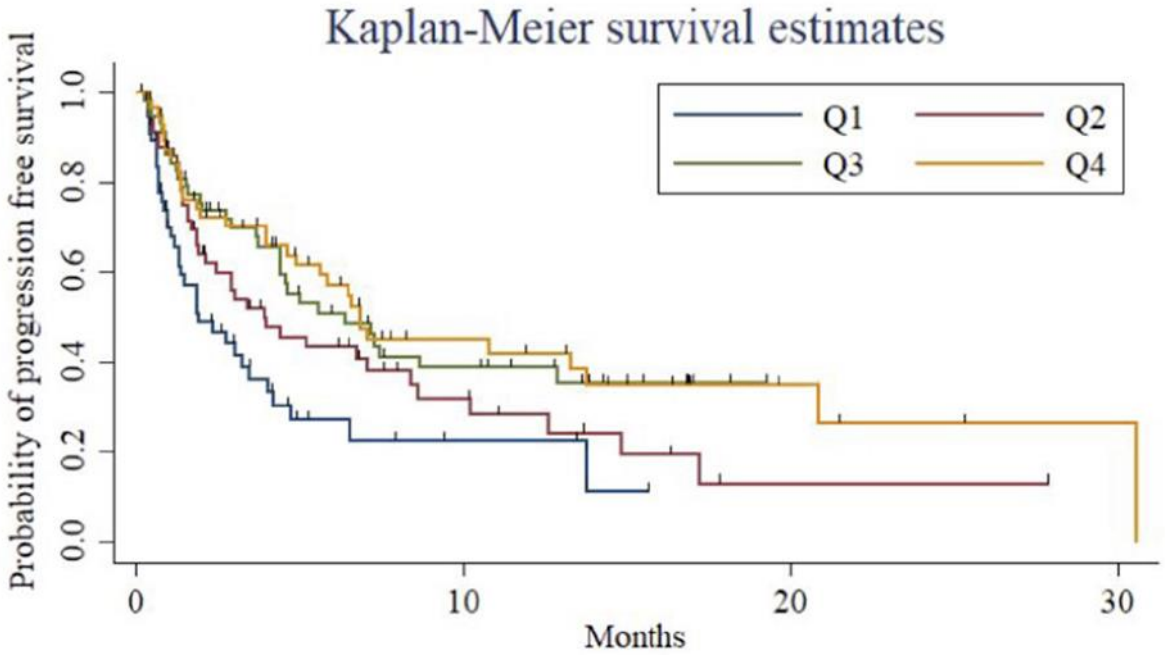
OPEN

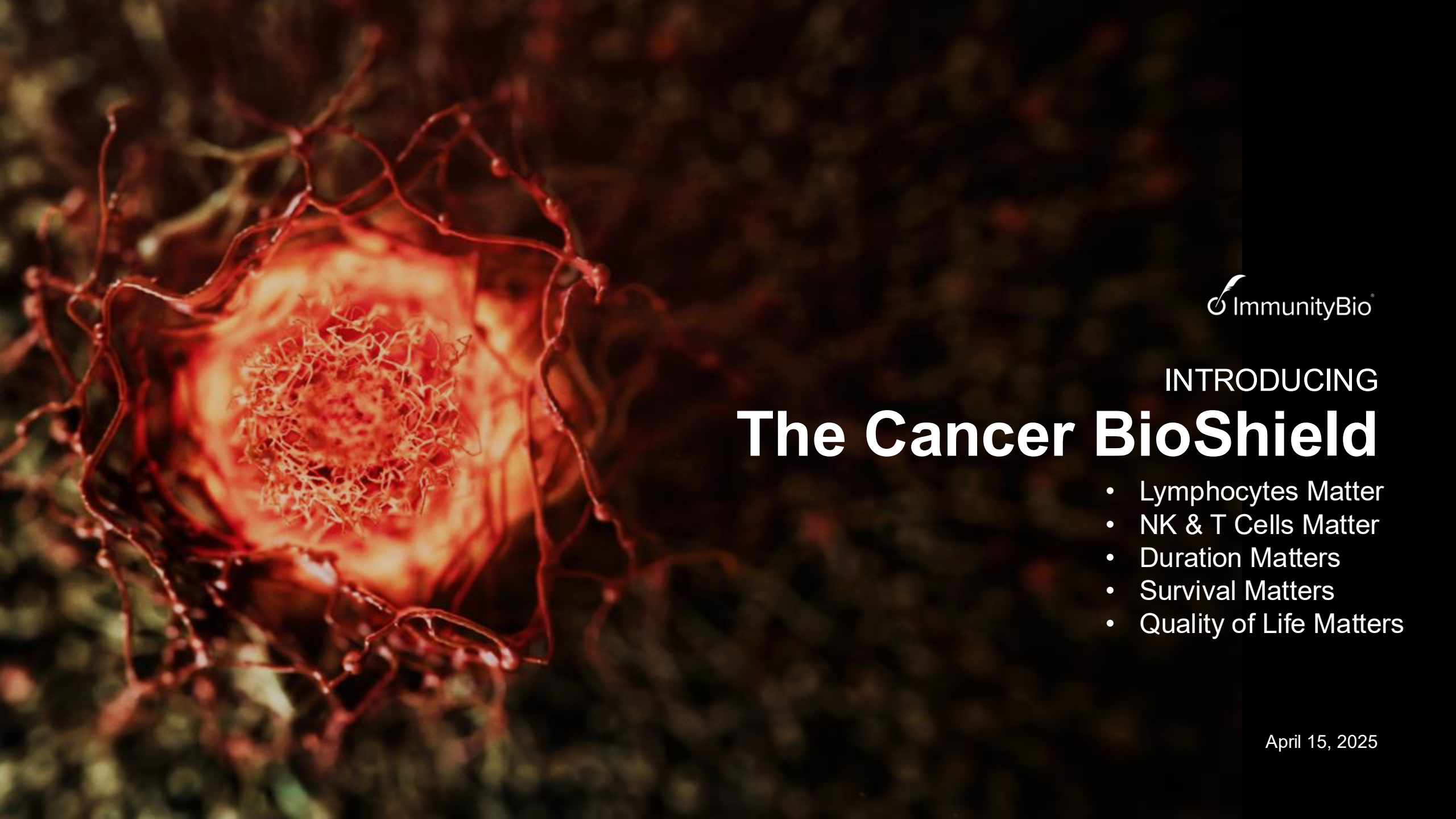
Peripheral lymphocyte count as a surrogate marker of immune checkpoint inhibitor therapy outcomes in patients with non-small-cell lung cancer

Ye Jin Lee[1], Young Sik Park[1], Hyun Woo Lee[2], Tae Yoen Park[2], Jung Kyu Lee[2] & Eun Young Heo[2]✉

Degree of expression of programmed death-ligand 1 (PD-L1) is related with Immune check point inhibitors (ICIs) response but it needs sufficient tumor tissue. There is unmet need for easily accessible and prognostic peripheral blood (PB) biomarkers. We investigated the application of serum peripheral lymphocyte count (PLC) as a predictive PB biomarker for ICI response in patients with NSCLC. We conducted a retrospective study and reviewed the patients with NSCLC who were treated with ICIs from April 1, 2016, to March 31, 2019. The PLC before and after 1 month of immunotherapy was collected. We evaluated the association between PLC and progression-free survival (PFS), overall survival (OS) and adverse events. A total of 231 patients were treated with ICIs for NSCLC. The median follow-up period was 4.7 months and the disease progressed in 138 patients (59.7%). Compared with the lowest quartile (Q1: the lowest 25%), the highest quartile (Q4: the highest 25%) of post-treatment PLC showed a significantly higher PFS (HR 0.28, 95% CI 0.16–0.52) and OS (HR 0.35, 95% CI 0.19–0.65) in the adjusted model. An association between adverse events and PLC was not observed. We revealed that an increased pre- and post-treatment PLC was associated with favorable PFS and OS with NSCLC patients treated with ICIs. PLC could be a helpful for ICI responses in NSCLC.

Post-treatment PLC, Quartile [min–max]				
1 [208.6–1178.6]	1 (reference)		1 (reference)	
2 [1181–1676.7]	0.61 (0.35, 1.06)	0.082	0.59 (0.32, 1.06)	0.09
3 [1686.7–2180]	0.40 (0.22, 0.73)	0.005	0.29 (0.15, 0.57)	< 0.001
4 [2186.9–5141.7]	0.28 (0.16, 0.52)	< 0.001	0.35 (0.19, 0.65)	< 0.001
P for trend	0.001		0.005	





ImmunityBio

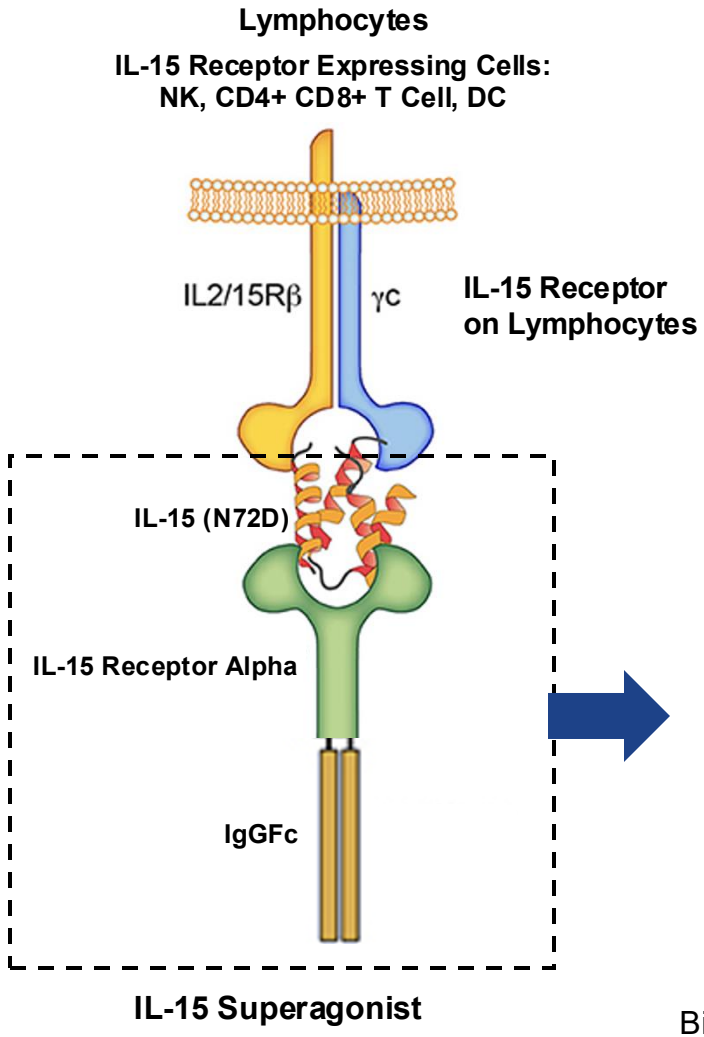
INTRODUCING

The Cancer BioShield

- Lymphocytes Matter
- NK & T Cells Matter
- Duration Matters
- Survival Matters
- Quality of Life Matters

April 15, 2025

ANKTIVA FDA Approved Mechanism of Action April 2024

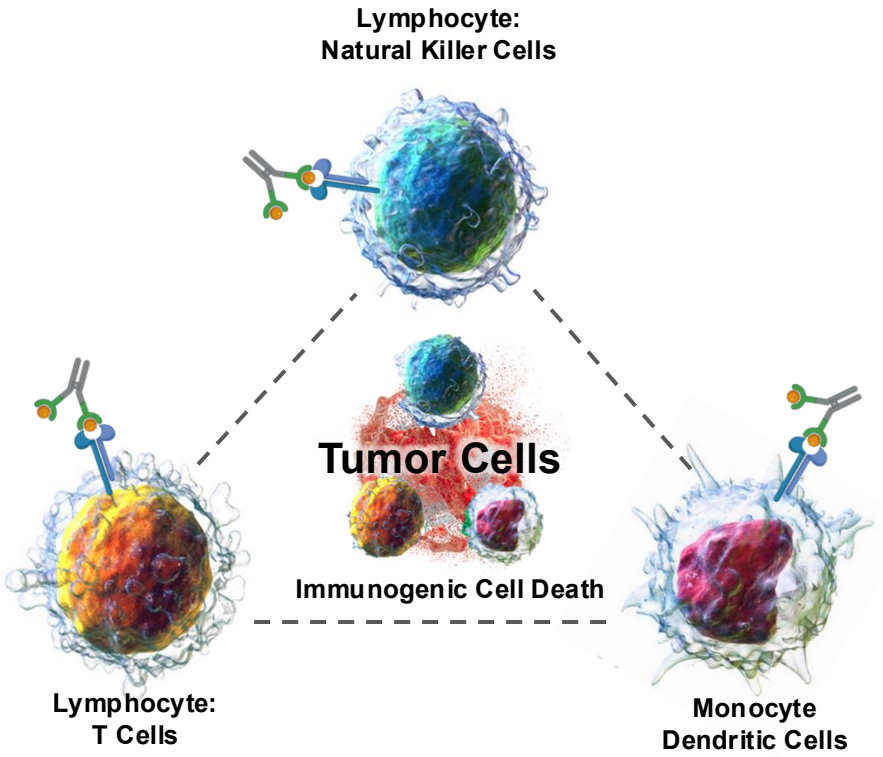


The Missing Link

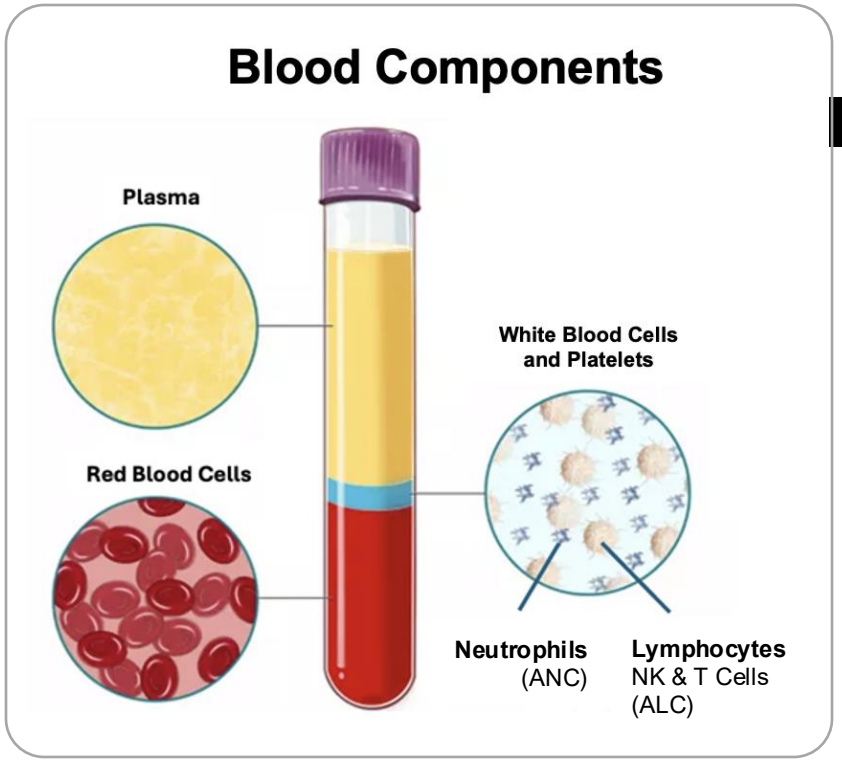
Nogapendekin alfa inbakicept (NAI)

Lymphocyte Stimulating Agent

Binding of nogapendekin alfa inbakicept-pmln to its receptor results in proliferation and activation of NK, CD8+, and memory T cells without proliferation of immuno-suppressive Treg cells.



Introducing Absolute Lymphocyte Count (ALC) and Lymphopenia



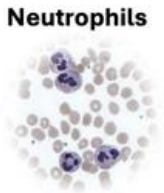
ANC: Absolute Neutrophil Count
ALC: Absolute Lymphocyte Count

Low Red Blood Count

Anemia

EPOGEN

Treats Anemia
Increases Red Blood Cell Production
1989

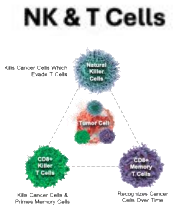


Low Neutrophil Count

Neutropenia

NEUPOGEN

Prevents Infection
Increases Neutrophil Production
1991



Low Lymphocyte Count

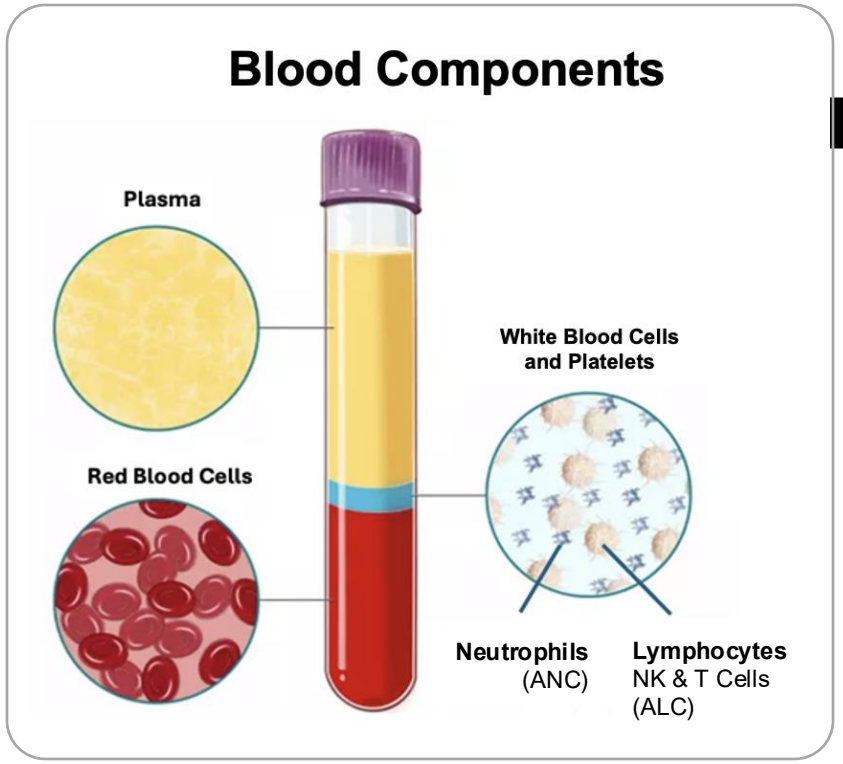
Lymphopenia

Loss of NK & T Cells
Which Kill Cancer &
Induce T Cell Memory

No Treatment for Over 50 Years
The Missing Link

Kills Cancer & Infected Cells

First Lymphocyte Rescue Agent in 50+ Years as Backbone to Chemo-Immunotherapy and Radiotherapy



ANC: Absolute Neutrophil Count
ALC: Absolute Lymphocyte Count

Red Blood Cell

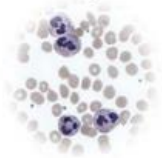
Low Red Blood Count

Anemia

EPOGEN

Treats Anemia
Increases Red Blood Cell Production
1989

Neutrophils



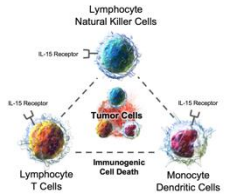
Low Neutrophil Count

Neutropenia

NEUPOGEN

Prevents Infection
Increases Neutrophil Production
1991

NK & T Cells



Low Lymphocyte Count

Lymphopenia

ANKTIVA

Induces Cancer Cell Death
Regenerates NK and T cells and Induces T Cell Memory

ANKTIVA Approved 2024

QUILT-1.004
Healthy Volunteers

2022: Phase I Trial Characterizing the PK Profile of NAI, a Chimeric IL-15 Superagonist, in Healthy Volunteers

Healthy Volunteers

2022

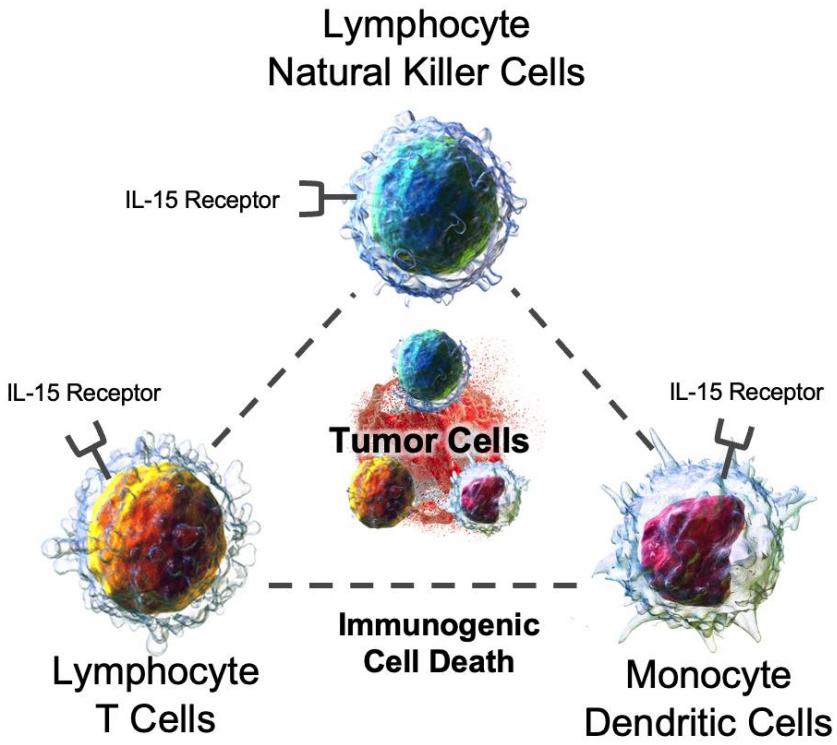
The Journal of Immunology

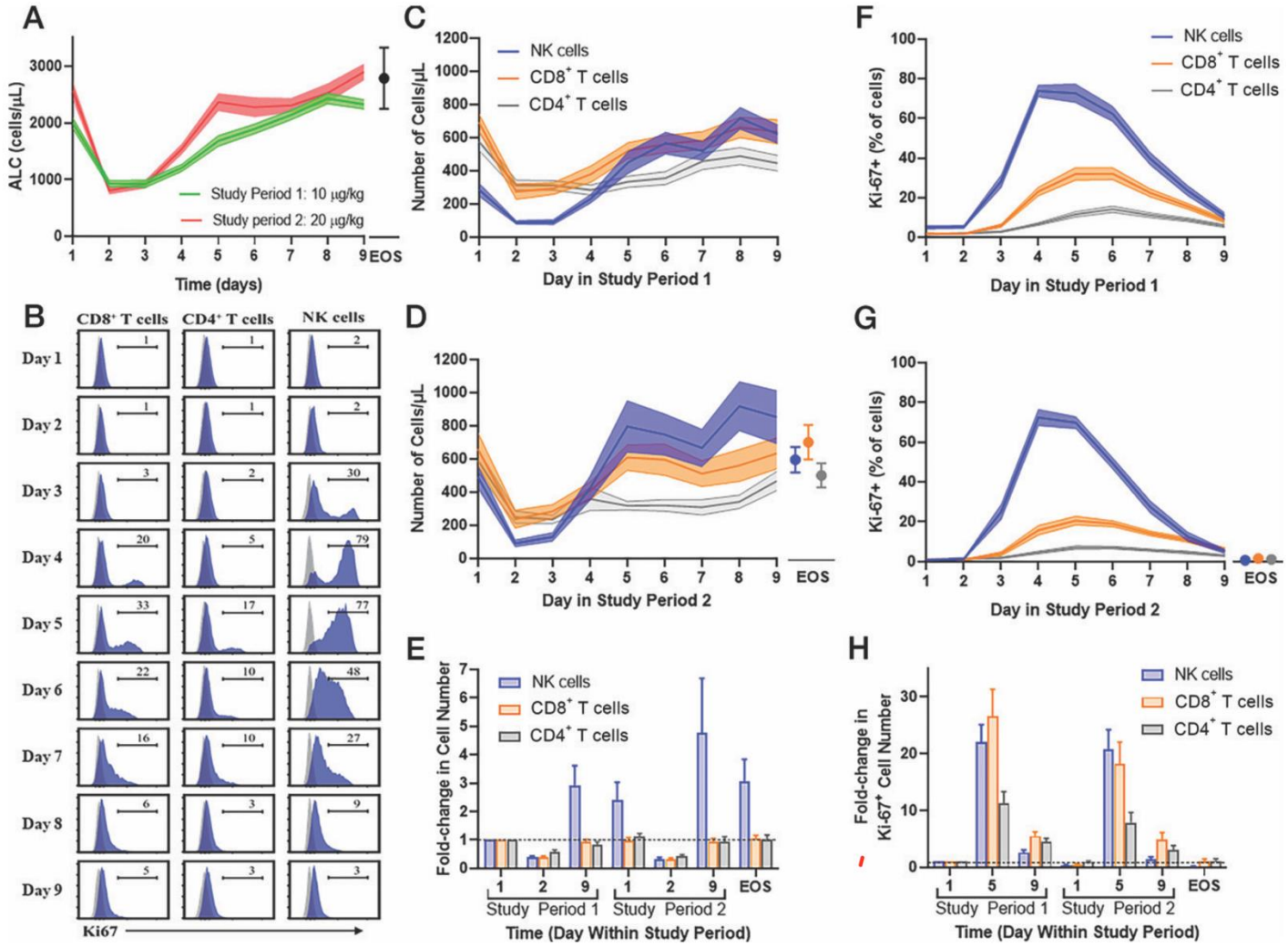
RESEARCH ARTICLE | MARCH 15 2022

Phase I Trial Characterizing the Pharmacokinetic Profile of N-803, a Chimeric IL-15 Superagonist, in Healthy Volunteers FREE

Mark P. Rubinstein; ... et. al

J Immunol (2022) 208 (6): 1362–1370.
https://doi.org/10.4049/jimmunol.2100066

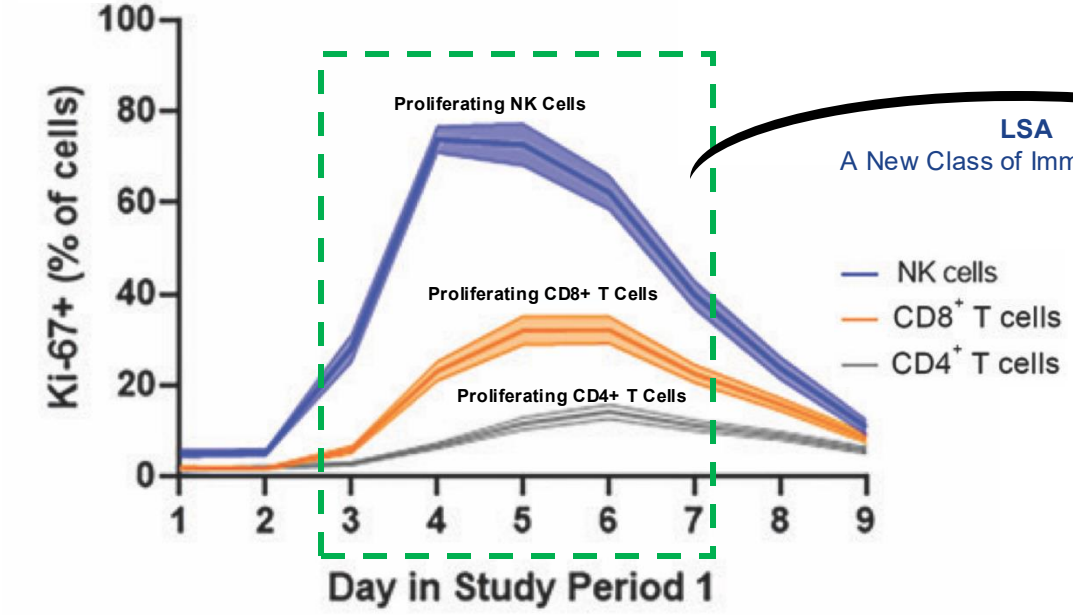




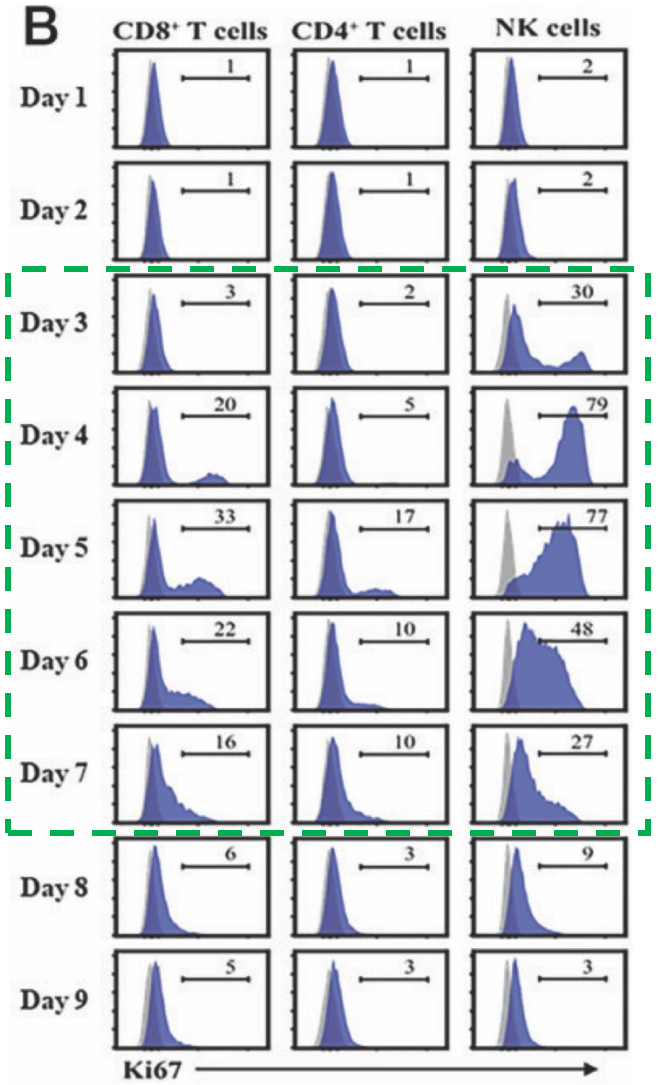
A New Class of Immunotherapy: Lymphocyte Stimulating Agent ANKTIVA – Proliferation of NK, CD4+ CD8+ T Cell

Lymphocyte Stimulating Agent
Proliferation

Proliferation Effect of ANNKTIVA on NK, CD4 CD8 T Cells
10µg/kg



LSA
A New Class of Immunotherapy



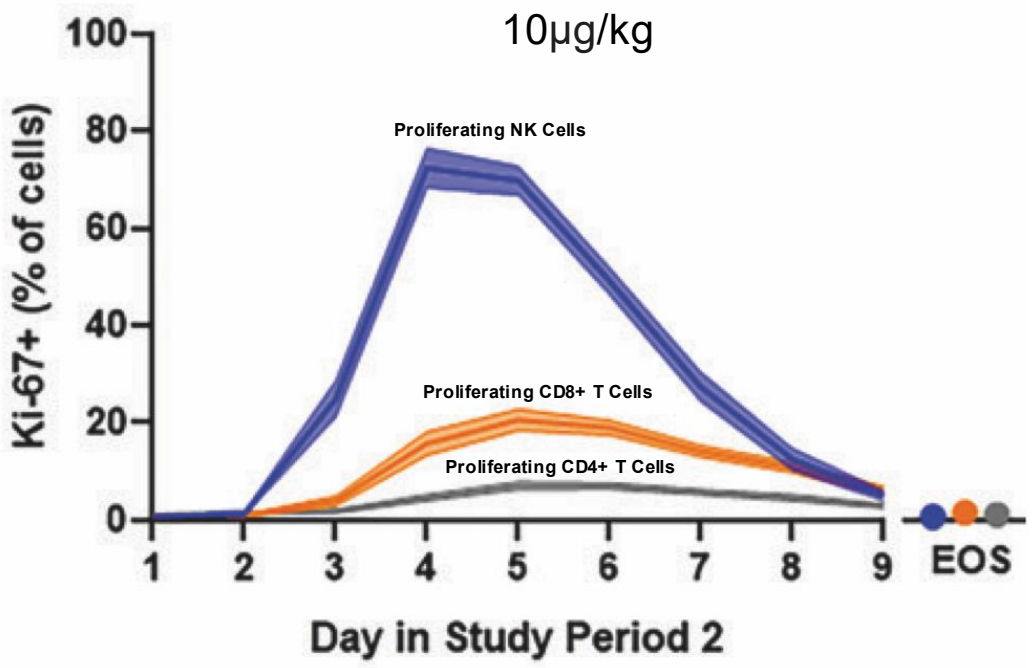
A New Class of Immunotherapy: Lymphocyte Stimulating Agent ANKTIVA – Proliferation of NK, CD4+ CD8+ T Cell Leading to Sustained Absolute Lymphocyte Count (ALC)

Lymphocyte Stimulating Agent (LSA)
Proliferation

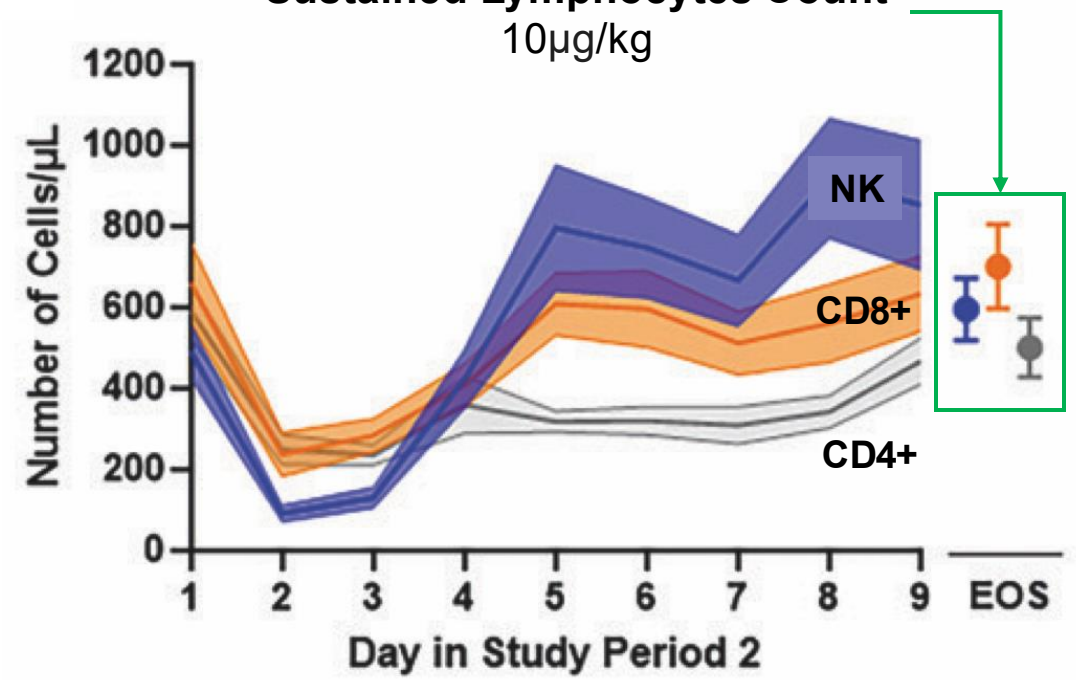
LSA
A New Class of Immunotherapy

Lymphocyte Stimulating Agent (LSA)
Increase in Lymphocyte Count

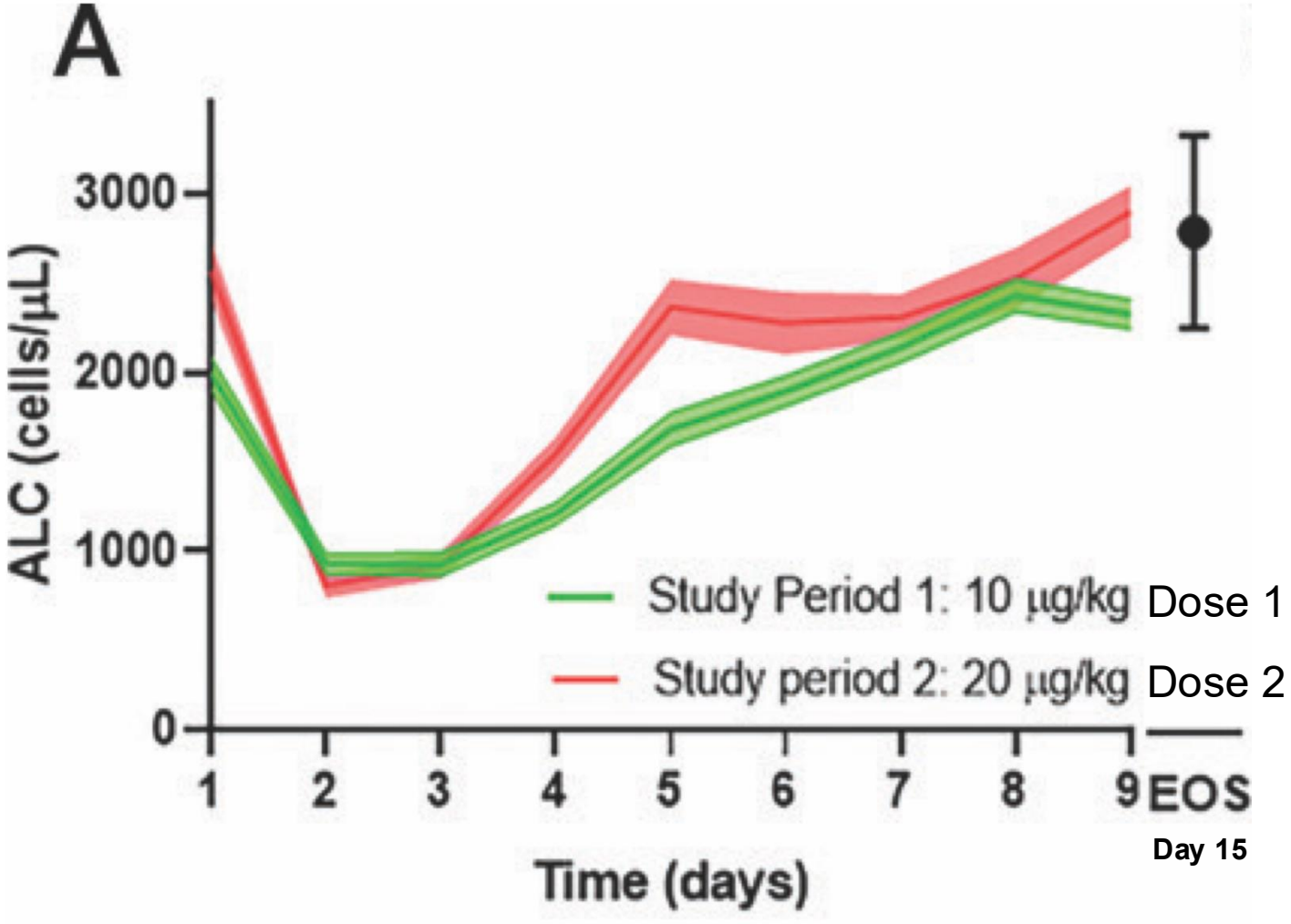
Proliferation Effect of ANNKTIVA on NK, CD4 CD8 T Cells
10µg/kg



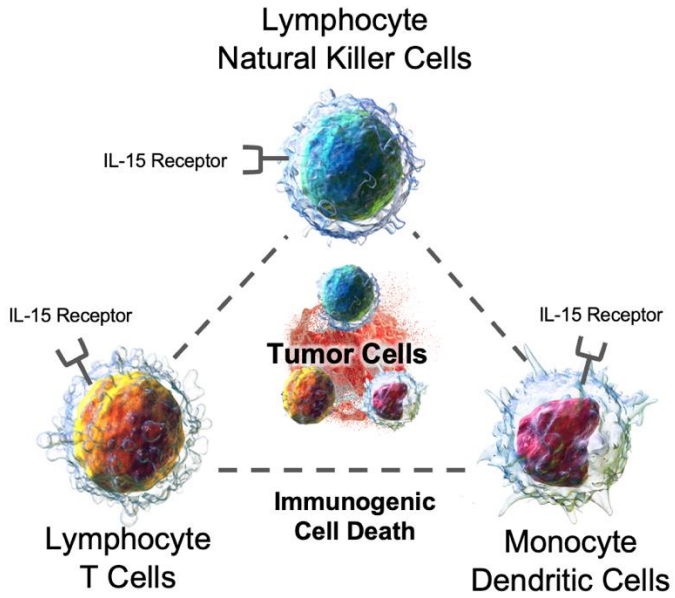
Sustained Lymphocytes Count
10µg/kg



Summary: A New Class of Immunotherapy: Lymphocyte Stimulating Agent ANKTIVA - Increase in ALC Count After Two Doses



Triangle Offense
A New Class of Immunotherapy
Lymphocyte Stimulating Agent (LSA)



(A) Mean absolute lymphocyte count in study period 1 (green), study period 2 (red), and EOS (black).

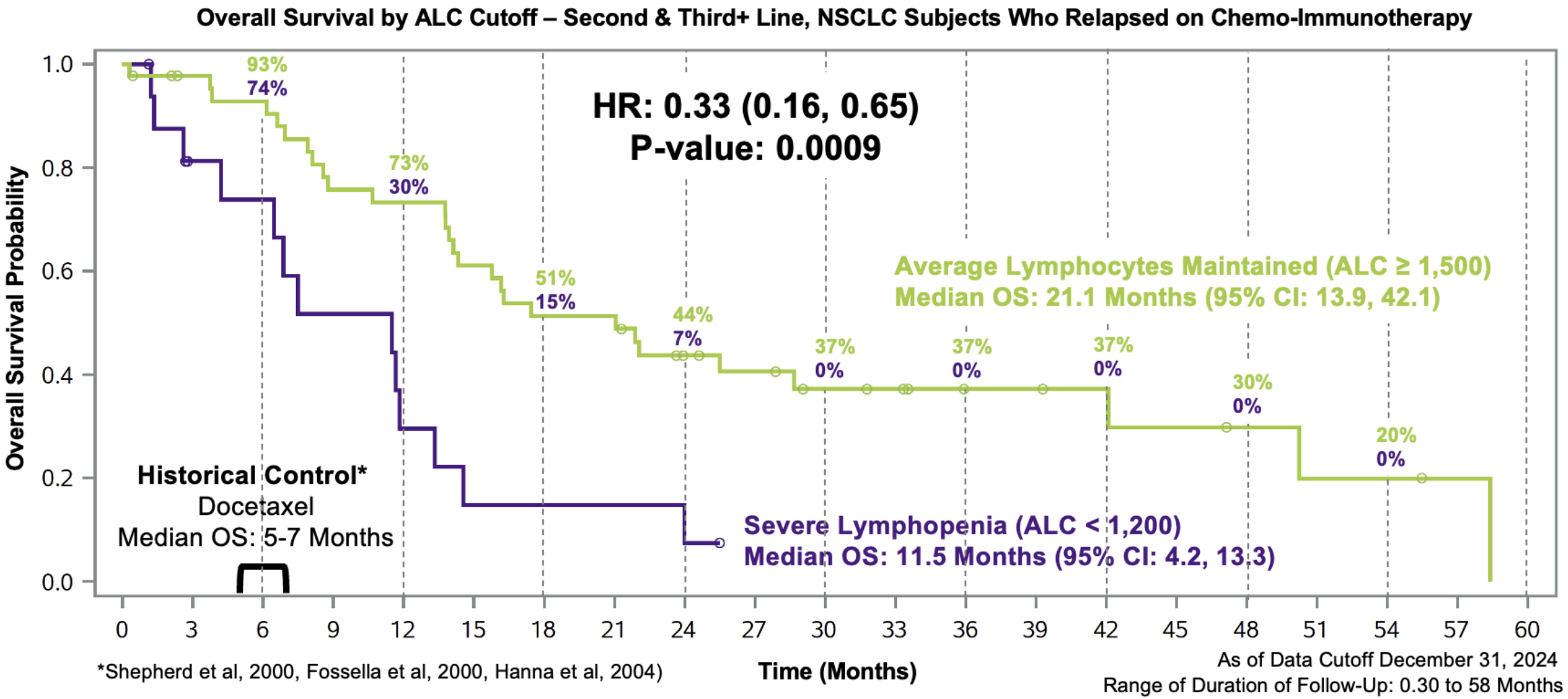
Lymphocyte Stimulating Agent Treats Lymphopenia and Prolongs Overall Survival Across All Tumor Types

QUILT-3.055 Second Line Non-Small Cell Lung Cancer (NSCLC)

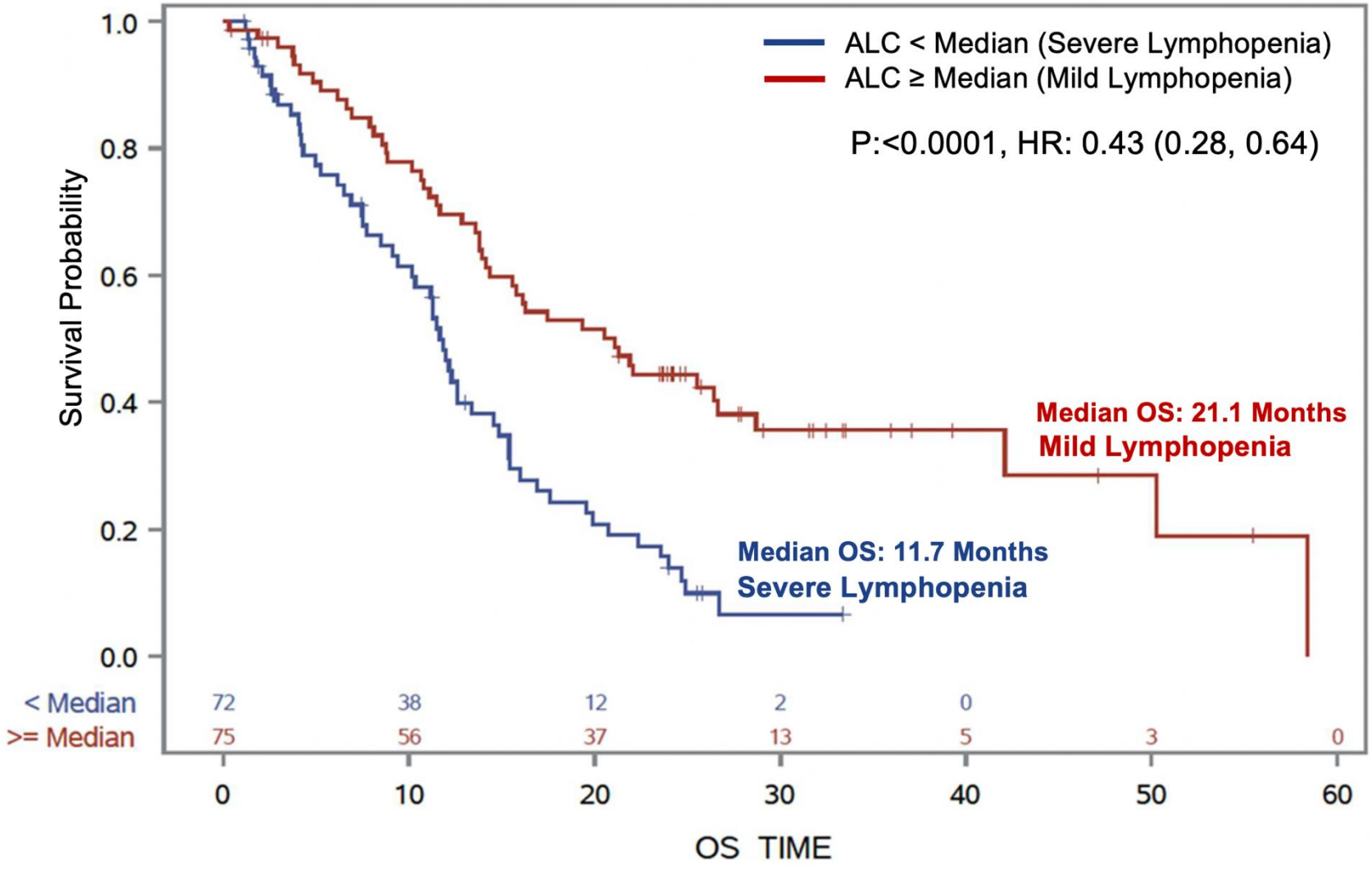
QUILT-3.055 Multiple Tumor Types Failing Checkpoint Inhibitors

QUILT-88 3rd Line or Greater Metastatic Pancreatic Cancer

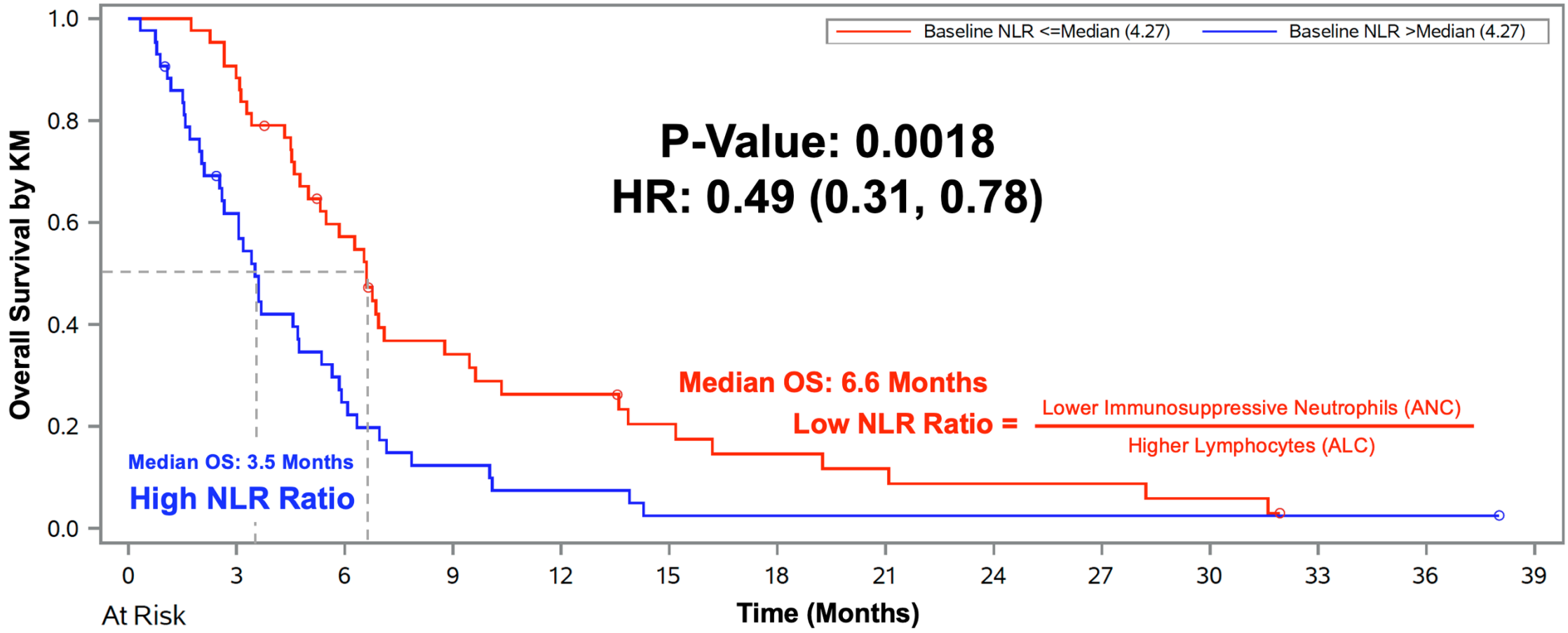
ANKTIVA: Lymphocyte Stimulating Agent in Lung Cancer



ANKTIVA: Lymphocyte Stimulating Agent in Multiple Tumors Improved Overall Survival – Tumor Agnostic



ANKTIVA: Lymphocyte Stimulating Agent in Metastatic Pancreatic Cancer Improved Overall Survival



February 28: RMAT Designation Granted for Reversing Lymphopenia Regenerative Medicine Advanced Therapy (RMAT)

Proposed Indications

- Reversing Lymphopenia in patients undergoing chemo & radiation therapy (e.g. NSCLC)
- Reversing Lymphopenia in patients with metastatic pancreatic cancer

FDA Grants RMAT Designation to Nogapendekin Alfa in Pancreatic Cancer

February 28, 2025
By Jordyn Sava
Fact checked by Jason M. Broderick

News *Article*

The FDA granted RMAT designation to nogapendekin alfa and CAR-NK for reversing lymphopenia in patients with cancer, with promising survival data in metastatic pancreatic cancer and non–small cell lung cancer.

- **The FDA granted Regenerative Medicine Advanced Therapy (RMAT) status to nogapendekin alfa (Anktiva) and CAR-NK (PD-L1 t-haNK) for reversing lymphopenia in patients undergoing chemotherapy/radiotherapy and treating metastatic pancreatic cancer.**
- **Significant overall survival (OS) correlations were observed in QUILT trials across multiple tumor types, including metastatic pancreatic cancer and non–small cell lung cancer (NSCLC).**
- **ImmunityBio plans to submit a biologic license application (BLA) for lymphopenia reversal and pancreatic cancer treatment.**

US FDA

The FDA has granted RMAT designation to nogapendekin alfa and CAR-NK for the reversal of lymphopenia in patients receiving standard-of-care chemotherapy or radiotherapy, as well as for the treatment of multiply relapsed locally advanced or metastatic pancreatic cancer.[1]

INTRODUCING

Fireside Chats

April 15, 2025

ImmunityBio

INTRODUCING

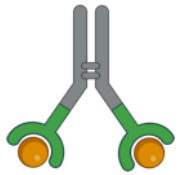
ImmunityBio Cancer BioShield Platforms

April 15, 2025

ImmunityBio Cancer BioShield

The Cancer BioShield

Fusion Proteins



NK & T Cell Activator
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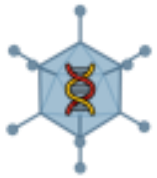

Adenovirus (hAd5)

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Phase 2

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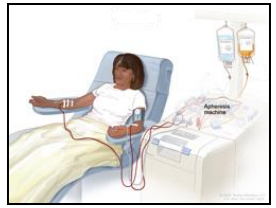

NK, iNKT &
Dendritic Cell Pathway

M-ceNK

Phase 2

Ex-Vivo Lymphocyte Rescue

INTRODUCING

Fireside Chats

April 15, 2025

Fireside Chats

Dr. Steven Finkelstein & Alan Portella: Radiation in Prostate Cancer

- Lymphopenia & Radiation
- Prostate Cancer Experience

Dr. David Kerr – Oxford University, Dr. Elizabeth Gabitzsch & Dr. Mark Lanasa

- Colon Cancer Experience
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- Lymphopenia & Radiation
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Dr. Steven Finkelstein

Mr. Alan Portella

Review

Combining Immunotherapy and Radiation for Prostate Cancer☆

Steven E. Finkelstein,[1] Sharon Salenius,[2] Constantine A. Mantz,[2] Neal D. Shore,[3] Eduardo B. Fernandez,[2] Jesse Shulman,[1] Francisco A. Myslicki,[1] Andre M. Agassi,[1] Yosef Rotterman,[1] Todd DeVries,[4] Robert Sims[4]

Abstract

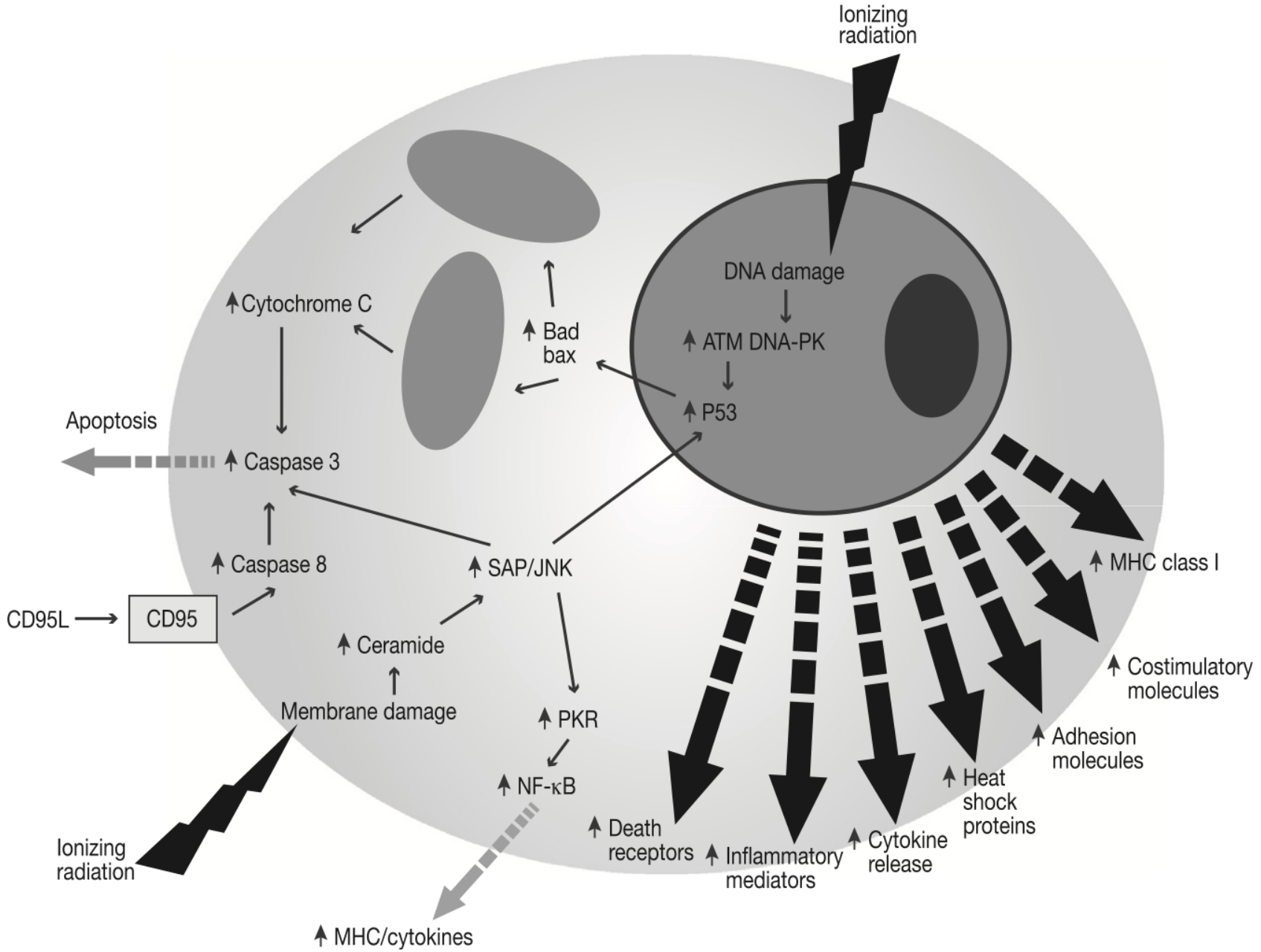
Radiotherapy has conventionally been viewed as immunosuppressive, which has precluded its use in combination with immunotherapy for prostate and other cancers. However, the relationship between ionizing radiation and immune reactivity is now known to be more complex than was previously thought, and data on the use of radiotherapy and immunotherapy are accumulating. Herein, we review this topic in the light of recently available data in the prostate cancer setting. Recent research has shown no significant lymphopenia in patients undergoing radiotherapy for high-risk adenocarcinoma of the prostate. In addition, emerging evidence suggests that radiotherapy can have immunostimulatory effects, and that tumor cell death, coupled with related changes in antigen availability and inflammatory signals, can affect lymphocyte and dendritic cell activation. Initial studies have focused on combinations of tumor irradiation and immunotherapy, such as the autologous cellular immunotherapy sipuleucel-T and the monoclonal antibody ipilimumab, in metastatic castration-resistant prostate cancer. These combinations appear to have clinical promise, and further investigation of the potentially synergistic combination of radiotherapy and immunotherapy is continuing in clinical trials.

Clinical Genitourinary Cancer, Vol. 13, No. 1, 1-9

Keywords: Cancer vaccine, Prostatic neoplasm, Radiation effects, Radiotherapy

Radiation Effects on Immune Cells and Consequent Modulation by Radiotherapy.

Apoptosis Can Be Initiated by Radiation-Induced DNA Damage and Upregulation of the p53 Tumor Suppressor Gene, and by Damage to the Cellular Lipid Membrane, Which Can Induce Ceramide Formation and Activate the SAPK/JNK Signaling Pathway. SAPK/JNK Can Upregulate PKR Expression, Which in Turn Induces MHC and Cytokines via NF-kB. Radiation Treatment Induces Cellular Expression of MHC Class I, Adhesion Molecules, Co-Stimulatory Molecules, Heat Shock Proteins, Inflammatory Mediators, Immunomodulatory Cytokines, and Death Receptors



Steven E. Finkelstein et al

Table 1 White Blood Cell Count (WBC) and Absolute Lymphocyte Counts (ALC) at Baseline and After Radiotherapy in 26 Patients With Adenocarcinoma of the Prostate[13]

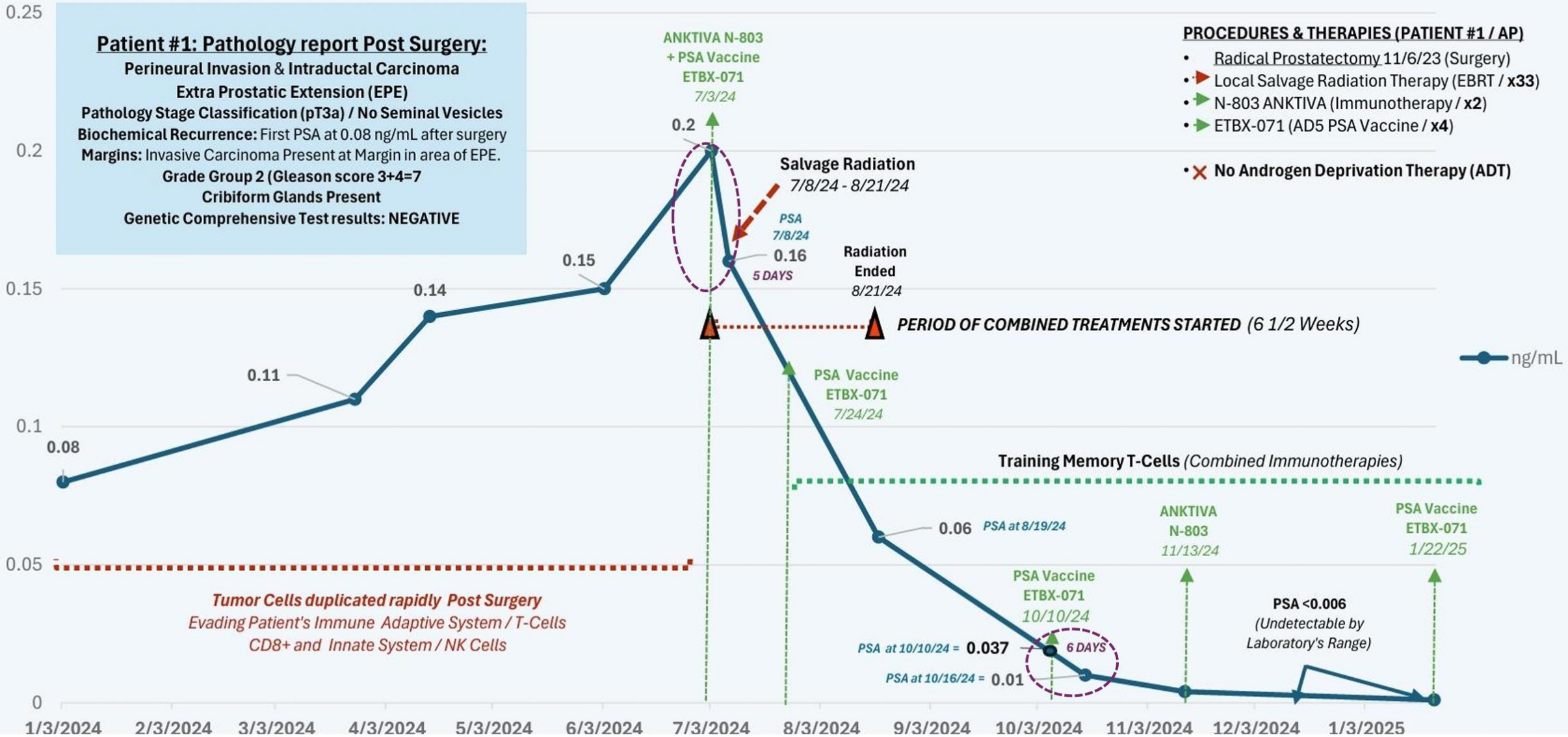
Parameter	Statistic	Baseline	Days After Radiotherapy			
			1-90	91-180	181-360	>360
WBC, Cells/μL	n	26	18	13	21	20
	Mean	6527	5806	6362	6038	6085
	Median	6050	5350	6000	5800	5200
	Minimum	4000	3500	3500	3400	4400
	Maximum	10,100	13,100	11,000	13,100	10,000
ALC, Cells/μL	n	21	11	9	10	8
	Mean	1680	1054	1059	1246	1275
	Median	1700	970	1100	1250	1350
	Minimum	700	700	500	590	1000
	Maximum	3100	1700	1500	2100	1400

Normal reference ranges were 3800 to 10,700 cells/μL for WBC and 910 to 4280 cells/μL for ALC.
Abbreviation: n = number of observations in an interval.

ALC Analysis on Prostate Cancer Post Radiation

RX Date	RT RX	Pre ALC DOS	Pre ALC	DATE OF RT	Post ALC DOS	Post ALC	% Change	LAB RANGES PER PERFORMING FACILITY
11/07/2024	Pros Rx 81 Prossvln 3 Phase	9/26/24	520.000	11/21/2024 to 01/28/2025	2/18/25	460.000	(0.115)	LYMPHOCYTES (ABSOLUTE)(950-3500)
07/25/2024	Pros Rx 70 LN	7/16/24	1,000.000	08/21/2024 to 10/03/2024	10/23/24	500.000	(0.500)	LYMPHS ABSOLUTE (0.7-3.1)
07/23/2024	Pros Rx 81 Pros LN w/LN bst	9/19/22	2,600.000	8/22/24 to 10/31/2024	11/18/24	700.000	(0.731)	LYMPH # (1.2-4.8)
06/19/2024	Pros Rx 81 Prossvln3pshr	5/31/24	1,000.000	07/15/2024 to 09/16/2024	12/13/24	700.000	(0.300)	LYMPH # (1.2-4.8)
06/14/2024	Pros Rx 81 Prossvln3pshr	6/12/24	2,400.000	07/10/2024 to 09/18/2024	11/26/24	800.000	(0.667)	LYMPH # (1.2-4.8)
06/11/2024	Pros Rx 81 Prossvln3pshr	5/17/24	2,400.000	06/20/2024 to 08/29/2024	10/14/24	1,300.000	(0.458)	LYMPH # (1.2-4.8)
04/03/2024	Pros Rx 81 Prossvln3ph	3/4/24	1,700.000	05/06/2024 to 07/11/2024	11/13/24	600.000	(0.647)	LYMPHOCYTES # BLD AUTO (0.6-4.6)
02/26/2024	Pros Rx 81 Pros LN	12/26/23	2,300.000	03/20/2024 to 05/24/2024	6/25/24	400.000	(0.826)	LYMPHS ABSOLUTE (0.7-3.1)
02/15/2024	Pros Rx LN	2/26/24	2,000.000	03/19/2024 to 05/23/2024	5/31/24	500.000	(0.750)	LYMPH # (1.2-4.8)
02/15/2024	Pros Rx 81 3PH	1/29/24	2,820.000	[illegible]	[illegible]	900.000	(0.681)	Abs. Lymphocyte 1.20-3.70 x 1000 / LYMPH # (1.2-4.8)
01/19/2024	Pros Rx 81 Prossvln3pshr	3/4/24	2,910.000	[illegible]	[illegible]	1,700.000	(0.416)	Lymphocytes Absolute 950-3500 / LYMPH # (1.2-4.8)
01/19/2024	Pros Rx 81 Pros LN w/LN bst	4/3/24	2,400.000	[illegible]	[illegible]	1,000.000	(0.583)	LYMPH # (1.2-4.8)
12/08/2023	Pros Rx 81 Prosallsvln	8/4/22	1,200.000	01/10/2024 to 03/12/2024	4/11/24	100.000	(0.917)	Lymphocytes Absolute 1.0-3.4 / LYMPH # (1.2-4.8)
09/15/2023	Pros Rx Prossvln3pshr	9/12/23	1,900.000	10/05/2023 to 12/14/2023	6/13/24	800.000	(0.579)	LYMPH # (0.5-5.0) / LYMPH # (1.2-4.8)
07/11/2023	Pros Rx 81 Prosallsvln25,5,15	4/24/23	2,000.000	08/03/2023 to 10/10/2023	7/10/24	900.000	(0.550)	LYMPH # (1.2-4.8)
06/27/2023	Pros Rx 81 Prosallsvln25,5,15	1/10/22	2,980.000	07/18/2023 to 09/21/2023	2/20/25	2,000.000	(0.329)	Abs Lymphocyte (1.20-3.70) / LYMPH # (1.2-4.8)
06/08/2023	Pros Rx 81 Prosallsvln25,5,15	3/21/23	1,760.000	07/05/2023 to 09/07/2023	5/30/24	920.000	(0.477)	LYMPH # (0.80-3.00)
05/25/2023	Pros Rx 81 Pros LN GTV2	11/23/22	1,760.000	06/06/2023 to 08/11/2023	9/19/24	800.000	(0.545)	Abs Lymph Auto (0.8-2.8)
05/19/2023	Pros Rx 81 Prosvslnsib25,20	4/20/22	1,400.000	05/25/2023 to 08/03/2023	10/28/24	800.000	(0.429)	Lymphocytes Absolute (0-3) / LYMPH # (1.2-4.8)
03/10/2023	Pros Rx 81 Prossvln3pshr	6/15/21	1,400.000	03/23/2023 to 05/30/2023	12/20/23	1,100.000	(0.214)	LYMPH # (1.2-4.8)
02/17/2023	Pros Rx 81 Prossvln3pshr	10/7/19	1,220.000	03/07/2023 to 05/10/2023	5/31/23	400.000	(0.672)	LYMPH # (1.2-4.8)
		Mean	1,889			828	(0.542)	
		Median	1,900.000			800.000	(0.550)	

PSA Velocity Post-Surgery, Radiation & Immunotherapies



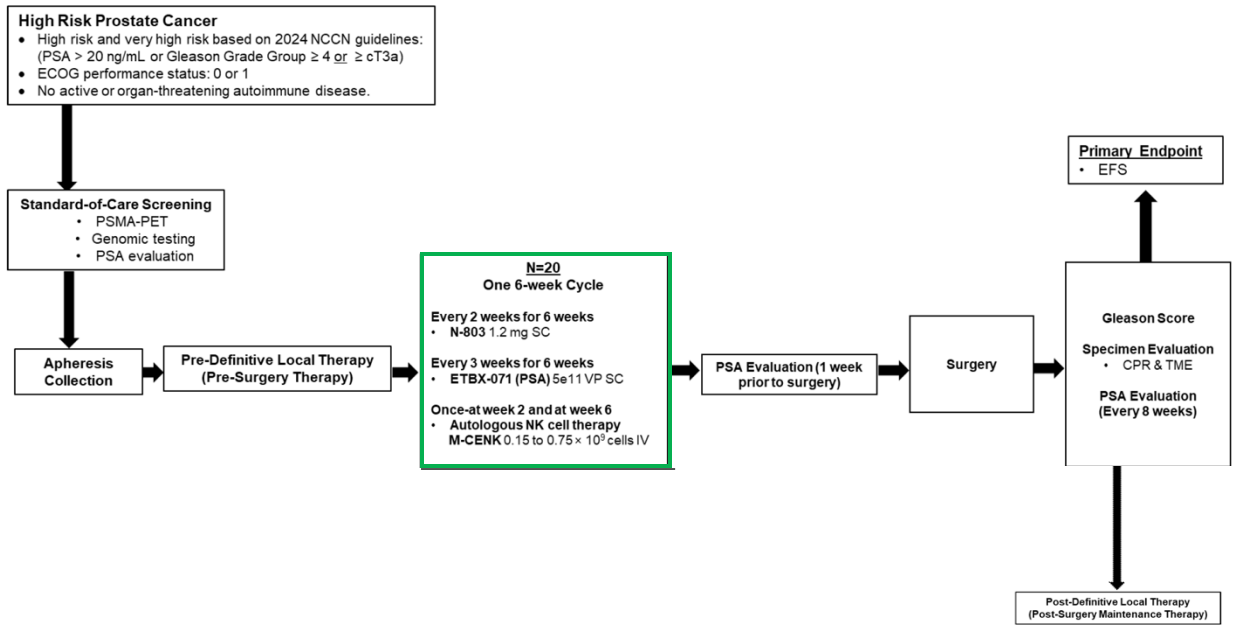
Planned Clinical Trials in Prostate Cancer
ResQ110A-PROS: High-Risk Prostate Cancer Pre-Prostatectomy

N-803, ETBX-071, M-CENK — ImmunityBio, Inc.
Clinical Trial Protocol: ResQ110A-PROS Version 1

OPEN-LABEL, PHASE 2 CLINICAL TRIAL OF PRE-SURGERY AND POST-SURGERY IMMUNOTHERAPY WITH N-803, ETBX-071, AND M-CENK IN COMBINATION WITH SURGERY FOR PARTICIPANTS WITH HIGH-RISK PROSTATE CANCER PRE-PROSTATECTOMY

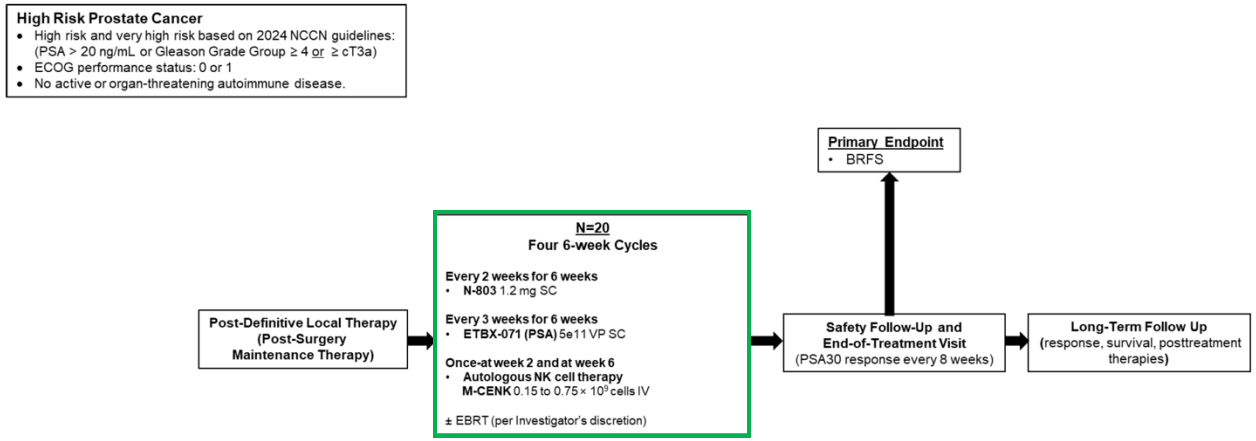
Pre-Surgery Neoadjuvant

Figure 7: Study Schema, Pre-Surgery Local Therapy



Post-Surgery Adjuvant

Figure 8: Study Schema, Post-Surgery Local Therapy



Planned Clinical Trials in Prostate Cancer

ResQ110B-PROS: High-Risk Prostate Cancer Pre-Radiation and Post-Radiation Immunotherapy

N-803, ETBX-071, M-CENK — ImmunityBio, Inc.
Clinical Trial Protocol: ResQ110B-PROS Version 1

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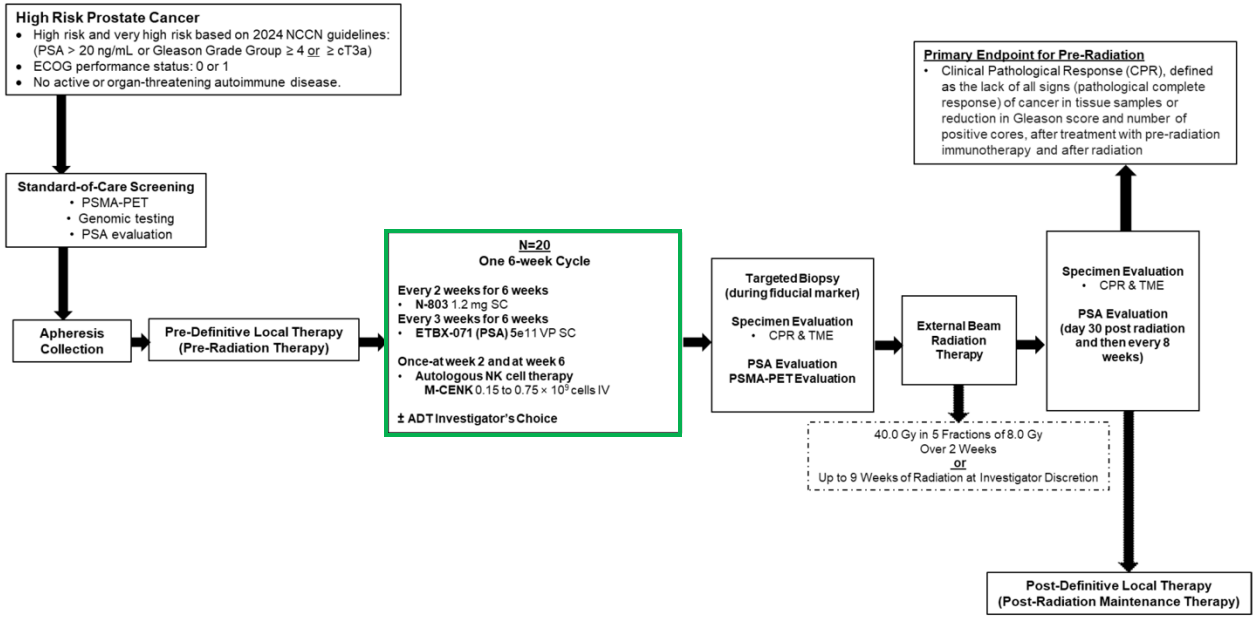
Pre-Radiation Neoadjuvant

Figure 7: Study Schema, Pre-Radiation Local Therapy



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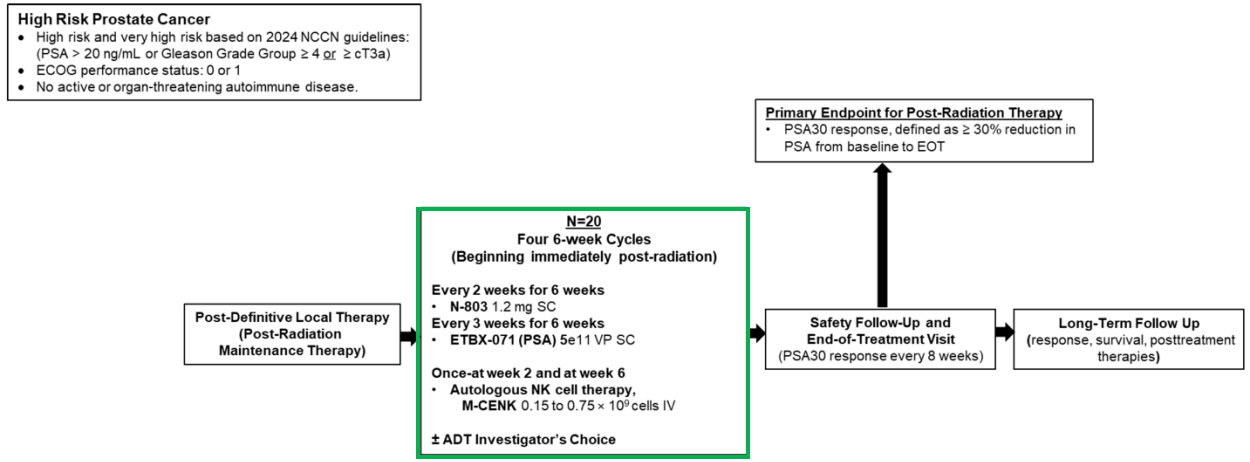

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- Colon Cancer Experience
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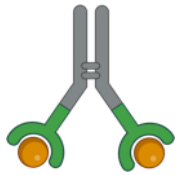

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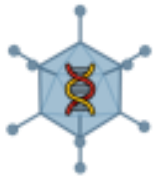

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Phase 2

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Off-The-Shelf
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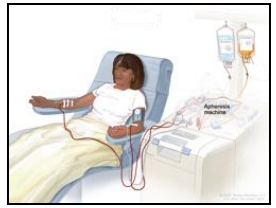

NK, iNKT &
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M-ceNK

Phase 2

Ex-Vivo Lymphocyte Rescue

Lynch Syndrome – Prevention of Colon Cancer and Endometrial Cancer

NIH NATIONAL CANCER INSTITUTE
Division of Cancer Prevention

Investigator Initiated Trial
Clinical Trials: NCT05419011

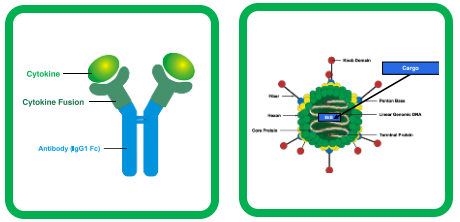
INT21-05-01
Protocol Version 7.0, 02/09/2023

COVER PAGE
DCP Protocol #: INT21-05-01

Local Protocol #: NCI21-05-01

A PHASE IIB CLINICAL TRIAL OF THE MULTITARGETED RECOMBINANT ADENOVIRUS 5 (CEA/MUC1/BRACHYURY) VACCINES (TRI-AD5) AND IL-15 SUPERAGONIST N-803 IN LYNCH SYNDROME

NIH NATIONAL CANCER INSTITUTE
Northwestern University
KU MEDICAL CENTER The University of Kansas
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
MAYO CLINIC
UNIVERSITY OF MICHIGAN
UCSF
University of Colorado Anschutz Medical Campus
Cleveland Clinic
THE UNIVERSITY OF ARIZONA Cancer Center
UNIVERSIDAD DE PUERTO RICO 1903
Fox Chase Cancer Center Temple Health
Dana-Farber Cancer Institute
City of Hope
Carbone Cancer Center UNIVERSITY OF WISCONSIN SCHOOL OF MEDICINE AND PUBLIC HEALTH
THE OHIO STATE UNIVERSITY WEXNER MEDICAL CENTER
THE UNIVERSITY OF CHICAGO



IL-15 Superagonist **hAd5**

Investigational Agents:
N-803 (Anktiva) + hAd5 CEA, MUC1, Brachyury

First large-scale multi-center clinical trial for the prevention of colon cancer by activating innate NK cells (with Anktiva) and inducing tumor specific CD4+, CD8+, and memory T cells (with hAd5 CEA, MUC1, Brachyury).

As of Jan 2025: Total enrollment is 101 subjects to date

www.impactjournals.com/oncotarget/ Oncotarget, Vol. 6, No. 31

The generation and analyses of a novel combination of recombinant adenovirus vaccines targeting three tumor antigens as an immunotherapeutic

Elizabeth S. Gabitzsch[1], Kwong Yok Tsang[2], Claudia Palena[2], Justin M. David[2], Massimo Fantini[2], Anna Kwilas[2], Adrian E. Rice[1], Yvette Latchman[1], James W. Hodge[2], James L. Gulley[3], Ravi A. Madan[3], Christopher R. Heery[2], Joseph P. Balint Jr.[1], Frank R. Jones[1,*], Jeffrey Schlom[2,*]

[1]Etubics Corporation, Seattle, WA, USA

[2]Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

[3]Genitourinary Malignancies Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

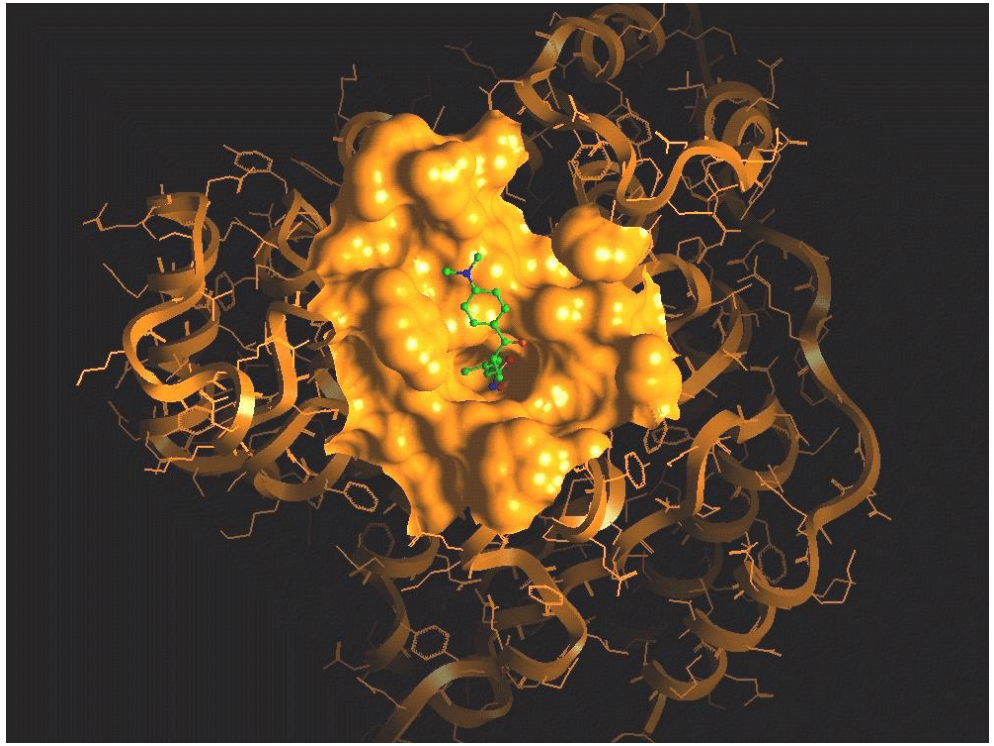
[*]These authors have contributed equally to this work

Correspondence to:
Jeffrey Schlom, **e-mail:** js141c@nih.gov

Keywords: *cancer vaccines, adenovirus vaccines, tumor antigens, immunotherapy, brachyury*

Received: *June 18, 2015* ***Accepted:*** *August 24, 2015* ***Published:*** *September 07, 2015*

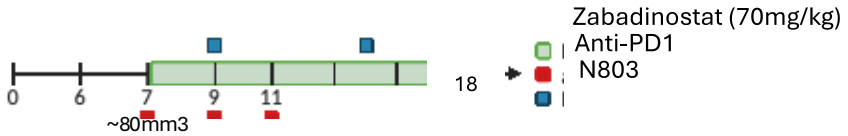
Zabadinostat: Potentially Best-in-Class HDAC Inhibitor

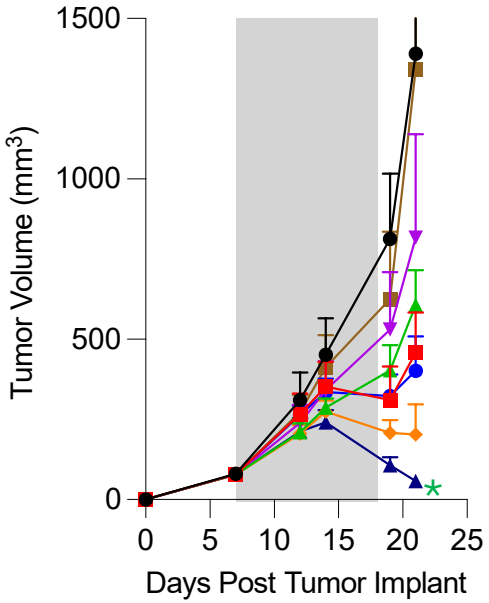


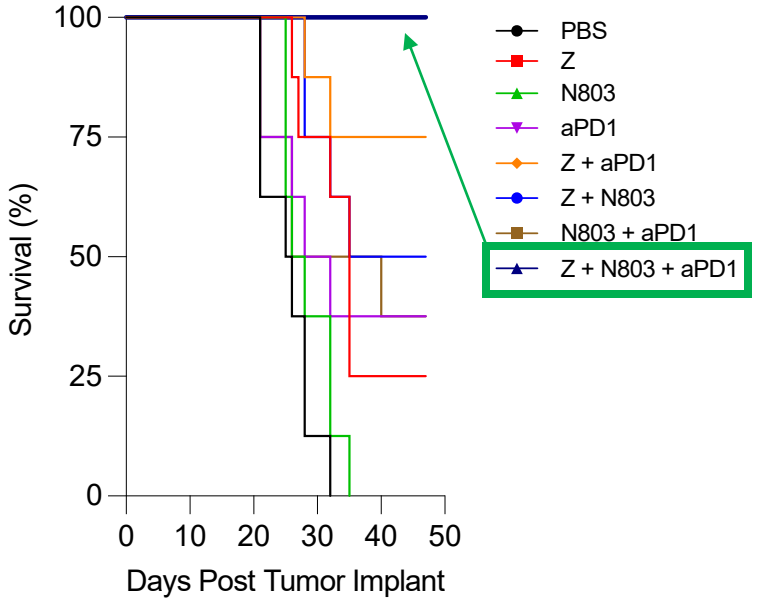
3D Model of zabadinostat (CXD101) in Complex with HDAC Class I

- Orally available, small molecule of benzamide chemical class; targeting HDAC1/2/3 (Class I specific; no activity against HDAC class II)
- MoA: Epigenetically upregulates genes involved in antigen presentation and activity of natural killer cells. Attracts CD8+ cytotoxic T-cells to tumours and killing cancer through the immune system
- Indications:
  - Microsatellite-Stable Colorectal Cancer (MSS CRC) Phase II,
  - Hepatocellular Carcinoma (HCC) Phase II,
  - Peripheral T-Cell Lymphoma (PTCL)
- Potential use as molecular adjuvant for vaccines (universal influenza)

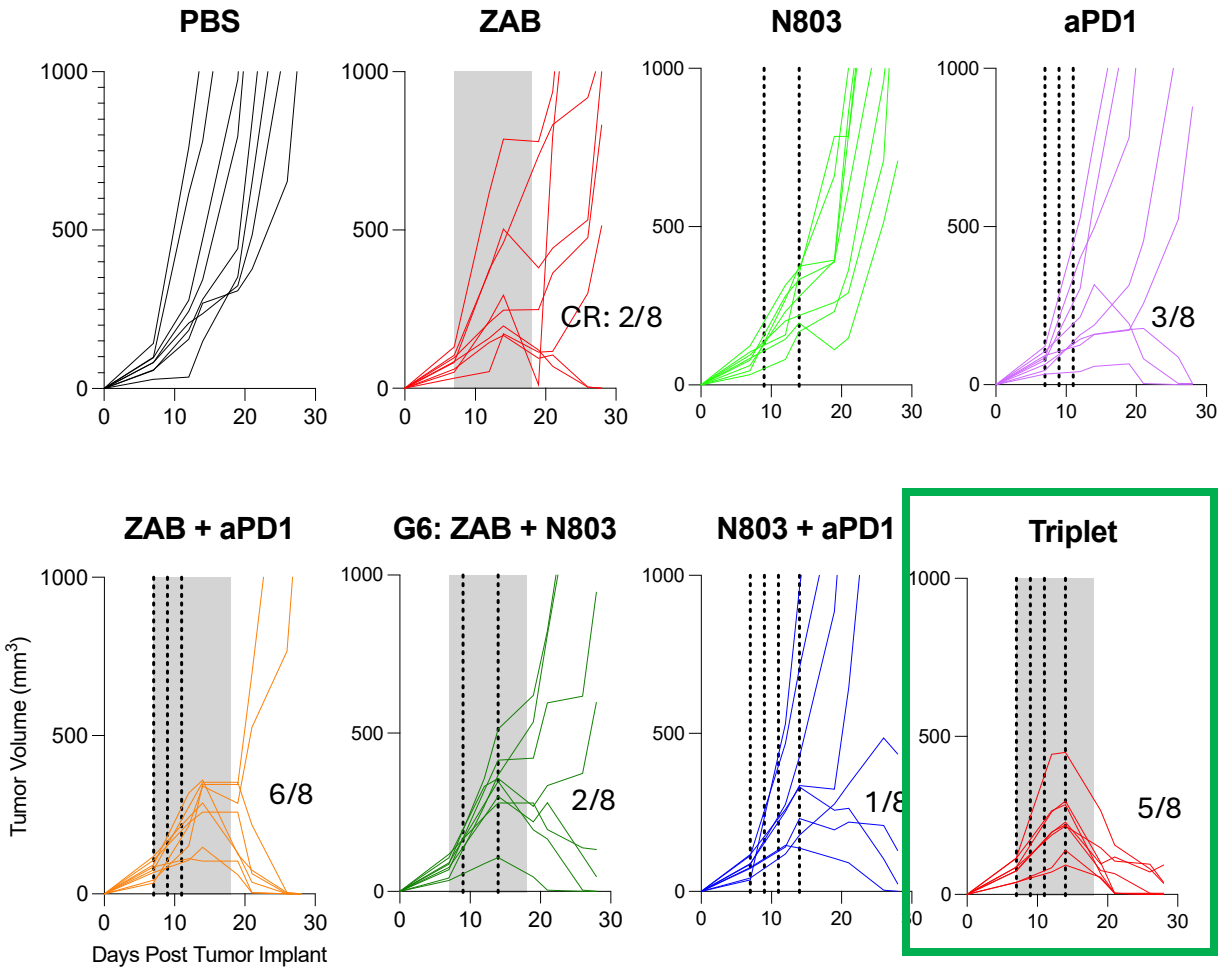
High Efficacy of Triplet Combination in Colon Cancer







CT26 (Colon Cancer Cell Line)



ResQ201A: Randomized 2nd Line NSCLC ANKTIVA + Tislelizumab

ResQ201A: Clinical Trial Of N-803 Plus TISLELIZUMAB And DOCETAXEL Versus DOCETAXEL Monotherapy In Participants With Advanced Or Metastatic Non-Small Cell Lung Cancer

ClinicalTrials.gov ID NCT06745908

Sponsor ImmunityBio, Inc.

Information provided by ImmunityBio, Inc. (Responsible Party)

Last Update Posted 2025-03-18

Phase 3, N=460

ANKTIVA + TISLELIZUMAB

Versus

Docetaxel

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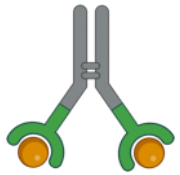

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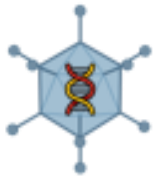

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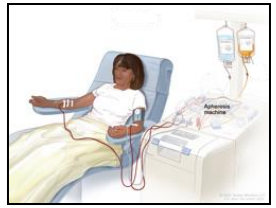


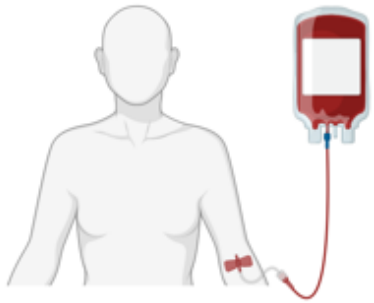
NK, iNKT &
Dendritic Cell Pathway

M-ceNK

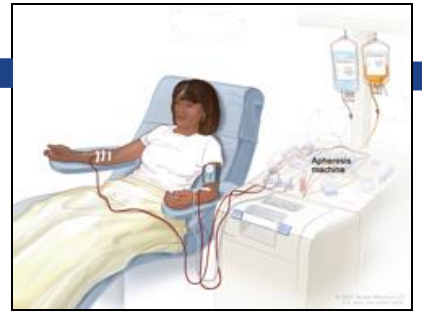
Phase 2

Ex-Vivo Lymphocyte Rescue

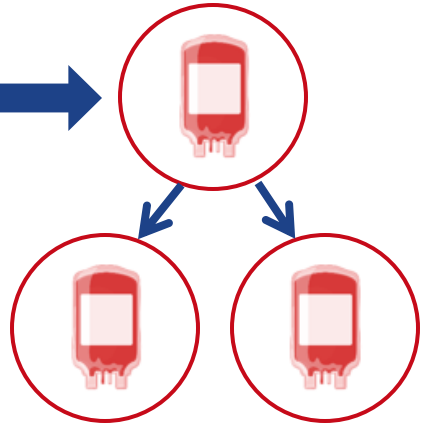
Apheresis Program: Autologous / Allogenic Cellular Vaccine Therapy Program



Apheresis Trifecta
NANT Cancer Vaccine



Single Apheresis



Non Cryopreserved
(Fresh) Apheresis

T Cell Pathway

Gamma Delta T Cell

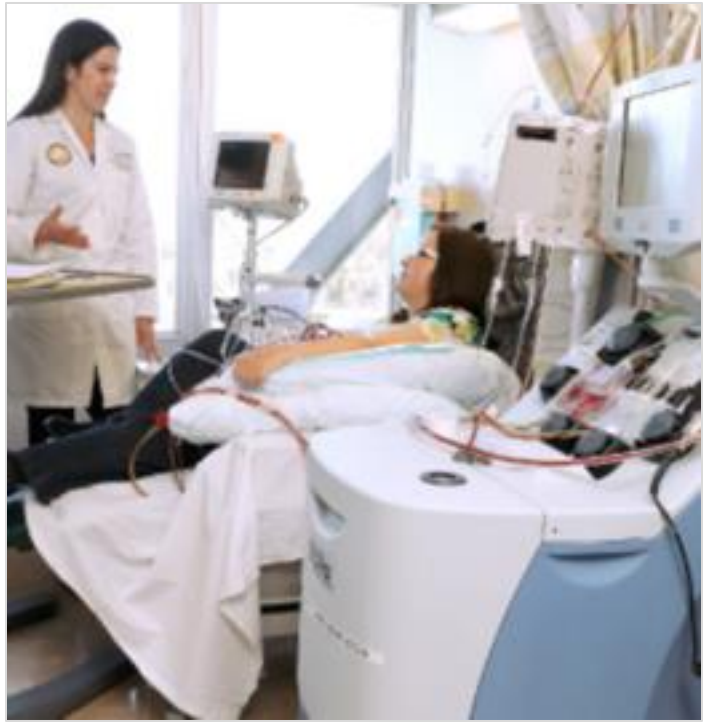
NK, iNKT & Dendritic Cell Pathway

M-ceNK
iNKT

Phase 2

Memory-Like Cytokine Enhanced Natural Killer (M-ceNK) Cells from Peripheral Blood First-in-Human Clinical Trials

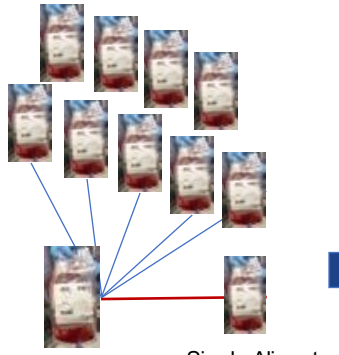
Day 1



Autologous Apheresis
Patient White Cell Collection

Day 1

Autologous
Apheresis
White Cells



Single Aliquot
For Enrichment

Aliquot One Bag into
10 Lots for
Cryopreservation

Day 17

Concentrate
0.3 – 1.0 x 10^9 NK Cells

Day 17

Autologous Cytokine
Enhanced Natural Killer Cells
for Transfusion
0.3 – 1.0 x 10^9 NK Cells


TSCD-
BIOHAZARD
For research use only
FOR AUTOLOGOUS USE ONLY
MNC APHERESIS
Do Not Use Leukoreduction Filters
Do Not Irradiate
For Further Processing
Chan Soon-Shiong Institute of Medicine
2040 E. Mariposa Avenue
El Segundo, CA 90245
ImmunityBio, Inc.
2040 E. Mariposa Avenue
El Segundo, CA 90245
Date of Birth: 21 MAR 1963
Recipient ID: MK2022-070-519
11 DEC 2024 13:38 PST
11 DEC 2024 21:38 UTC)
09 DEC 2024 13:38 PST
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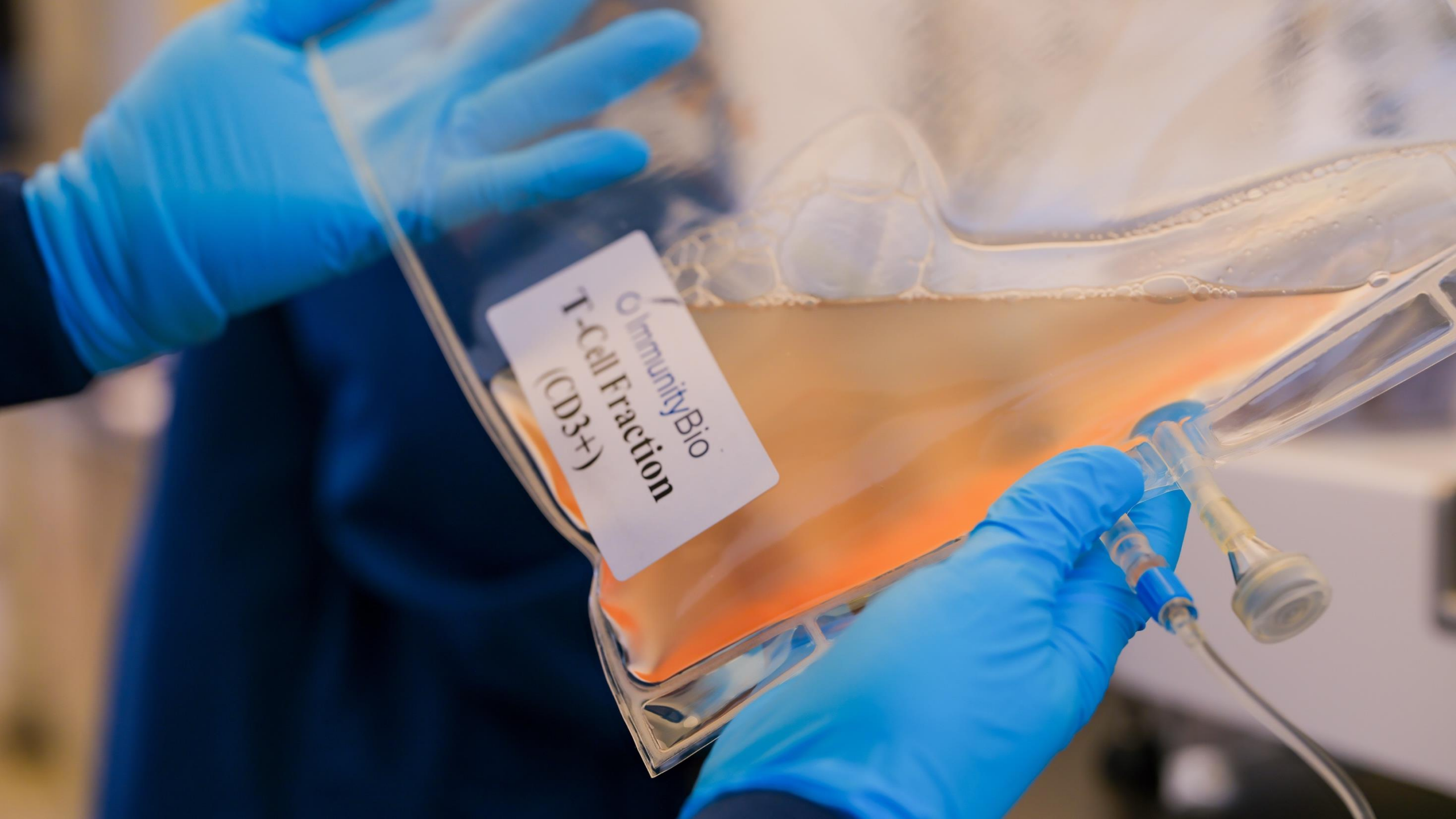
ImmunityBio
T-Cell Fraction
(CD3+)

Fireside Chats

Dr. Carlos Cardo-Cordon & Dr. Timothy Henrich

- Long-COVID Persistence
- Oncogenic Potential of SARS-CoV-2

Dr. Carlos Cardo-Cordon

Dr. Timothy Henrich

Dr. Timothy Henrich – Long COVID

nature immunology

Letter

https://doi.org/10.1038/s41590-023-01724-6

Long COVID manifests with T cell dysregulation, inflammation and an uncoordinated adaptive immune response to SARS-CoV-2

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Check for updates

Kailin Yin[1,2,9], Michael J. Peluso[3,9], Xiaoyu Luo[1,2], Reuben Thomas[1], Min-Gyoung Shin[1], Jason Neidleman[1,2], Alicer Andrew[1,2], Kyrlia C. Young[1,2], Tongcui Ma[1,2], Rebecca Hoh[3], Khamal Anglin[3], Beatrice Huang[3], Urania Argueta[3], Monica Lopez[3], Daisy Valdivieso[3], Kofi Asare[3], Tyler-Marie Deveau[4], Sadie E. Munter[4], Rania Ibrahim[3], Ludger Ständker[5], Scott Lu[6], Sarah A. Goldberg[6], Sulggi A. Lee[7], Kara L. Lynch[8], J. Daniel Kelly[6], Jeffrey N. Martin[6], Jan Münch[5], Steven G. Deeks[3], Timothy J. Henrich[4] ✉ & Nadia R. Roan[1,2] ✉

nature immunology

Letter

https://doi.org/10.1038/s41590-023-01724-6

Long COVID manifests with T cell dysregulation, inflammation and an uncoordinated adaptive immune response to SARS-CoV-2

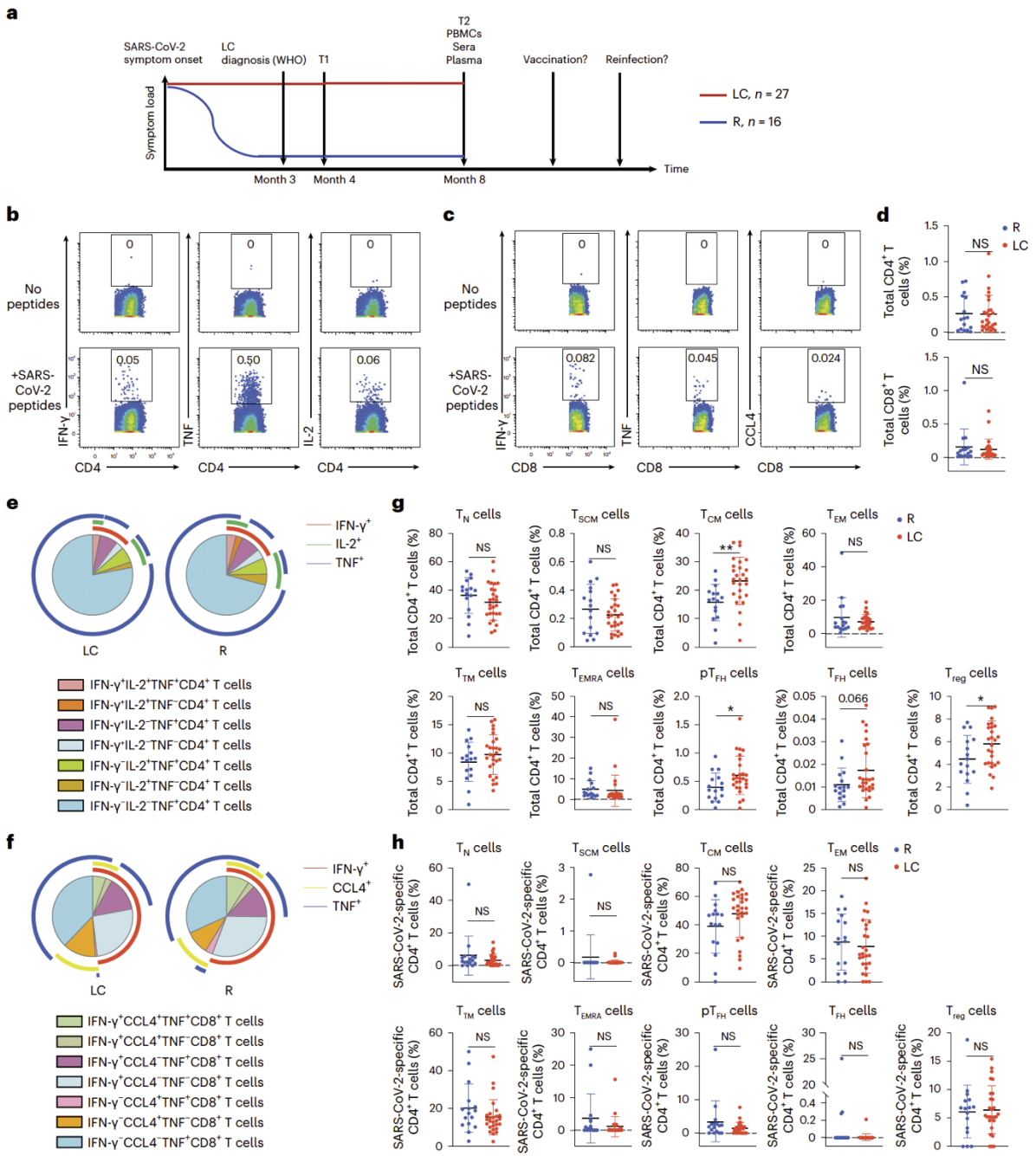

Fig. 1 | CD4+ T cell phenotypes are perturbed in individuals with LC

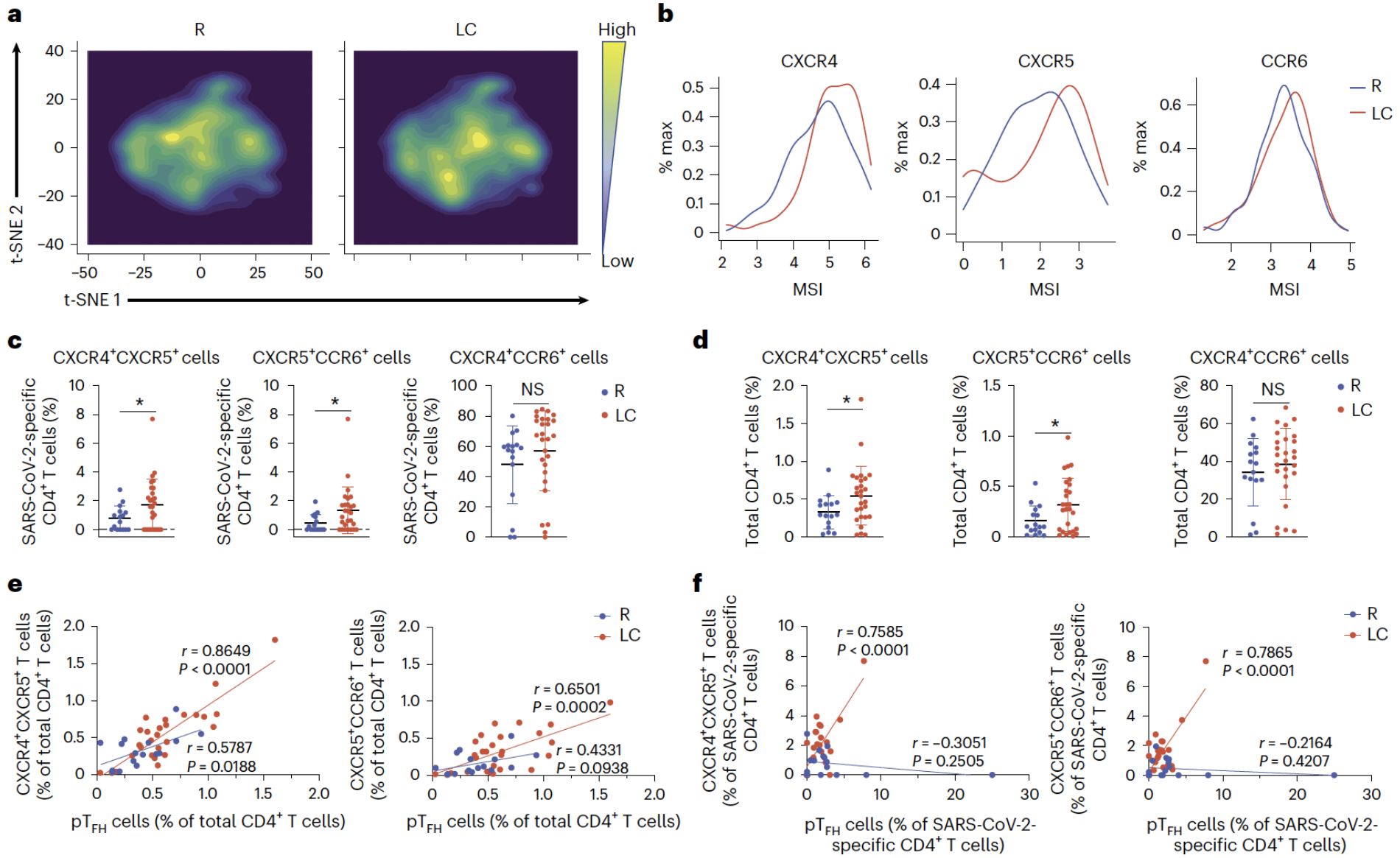

Fig. 2 | SARS-CoV-2-specific CD4+ T cells from individuals with LC preferentially express homing receptors associated with migration to inflamed tissues

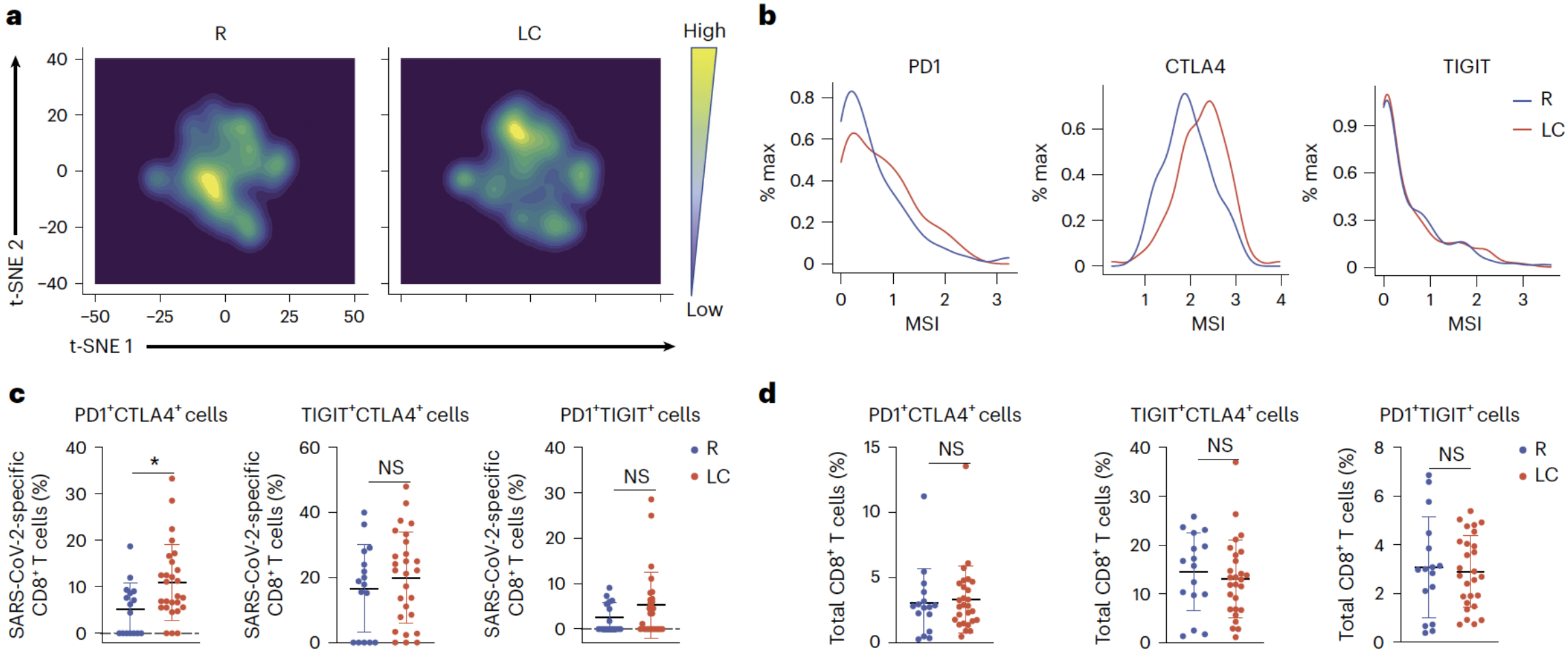

Fig. 3 | SARS-CoV-2-specific CD8⁺ T cells from individuals with LC preferentially express the exhaustion markers PD1 and CTLA4. a, t-SNE contour depiction of SARS-CoV-2-specific CD8⁺ T cells from LC and R individuals. **b**, Expression of PD1, CTLA4 and TIGIT on SARS-CoV-2-specific CD8⁺ T cells from LC and R individuals. **c**,**d**, Percentages of PD1⁺CTLA4⁺CD8⁺, TIGIT⁺CTLA4⁺CD8⁺ and PD1⁺TIGIT⁺CD8⁺ SARS-CoV-2-specific (**c**) and total (**d**) CD8⁺ T cells in LC and R individuals. *$P < 0.05$ (two-sided Student's t test). Horizontal bars indicate mean, error bars indicate s.d. and dots represent individuals, with $n = 27$ LC and $n = 16$ R (**c**,**d**).

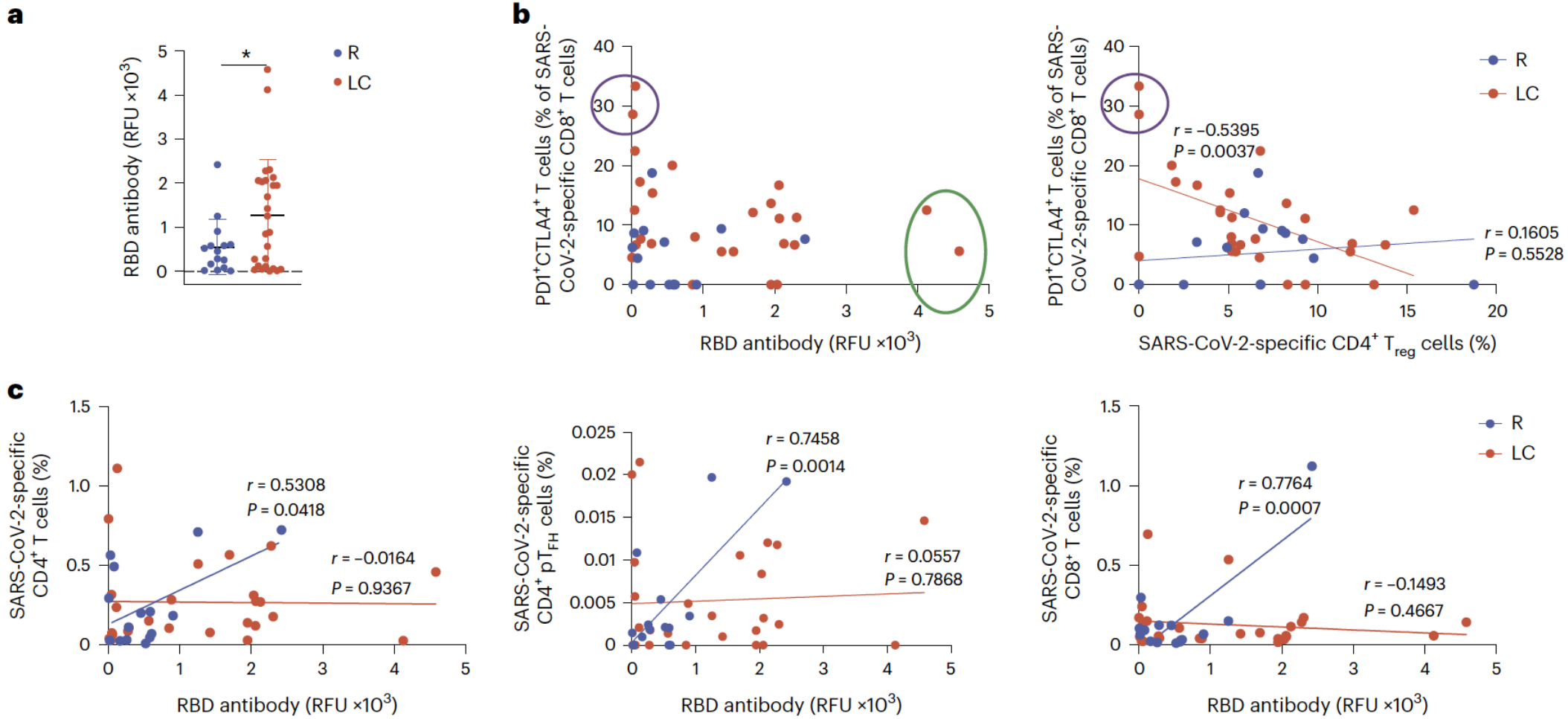

Fig. 4 | Humoral and cellular immunity are discoordinated in individuals with LC. a, Total SARS-CoV-2 RBD-specific antibody levels in LC and R individuals. $^*P < 0.05$ (two-sided Student's *t* test). Horizontal bars indicate mean, error bars indicate s.d. and dots represent individuals. LC ($n = 26$), R ($n = 15$). **b**, Plot depicting the percentage of $PD1^+CTLA4^+$ cells among SARS-CoV-2-specific $CD8^+$ T cells and RBD antibody levels in LC and R individuals. Individuals with the highest humoral response are circled in green, and those with the highest percentages of $PD1^+CTLA4^+$ SARS-CoV-2-specific $CD8^+$ T cells are circled in purple (left). **c**, Plot depicting the association between RBD antibody levels and the percentages of SARS-CoV-2-specific $CD4^+$ T cells, SARS-CoV-2-specific $CD4^+$ pT_{FH} cells (middle) and SARS-CoV-2-specific $CD8^+$ T cells (right) in LC and R individuals. Data were analyzed by Pearson correlation coefficient and two-tailed unpaired *t* tests.

Pathophysiology of PASC through Molecular Profiling of Autopsies and Biopsy Samples. Defining the Potential Tumorigenic Effects of SARS-CoV-2:

Generating an Atlas of Viral Persistence, a Test for Risk Stratification and Therapeutic intervention, and Defining the Potential Tumorigenesis and Clinical Implications of SARS-CoV-2.

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Icahn School of Medicine at Mount Sinai
One Gustave L. Levy Place
New York, NY 10029
Phone: 212-241-8762
E-mail: carlos.cordon-cardo@mssm.edu

Pathophysiology of PASC through Molecular Profiling of Autopsies

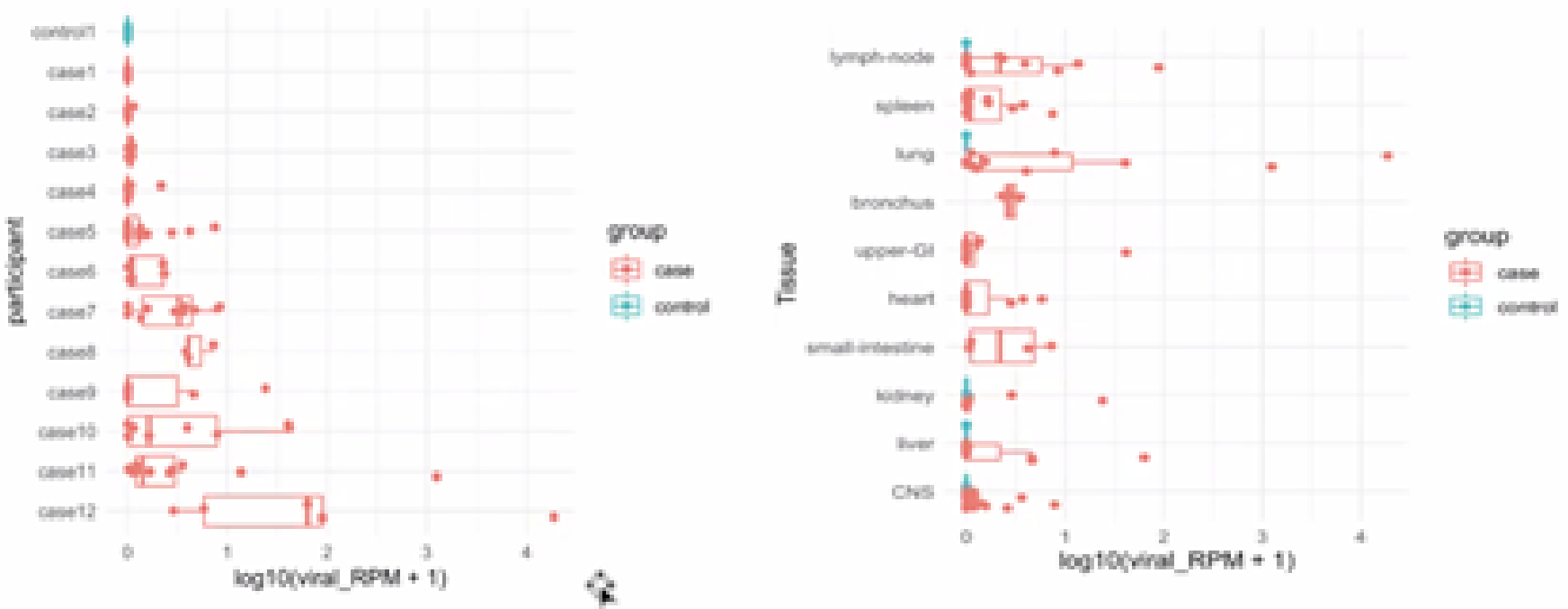
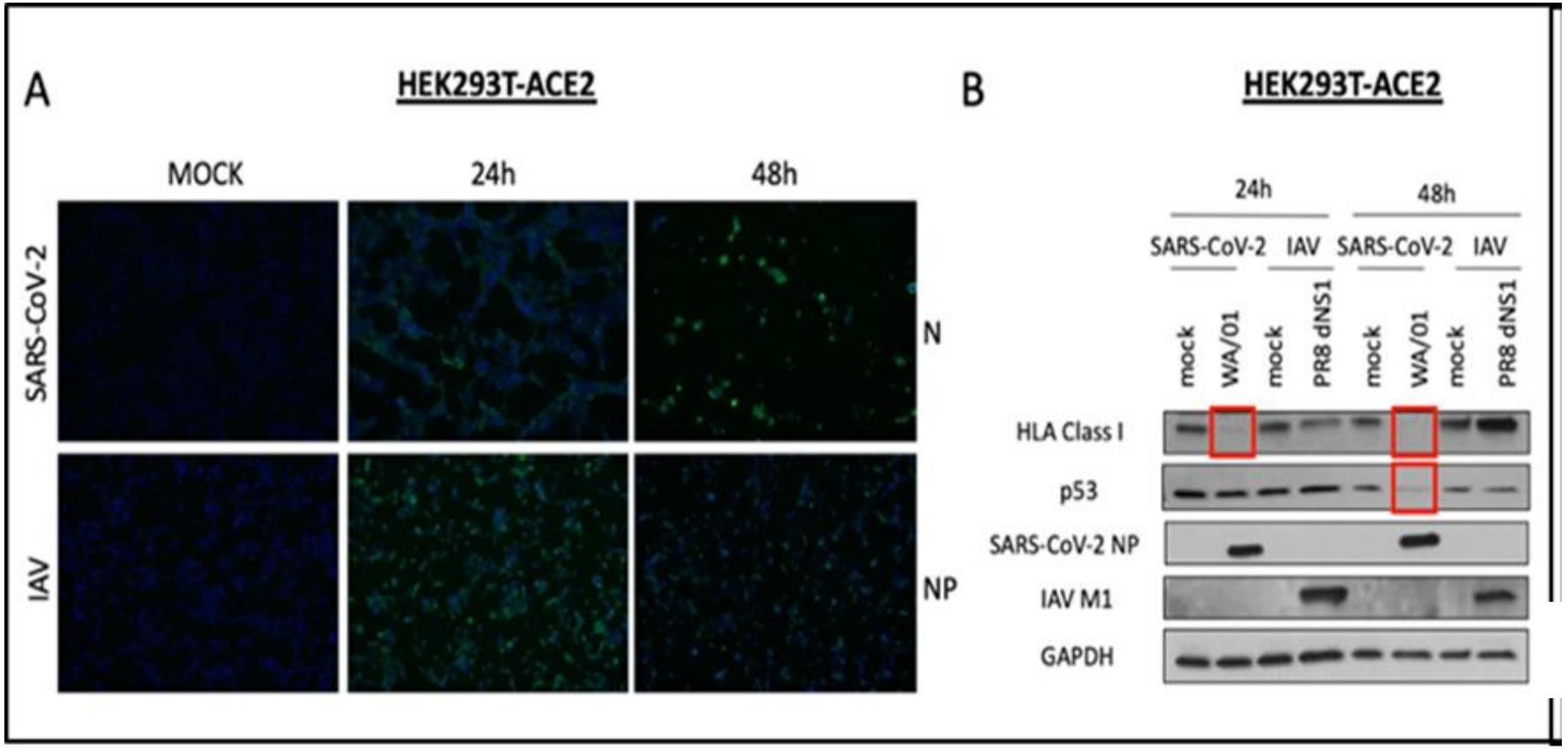


Figure 1. Bulk RNA sequencing of tissues from rapid COVID-19 autopsies revealed the presence of viral RNA across organs. Fresh-frozen tissue was obtained at the time of autopsy for patients affected by acute and post-acute COVID-19. Bulk RNA-sequencing revealed moderate to high viral RNA mapping to SARS-CoV-2 reference genome in lung, lymph-node and small intestine; and low to undetectable in upper-GI and kidney.

Pathophysiology of PASC through Molecular Profiling of Autopsies



SARS-CoV-2 (WA1

PR8-ΔNS1 MC

Pathophysiology of PASC through Molecular Profiling of Autopsies

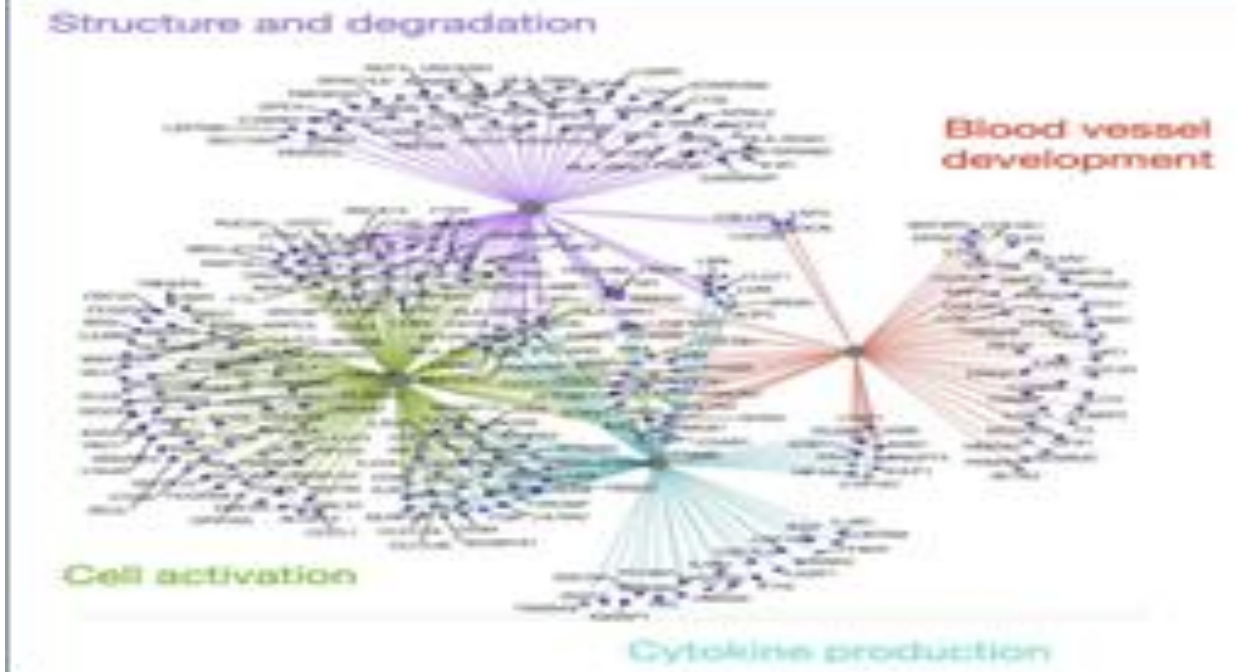
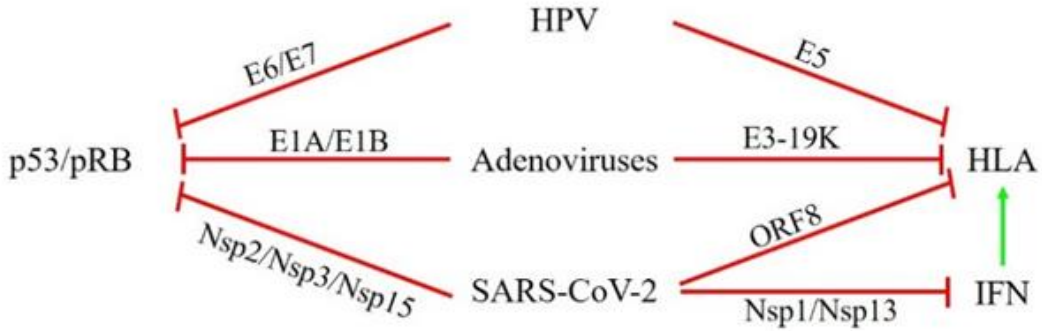
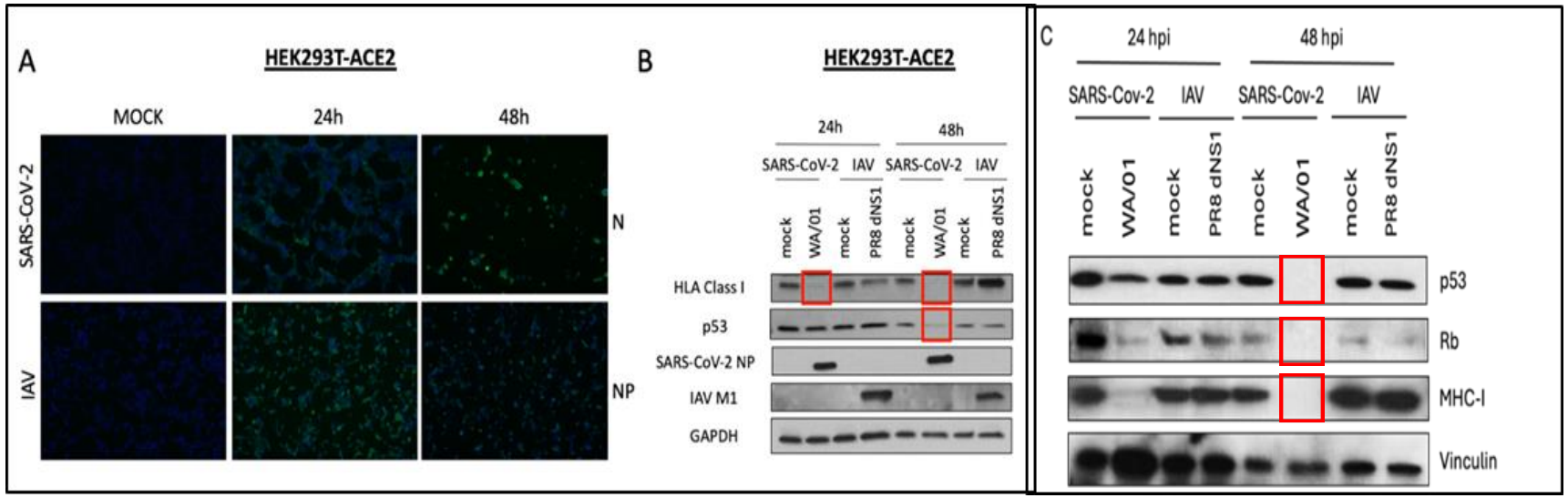


Figure 2: Preliminary data showing pathway analysis of infected vs. uninfected tissues in a COVID-19 patient. Reads mapping to the SARS-CoV-2 genome in unenriched host tissue were detected in nasopharynx and lung, while no reads were detected in olfactory bulb, pre-frontal cortex, oropharynx, salivary gland, tongue, heart, liver or kidney. Differential gene expression analysis between infected and uninfected tissues resulted in 4,376 differentially expressed genes (FDR <0.05). Visualization of Gene Set Enrichment Analysis showing the top 4 most significant pathways.

Pathophysiology of PASC through Molecular Profiling of Autopsies



MHC-I, p53, and Rb Downregulation by SARS-CoV-2



SARS-CoV-2 (WA1) MOI=0.1
PR8-ΔNS1 MOI=0.1

Fireside Chats

Dr. Krishnansu Tewari
Dr. Lennie Sender
Dr. Patrick Soon-Shiong

- Ovarian Cancer Trial
- Ovarian Cancer Patient

Dr. Krishnansu Tewari

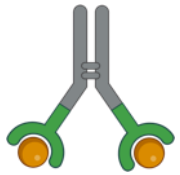
Dr. Lennie Sender

Dr. Patrick Soon-Shiong

ImmunityBio Cancer BioShield

The Cancer BioShield

Fusion Proteins



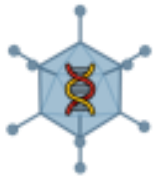
NK & T Cell Activator
Memory T Cell

ANKTIVA

FDA Approved April 2024

In-Vivo Lymphocyte Rescue

DNA Vaccine



Adenovirus (hAd5)

hAd5 CEA, MUC1, Brachyury

hAd5 PSA

hAd5 HPV

Phase 2

In-Vivo Lymphocyte Rescue

Cell Therapy

CAR-NK

Off-The-Shelf
CAR-NK

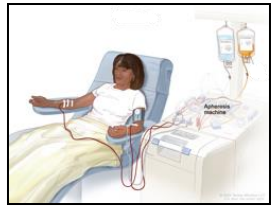
PD-L1 t-haNK

CD19 t-haNK

Phase 2

Ex-Vivo Lymphocyte Rescue

M-ceNK



NK, iNKT &
Dendritic Cell Pathway

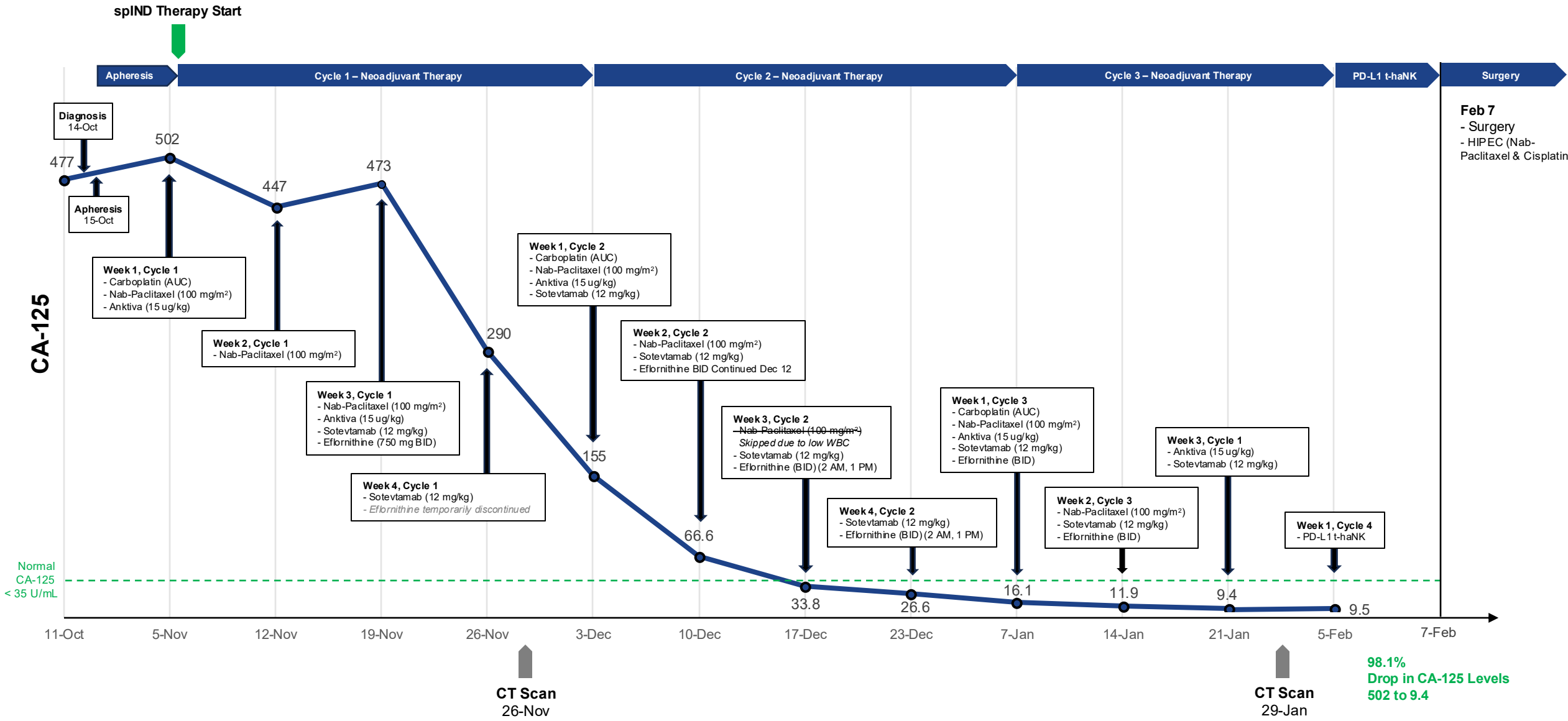
M-ceNK

Phase 2

Ex-Vivo Lymphocyte Rescue

Ovarian Cancer Stage 3C

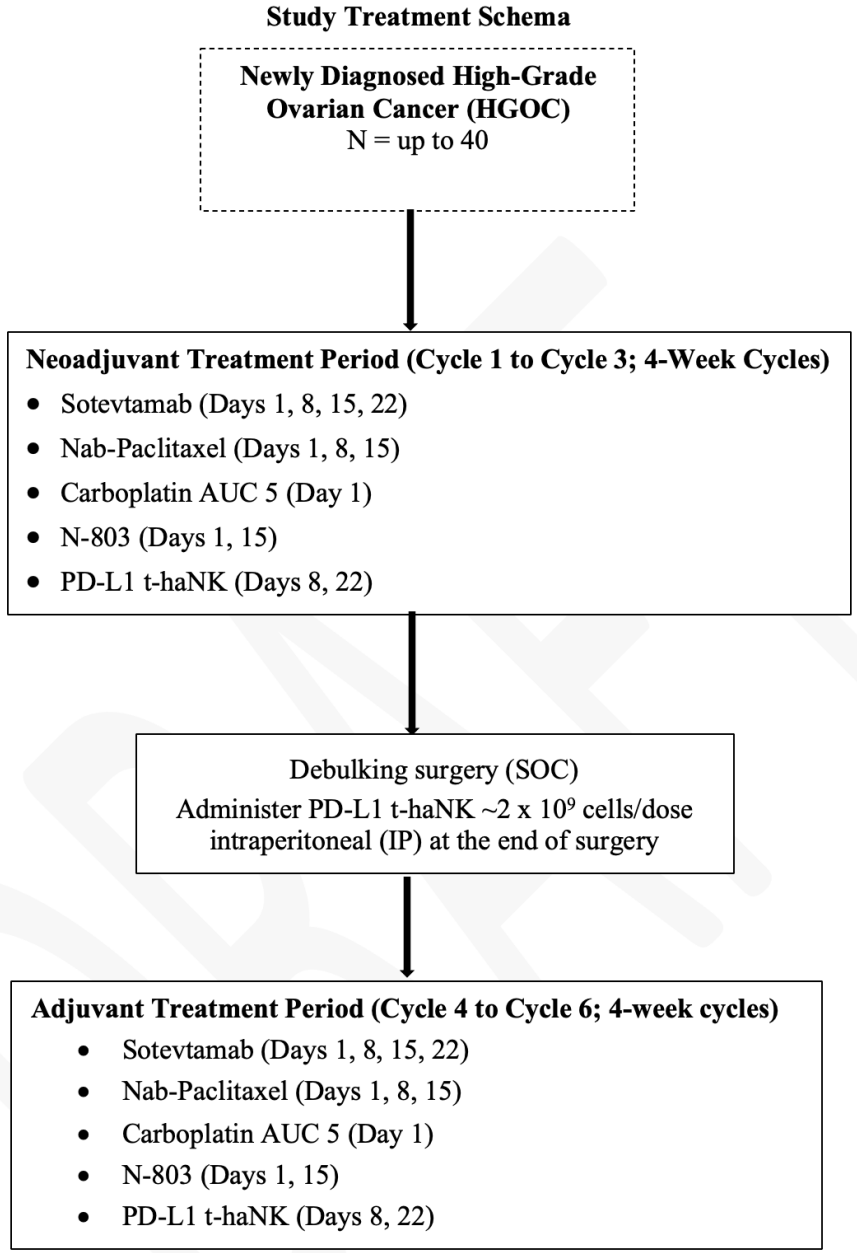
CA-125 Levels



		Neoadjuvant Treatment Start (Cycle 1)				Neoadjuvant Treatment Start (Cycle 2)				Neoadjuvant Treatment Start (Cycle 3)			PD-L1 t-haNK
	10/15 Apheresis	11/5 W1C1	11/12 W2C1	11/19 W3C1	11/26 W4C1	12/3 W1C2	12/10 W2C2	12/17 W3C2	12/23 W4C2	1/7 W1C3	1/14 W2C3	1/21 W3C3	2/5 W1C4
WBC (10^3/µL) White Blood Cell	5.77	5.74	3.26	3.06	4.41	4.47	2.77	2.44	3.14	4.70	2.59	2.78	5.39
RBC (10^6/µL) Red Blood Cell	4.87	4.92	4.52	4.06	3.72	4.06	3.63	3.56	3.47	3.88	3.67	3.53	4.02
Hgb (g/dL) Hemoglobin	14.0	14.1	13.0	11.7	10.7	11.8	10.6	10.3	10.3	11.6	11.1	10.8	12.3
HCT (%) Hematocrit	43.8	44.1	40.1	36.8	33.1	37.4	32.7	32.7	32.3	37.1	34.5	33.4	38.0
MCV (fL) Mean Corpuscular Volume	89.9	89.6	88.7	90.6	89.0	92.1	90.1	91.9	93.1	95.6	94.0	94.6	94.5
MCH (pg) Mean Corpuscular Hgb	28.7	28.7	28.8	28.8	28.8	29.1	29.2	28.9	29.7	29.9	30.2	30.6	30.6
MCHC (g/dL) Mean Corpuscular Hgb Conc.	32.0	32.0	32.4	31.8	32.3	31.6	32.4	31.5	31.9	31.3	32.2	32.3	32.4
RDW-CV (%) Red Cell Distribution Width	13.2	12.7	12.7	12.8	13.5	14.7	14.6	14.7	15.7	16.6	15.7	15.8	15.6
PLT (10^3/µL) Platelet Count	249	294	157	238	145	261	141	217	145	221	181	233	160
MPV (fL) Mean Platelet Volume	9.2	9.2	9.9	9.0	9.3	8.6	9.6	9.0	8.9	8.6	9.1	9.0	8.5
NEUT # (10^3/µL)	3.41	3.47	1.47	1.05	2.58	1.97	1.22	0.71	1.24	2.52	0.95	1.16	3.11
LYMPH # (10^3/µL)	1.86	1.83	1.48	1.76	1.51	1.96	1.34	1.51	1.44	1.74	1.36	1.41	1.83
Neutrophil-Lymphocyte Ratio (NLR)	1.83	1.90	0.99	0.60	1.71	1.01	0.91	0.47	0.86	1.45	0.70	0.82	1.70
MONO # (10^3/µL)	0.36	0.36	0.21	0.18	0.22	0.36	0.15	0.15	0.37	0.26	0.08	0.14	0.29
EO # (10^3/µL)	0.12	0.05	0.08	0.05	0.08	0.14	0.05	0.04	0.05	0.16	0.18	0.05	0.13
BASO # (10^3/µL)	0.02	0.02	0.01	0.01	0.01	0.02	0.00	0.01	0.03	0.01	0.01	0.01	0.02
IG # (10^3/µL)	0.00	0.01	0.01	0.00	0.01	0.02	0.01	0.02	0.01	0.01	0.01	0.01	0.01
NRBC (10^3/µL)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00
NEUT %	59.2	60.4	45.1	34.4	58.6	44.2	44.0	29.2	39.4	53.7	36.7	41.7	57.6
LYMPH %	32.2	31.9	45.4	57.5	34.2	43.8	48.4	61.9	45.9	37.0	52.5	50.7	34.0
MONO %	6.2	6.3	6.4	6.2	5.0	8.1	5.4	6.1	11.8	5.5	3.1	5.0	5.4
EO %	2.1	0.9	2.5	1.6	1.8	3.1	1.8	1.6	1.6	3.4	6.9	1.8	2.4
BASO %	0.3	0.3	0.3	0.3	0.2	0.4	0.0	0.4	1.0	0.2	0.4	0.4	0.4
IG %	0.0	0.2	0.3	0.0	0.2	0.4	0.4	0.8	0.3	0.2	0.4	0.4	0.2
NRBC % (% / 100 WBC)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.4	0.0
Absolute Lymphocyte Count (ALC)	1858	1831	1480	1760	1508	1958	1341	1510	1441	1739	1359	1409	1833
CA-125		502	447	473	290	155	66.6	33.8	26.6	16.1	11.9	9.4	9.5

PD-L1 t-haNK, N-803, and Sotevtamab

Clinical Trial Protocol: ResQ109A-OVN

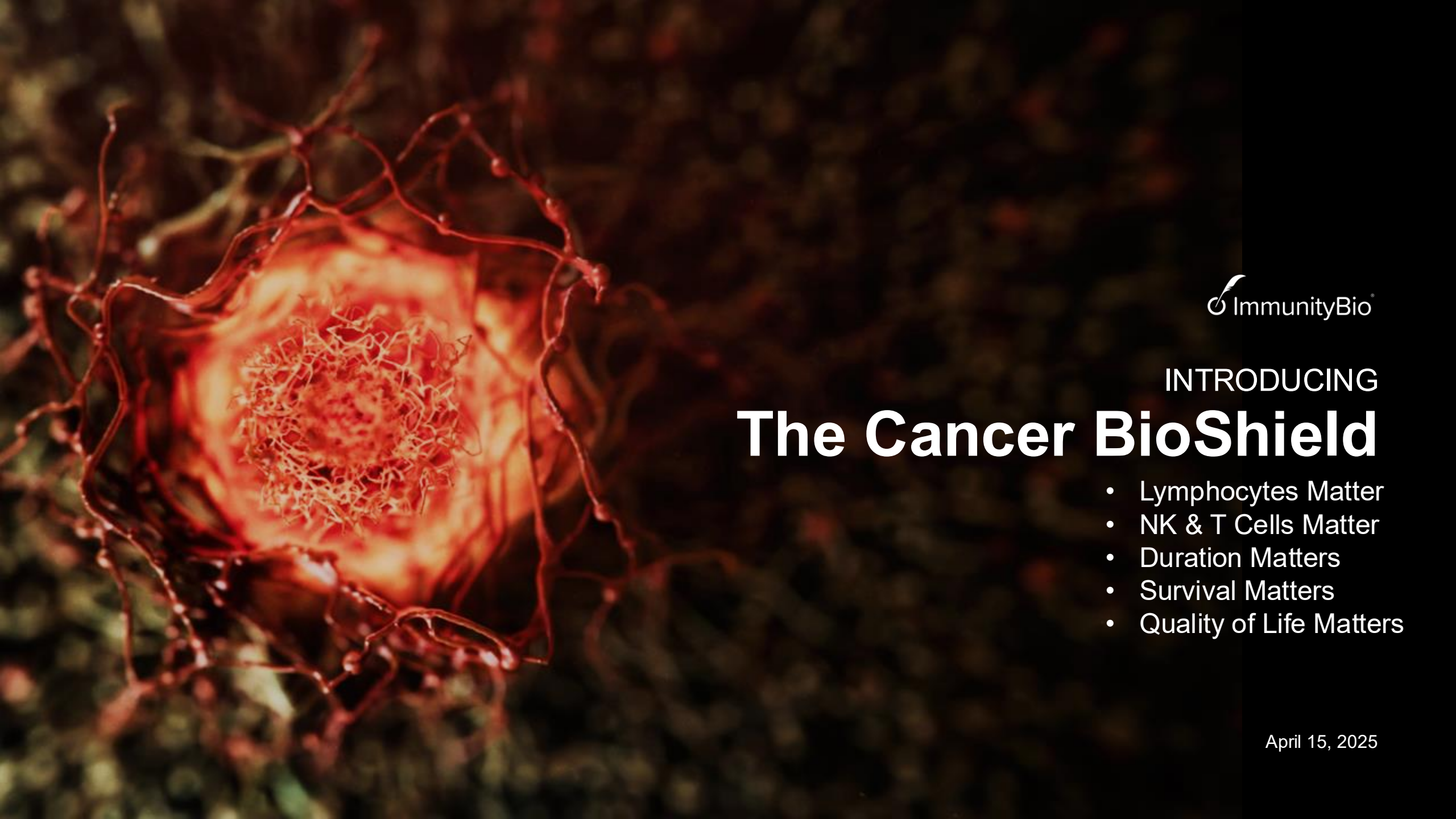


CEO’s Report

Rich Adcock
President & Chief Executive Officer

Summary & Ending Thoughts

Dr. Patrick Soon-Shiong



ImmunityBio

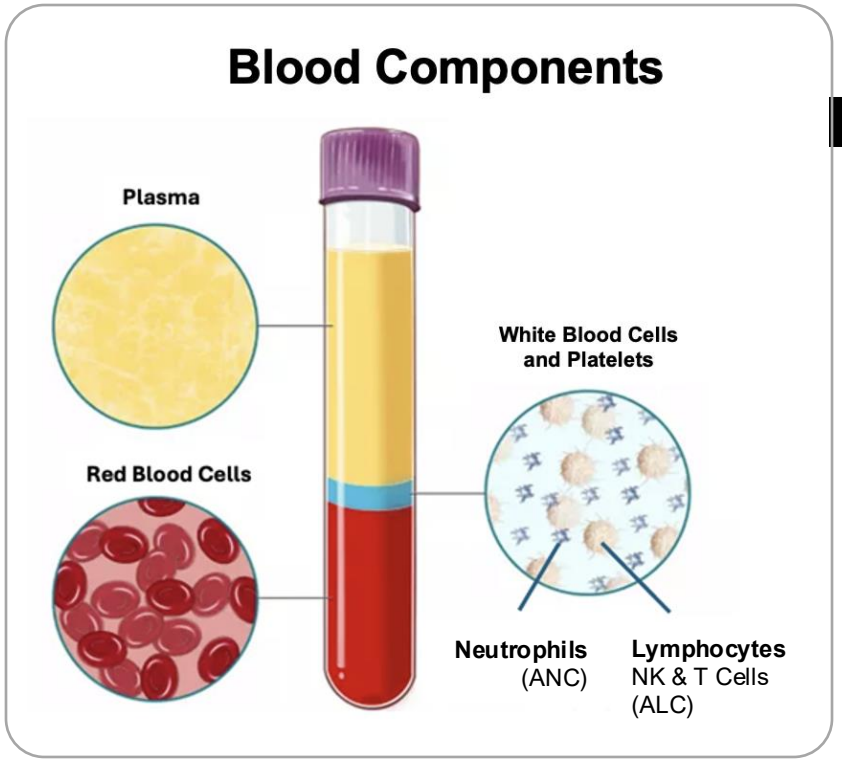
INTRODUCING

The Cancer BioShield

- Lymphocytes Matter
- NK & T Cells Matter
- Duration Matters
- Survival Matters
- Quality of Life Matters

April 15, 2025

Introducing Absolute Lymphocyte Count (ALC) and Lymphopenia



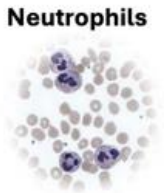
ANC: Absolute Neutrophil Count
ALC: Absolute Lymphocyte Count

Low Red Blood Count

Anemia

EPOGEN

Treats Anemia
Increases Red Blood Cell Production
1989

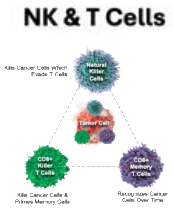


Low Neutrophil Count

Neutropenia

NEUPOGEN

Prevents Infection
Increases Neutrophil Production
1991



Low Lymphocyte Count

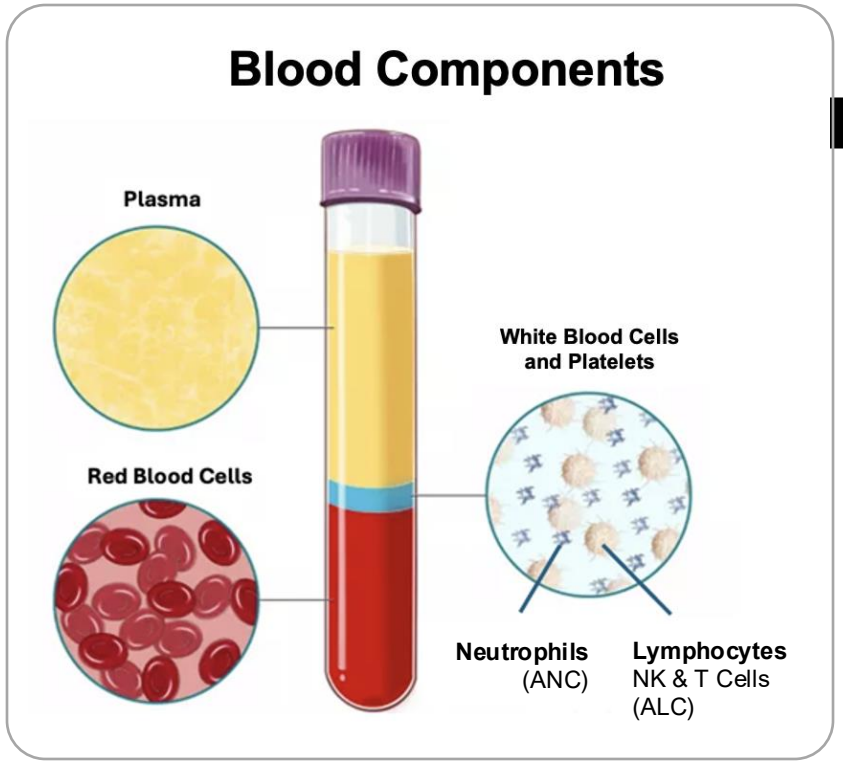
Lymphopenia

Loss of NK & T Cells
Which Kill Cancer &
Induce T Cell Memory

No Treatment for Over 50 Years
The Missing Link

Kills Cancer & Infected Cells

First Lymphocyte Rescue Agent in 50+ Years as Backbone to Chemo-Immunotherapy and Radiotherapy



ANC: Absolute Neutrophil Count
ALC: Absolute Lymphocyte Count

Red Blood Cell

Low Red Blood Count

Anemia

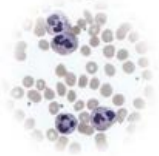
EPOGEN

Treats Anemia

Increases Red Blood Cell Production

1989

Neutrophils



Low Neutrophil Count

Neutropenia

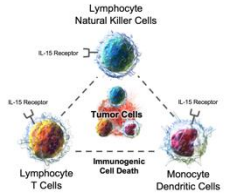
NEUPOGEN

Prevents Infection

Increases Neutrophil Production

1991

NK & T Cells



Low Lymphocyte Count

Lymphopenia

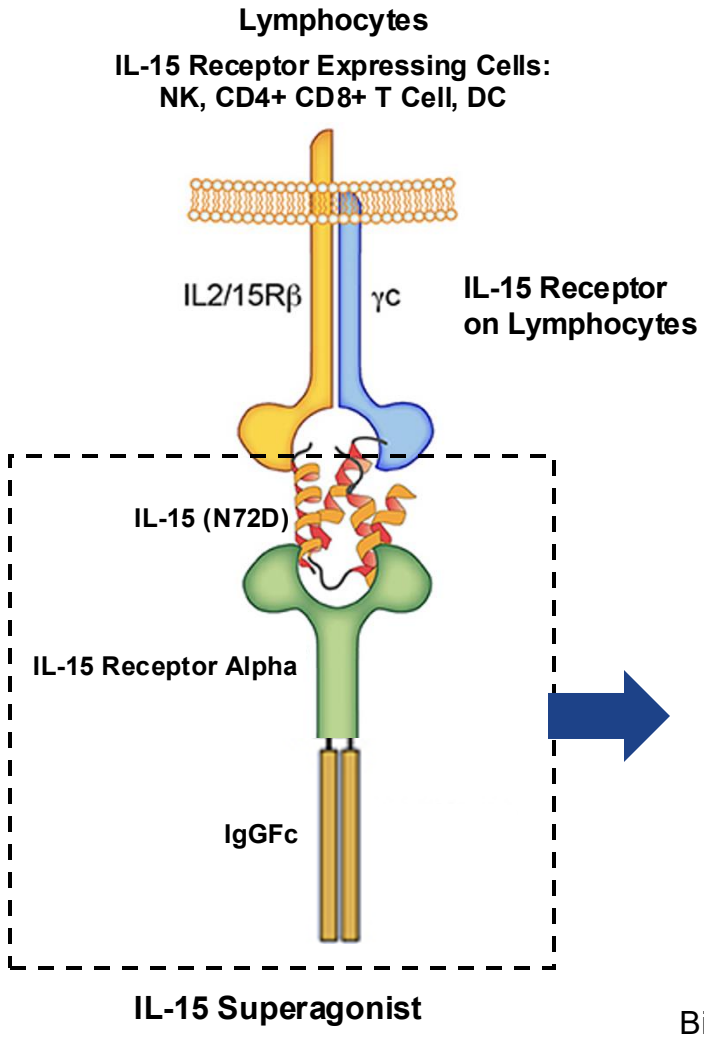
ANKTIVA

Induces Cancer Cell Death

Regenerates NK and T cells and Induces T Cell Memory

ANKTIVA Approved 2024

ANKTIVA FDA Approved Mechanism of Action April 2024

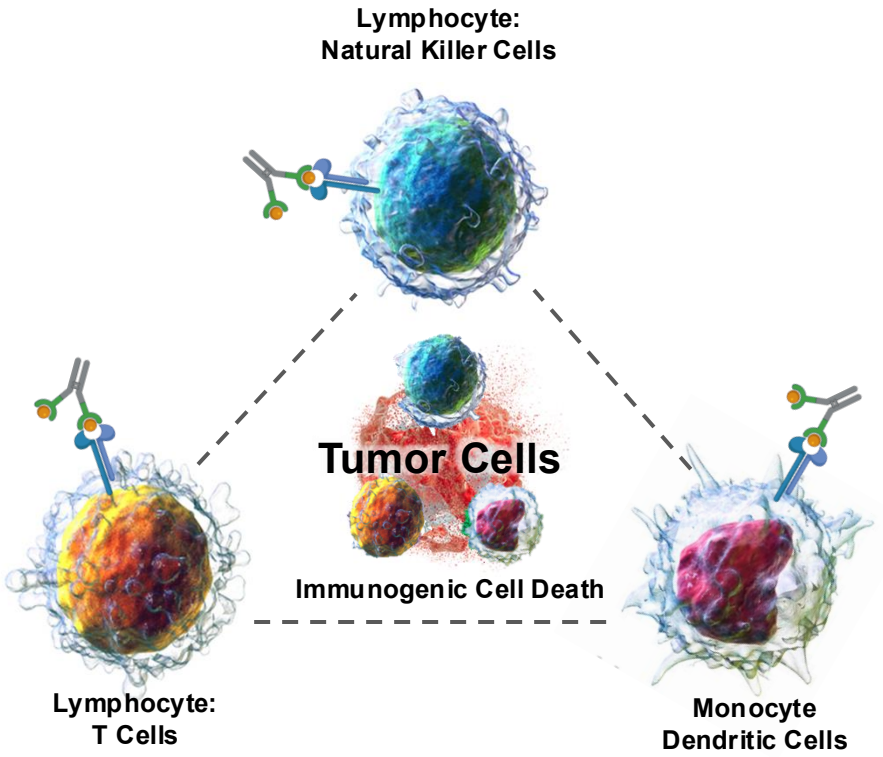


The Missing Link

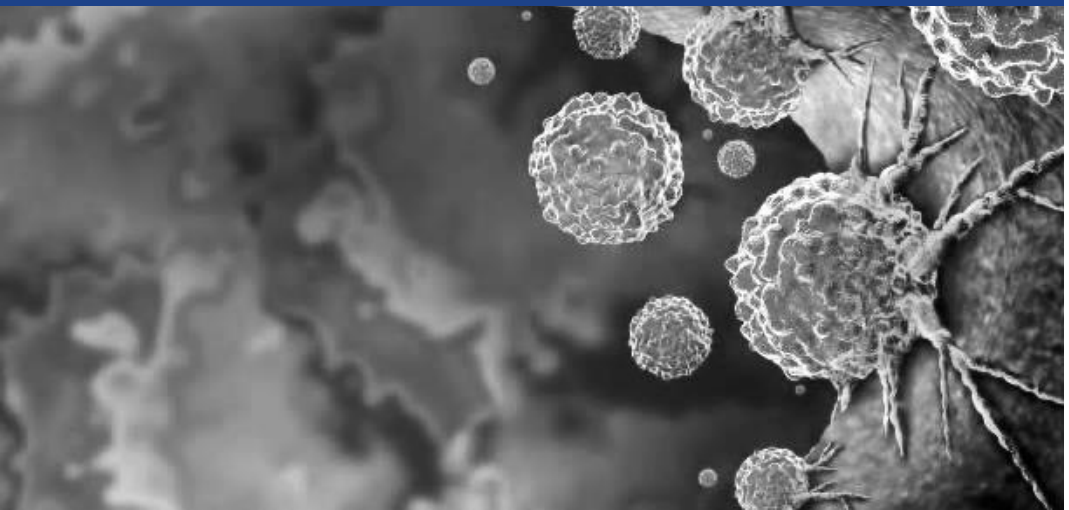
Nogapendekin alfa inbakicept (NAI)

Lymphocyte Stimulating Agent

Binding of nogapendekin alfa inbakicept-pmln to its receptor results in proliferation and activation of NK, CD8+, and memory T cells without proliferation of immuno-suppressive Treg cells.



ImmunityBio®



Thank You

ImmunityBio Investor Day
The Westin Hotel LAX
10:00am – 3:30pm Pacific
April 15, 2025