Supercharged rBCG with Potential Increased Tolerability Compared to TICE BCG

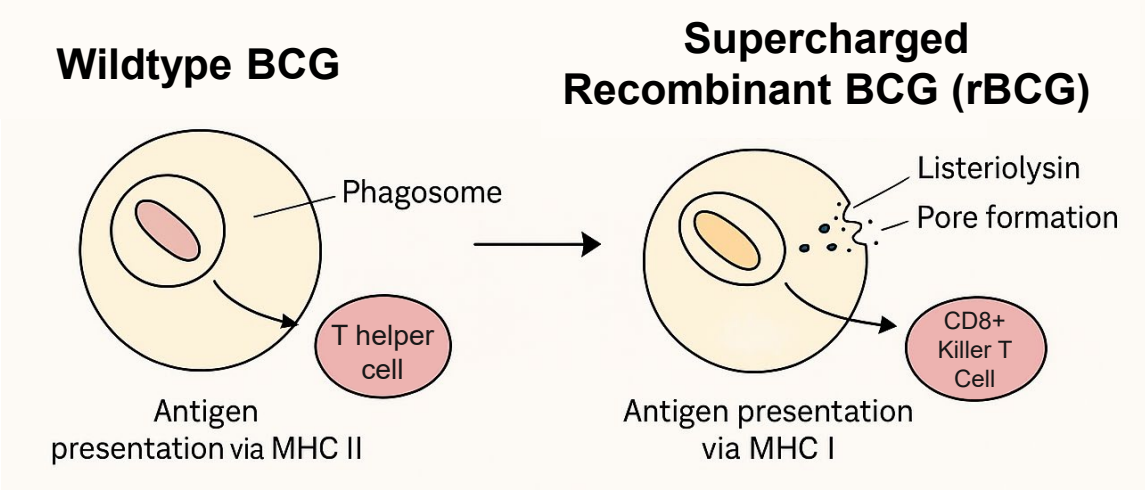
Recombinant BCG (rBCG)

- Recombinant BCG (rBCG) is a recombinant Mycobacterium bovis BCG engineered to increase induction of CD8+ T cell immune response

To sign up and receive rBCG for your patients

- **rBCG is a Biosafety Level 1 (BSL-1) immunotherapy designed to improve anti-tumor efficacy and tolerability**

Overcoming the BCG shortage



rBCG Available Nationwide via Expanded Access Program

AUA 2025 Las Vegas APR 26-29

The Power of ANKTIVA to Overcome Lymphopenia Through NK & Memory T Cells to Achieve Durable Responses in Urological Diseases - Duration Matters

Keynote Speaker:
Patrick Soon-Shiong, MBBCh, MSc, FRCS(C), FACS

Sunday, April 27, 2025
1:30 – 2:15pm Pacific

ImmunityBio®

AUA 2025 APRIL 26-29 Las Vegas

The Superpower of Lymphocytes in Prolonging Survival in Patients with Cancer

I. Supercharged Recombinant BCG: Stimulating CD8+ T Cells

II. Unrecognized Lymphocytes as a ‘Organ at Risk’

III. The Missing Link: Treating Lymphopenia ‘The Cancer BioShield’

IV. Unprecedented Duration of Response & Bladder Sparing

   A. NMIBC CIS Disease: Prolonged Complete Remission >45mo with Bladder Sparing of 84% at 36 Months with Five Year Update

   B. NMIBC Papillary Disease: Prolonged Disease-Free Survival with Bladder Sparing of 82% at 36 Months

V. Awaiting FDA Review & NCCN Guideline Update on NMIBC Papillary Disease

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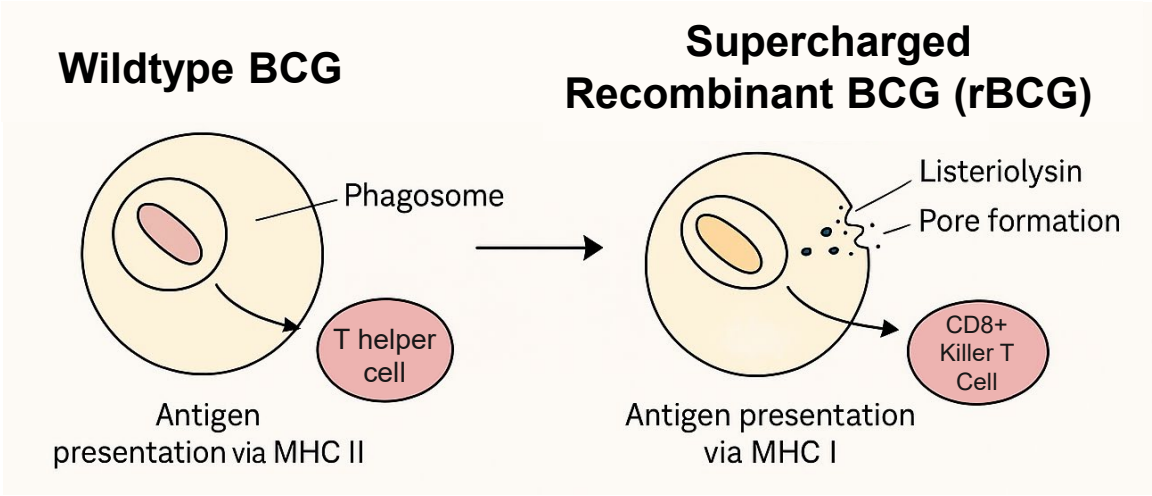
- Recombinant BCG (rBCG) is a recombinant Mycobacterium bovis BCG engineered to increase induction of CD8+ T cell immune response
- Gene modifications have been implemented in BCG to improve its immunogenicity and safety leading to rBCG for bladder cancer
- In contrast to BCG, which is trapped inside the phagosome and thus is conducted towards the MHC II pathway, rBCG moves from the intracellular compartment of the phagosome via listeriolysin-formed pores into the cytoplasm, leading to MHC I presentation of bacterium-derived peptides and thus increase CD8+ T cell immunogenicity
- **rBCG is a Biosafety Level 1 (BSL-1) immunotherapy designed to improve anti-tumor efficacy and tolerability**



rBCG Available Nationwide via Expanded Access Program

To sign up and receive rBCG

BCG@ImmunityBio.com

Supercharged rBCG Alone with 42% Recurrence Free Rate at 4 Years in NMIBC Phase 1, 2 After Recurrence From Convention BCG

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)

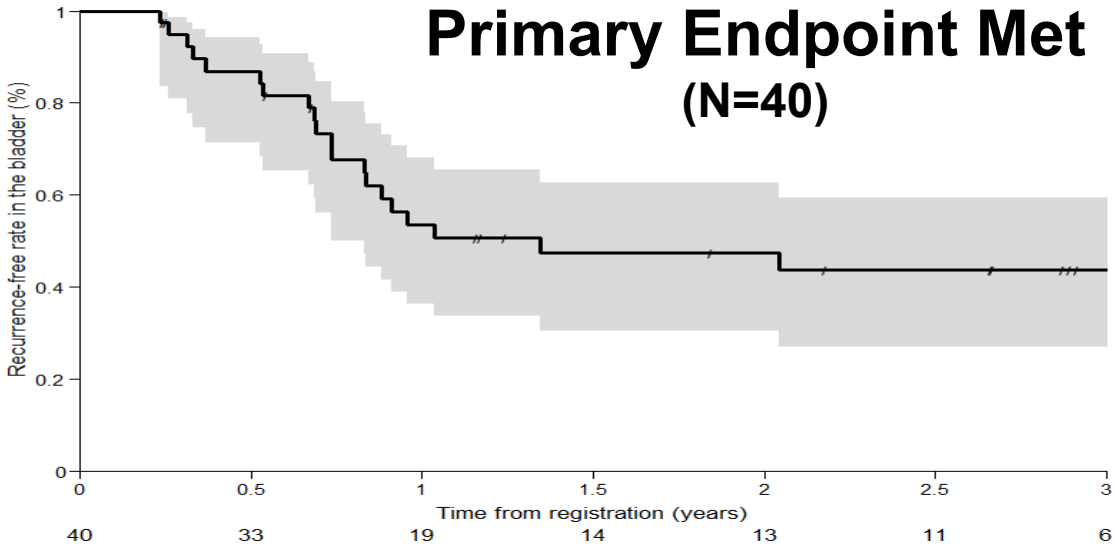
EUROPEAN UROLOGY ONCOLOGY 5 (2022) 195–202

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]*



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%]**

Recombinant BCG Available Now on a Nationwide Basis

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.

Scan QR code to receive rBCG for your patients

AUA 2025 APRIL 26-29 Las Vegas

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Effect of Chemotherapy Induced Lymphopenia on Rapid Progression and Reduced Overall Survival Across All Tumor Types

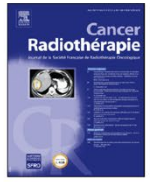
Lymphocytes as a “New Organ” at Risk

2023

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

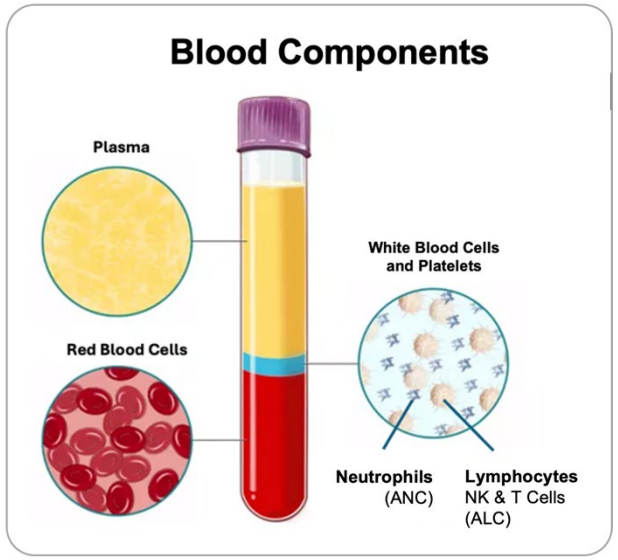
P.A. Laurent[a,b], É. Deutsch[a,b,*]

[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

The Unrecognized Absolute Lymphocyte Count (ALC) and Lymphopenia (Low ALC) in 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

The Barrier to the Cure
Chemotherapy Induced Lymphopenia

2009

The unrecognized damage to the immune system for over 30 years

1994

NIH Public Access
Author Manuscript
Cancer Res. Author manuscript; available in PMC 2010 July 1.

Published in final edited form as:
Cancer Res. 2009 July 1; 69(13): 5383–5391. doi:10.1158/0008-5472.CAN-08-3845.

LYMPHOPENIA AS A PROGNOSTIC FACTOR FOR OVERALL SURVIVAL IN ADVANCED CARCINOMAS, SARCOMAS AND LYMPHOMAS

Isabelle Ray-Coquard[1], Claire Cropet[2], Martine Van Glabbeke[3], Catherine Sebban, MD[1], Axel Le Cesne[4], Ian Judson[5], Olivier Tredan[1], Jaap Verweij[6], Pierre Biron[1], Inthidar Labidi[1], Jean-Paul Guastalla[1], Thomas Bachelot[1], David Perol[2], Sylvie Chabaud[2], Pancras C.W. Hogendoorn[7], Philippe Cassier[8], Armelle Dufresne[8], and Jean-Yves Blay[8,9] on behalf of the EORTC Soft Tissue and Bone Sarcoma Group

blood®
Volume 84, Issue 7, 1 October 1994, Pages 2221-2228

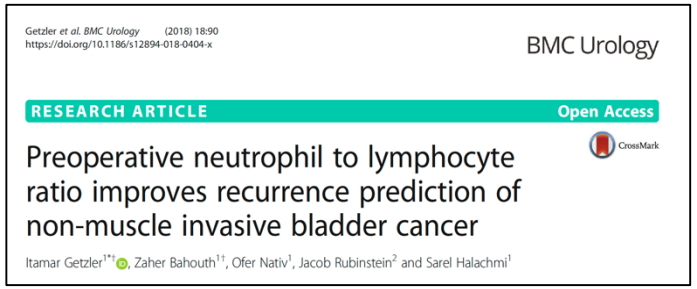
Article

Lymphocyte Depletion During Treatment With Intensive Chemotherapy for Cancer

Crystal L. Mackall, Thomas A. Fleisher, Margaret R. Brown, Ian T. Magrath, Aziza T. Shad, Marc E. Horowitz, Leonard H. Wexler, Melissa A. Adde, Linda L. McClure, Ronald E. Gress

Immunosuppression Combined with Low Lymphocytes Ratio Predicts High Recurrence in NMIBC

2018



Getzler et al. BMC Urology (2018) 18:90
https://doi.org/10.1186/s12894-018-0404-x

BMC Urology

RESEARCH ARTICLE Open Access

Preoperative neutrophil to lymphocyte ratio improves recurrence prediction of non-muscle invasive bladder cancer

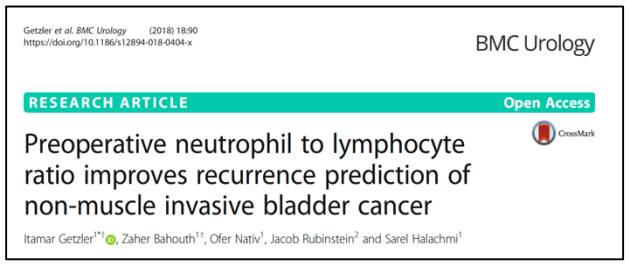
Itamar Getzler[1*†], Zaher Bahouth[1†], Ofer Nativ[1], Jacob Rubinstein[2] and Sarel Halachmi[1]

Results: The study cohort included 96 men and 17 women with a median age of 72 years. Sixty-four patients (56.6%) have had a recurrence during the study occurring at the median time of 9 months (IQR 6, 13), while the median follow-up time for patients without recurrence was 18 months (IQR 10, 29). Univariate Cox regressions for recurrence demonstrated significance for NLR > 2.5 for the whole cohort ($p = 0.011$, HR 2.015, CI 1.175–3.454) and for the BCG sub-group ($p = 0.023$, HR 3.7, CI 1.2–11.9), while the EORTC score demonstrated significance for the 'No Treatment' subgroup ($p = 0.024$, HR 1.278, CI 1.03–1.58). When analyzed together as a multivariate Cox model, the NLR > 2.5 and EORTC score retained their significance for the aforementioned groups, while also improving the EORTC score significance for the whole cohort.

Conclusion: NLR > 2.5 was found to be a significant predictor of disease recurrence and demonstrated high hazard ratio and worse recurrence-free survival in patients with NMIBC, especially in those treated with BCG. Additionally, our data demonstrated statistical evidence that NLR > 2.5 might have an improving effect on the EORTC score's prediction when analyzed together.

Lymphopenia Results in Rapid Recurrence in NMIBC

2018


Getzler et al. BMC Urology (2018) 18:90
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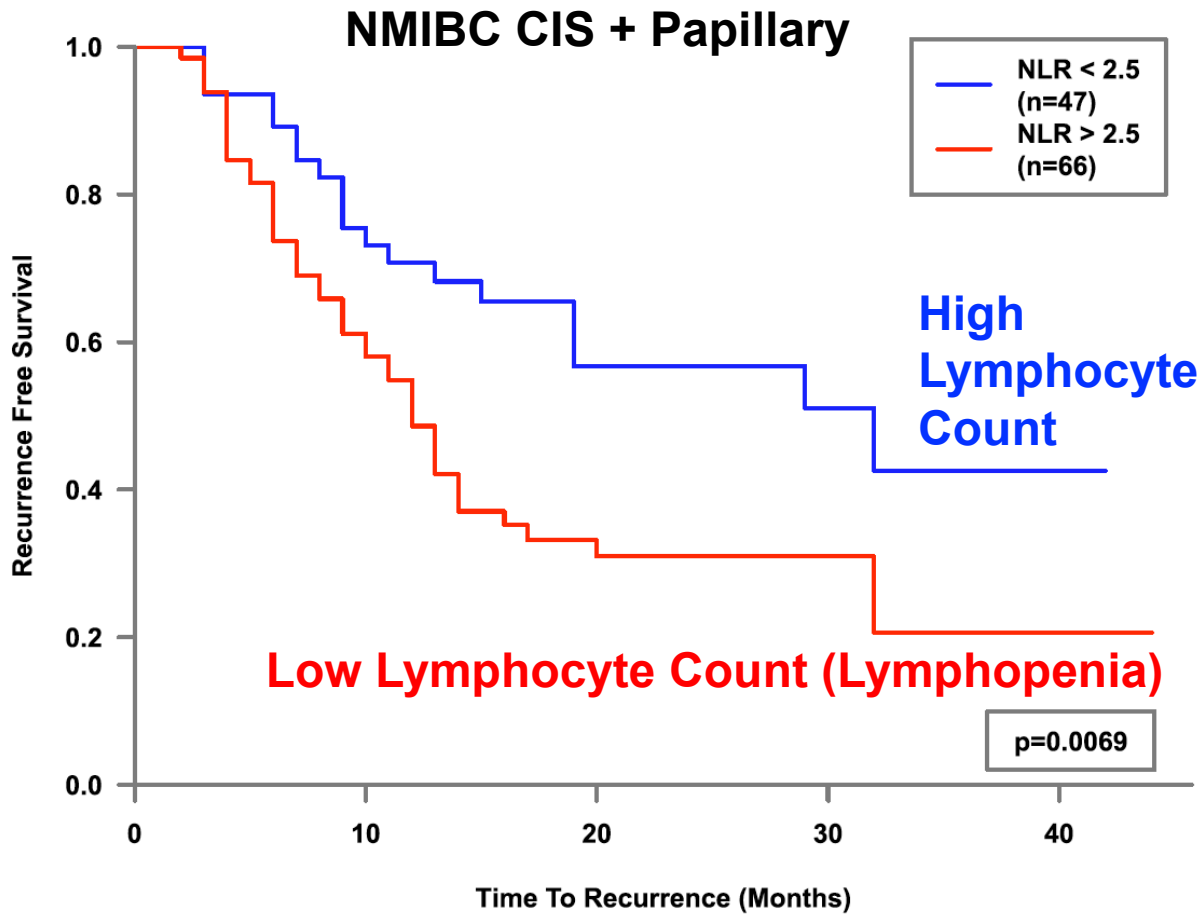

Fig. 1 Kaplan-Meier estimates of recurrence-free survival factored by NLR 2.5 - whole cohort analysis

High Immunosuppressive Neutrophil Count + Low Lymphocyte Count = High NLR Ratio = Recurrence

Lymphopenia Induces Rapid Recurrence in NMIBC

2018

Getzler et al. BMC Urology (2018) 18:90
https://doi.org/10.1186/s12894-018-0404-x

BMC Urology

RESEARCH ARTICLE Open Access

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Conclusions

NLR > 2.5 was found to be a significant predictor of disease recurrence and demonstrated high hazard ratio and worse recurrence-free survival in patients with NMIBC, especially in those treated with BCG. Additionally, our data demonstrated statistical evidence that NLR > 2.5 might have an improving effect on the EORTC score's prediction when calculated together. Thus, we propose to consider the incorporation of NLR > 2.5 in the next revisions of the EORTC score.

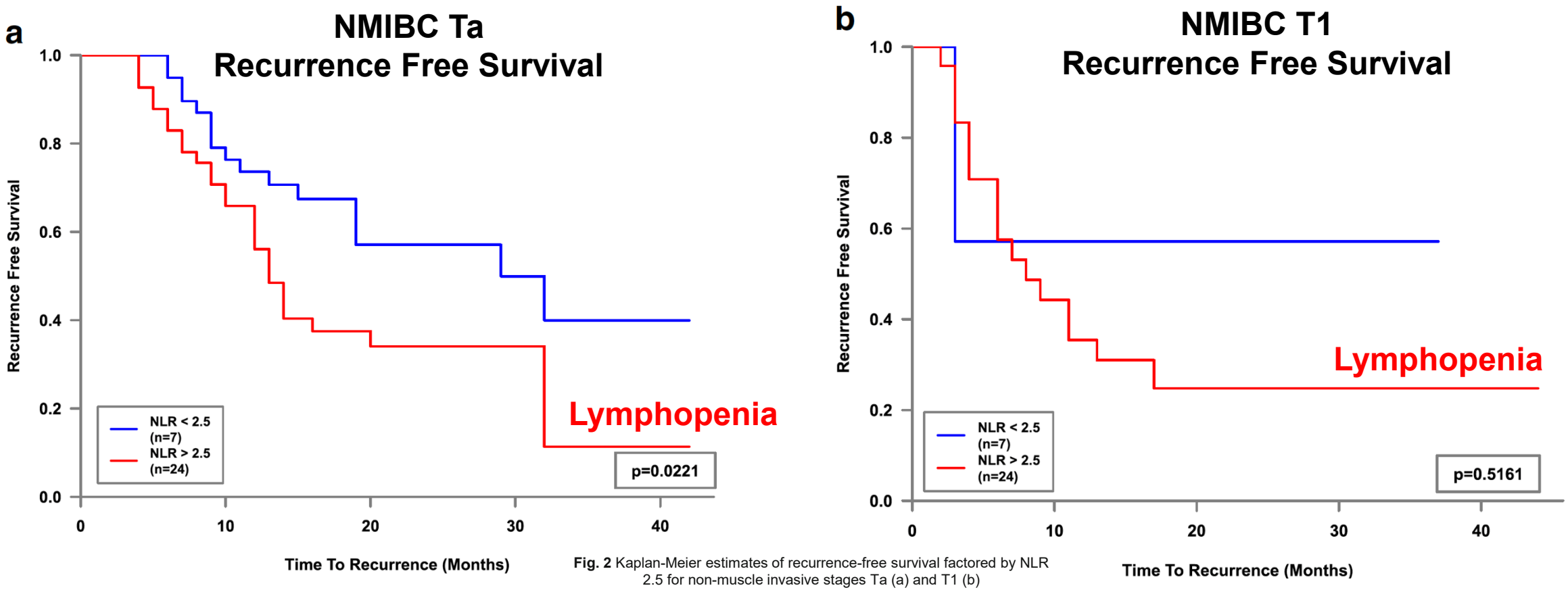


Fig. 2 Kaplan-Meier estimates of recurrence-free survival factored by NLR 2.5 for non-muscle invasive stages Ta (a) and T1 (b)

Lymphopenia Results in Significantly Decreased Survival in Renal Cancer and Bladder Cancer

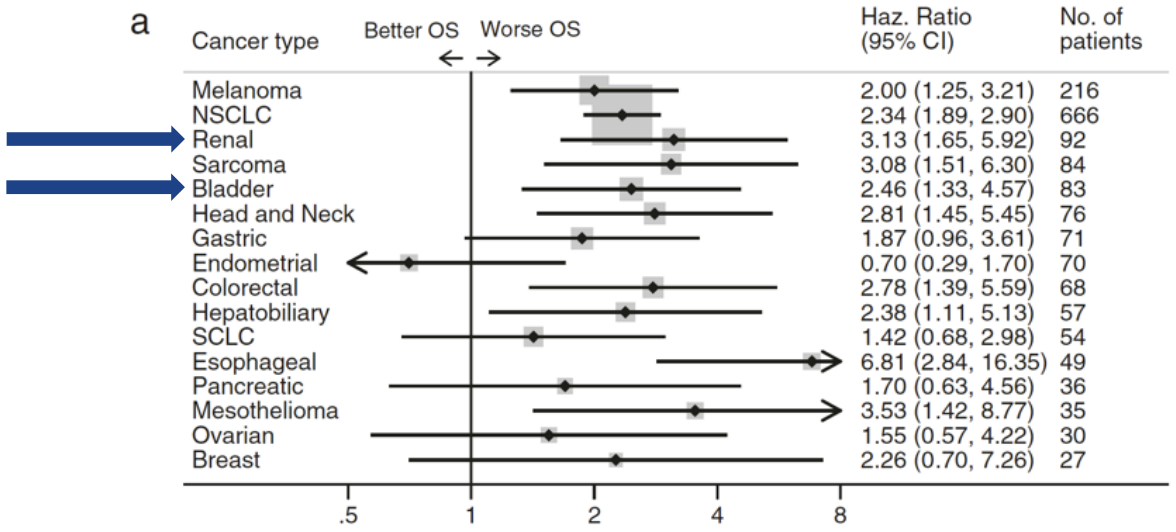
nature COMMUNICATIONS

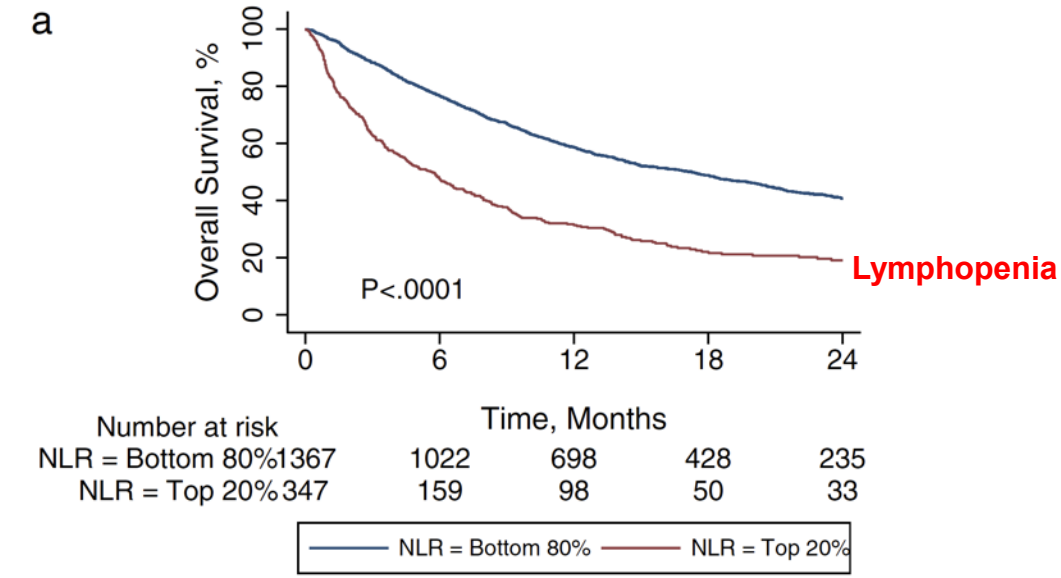
ARTICLE

https://doi.org/10.1038/s41467-021-20935-9 OPEN

Pretreatment neutrophil-to-lymphocyte ratio and mutational burden as biomarkers of tumor response to immune checkpoint inhibitors

Cristina Valero[1,2,3], Mark Lee[2,3], Douglas Hoen[2,3], Kate Weiss[2,3], Daniel W. Kelly[4], Prasad S. Adusumilli[1], Paul K. Paik[5], George Plitas[1], Marc Ladanyi[6], Michael A. Postow[5], Charlotte E. Ariyan[1], Alexander N. Shoushtari[5], Vinod P. Balachandran[1], A. Ari Hakimi[1,2,3], Aimee M. Crago[1], Kara C. Long Roche[1], J. Joshua Smith[1], Ian Ganly[1,2,3], Richard J. Wong[1], Snehal G. Patel[1], Jatin P. Shah[1], Nancy Y. Lee[7], Nadeem Riaz[2,3,7], Jingming Wang[2,3], Ahmet Zehir[6], Michael F. Berger[6], Timothy A. Chan[2,3,7,9]✉, Venkatraman E. Seshan[8,9]✉ & Luc G. T. Morris[1,2,3,9]✉





Lymphopenia

Lymphopenia Associated with Significant Lower OS (p=0.006) with Checkpoint Inhibitors

2024

ARTICLE OPEN

Check for updates

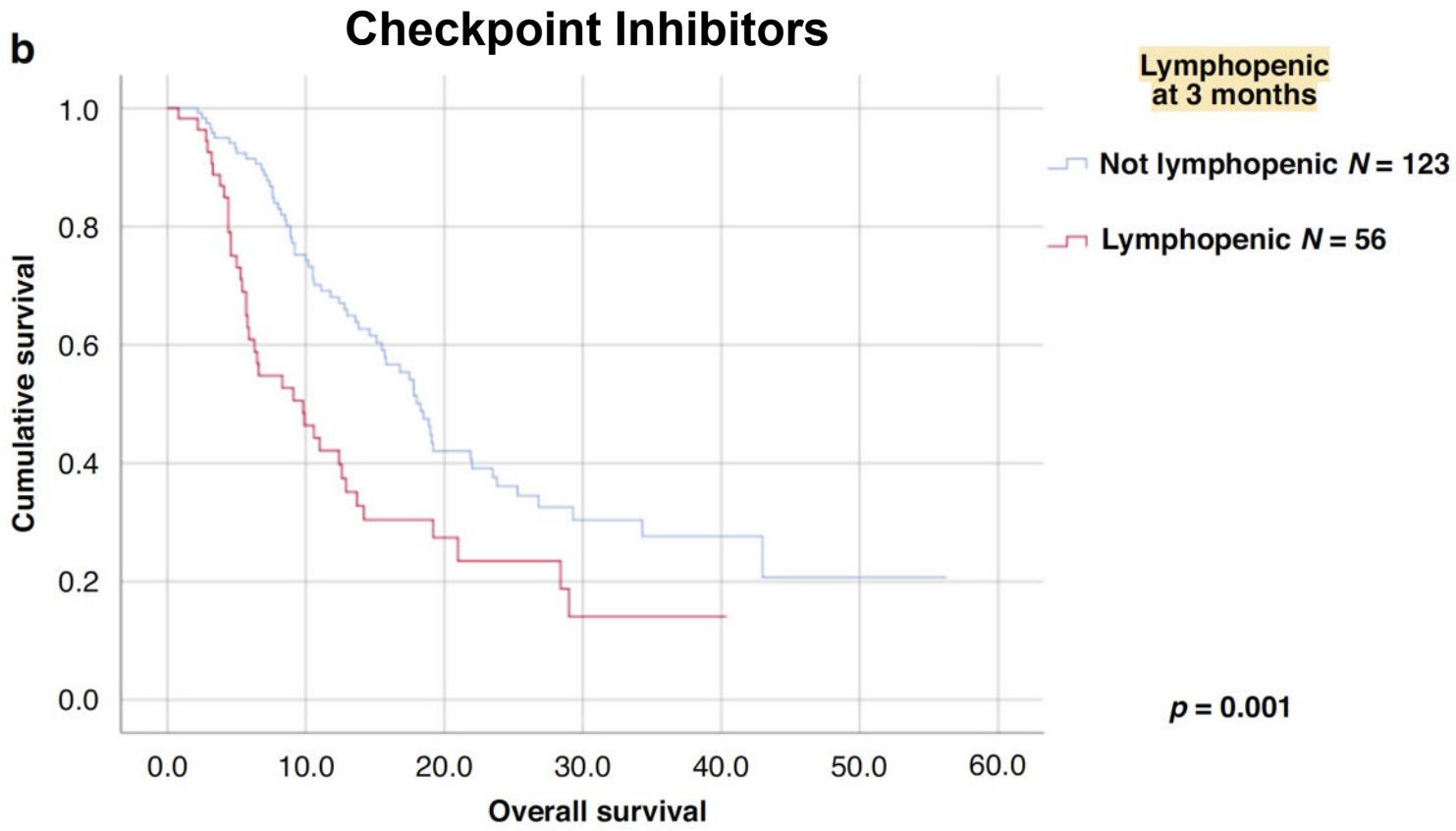
Exploring the prognostic impact of absolute lymphocyte count in patients treated with immune-checkpoint inhibitors

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.



Lymphopenia as a Poor Prognostic Indicator Across All Tumor Types

2018

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*

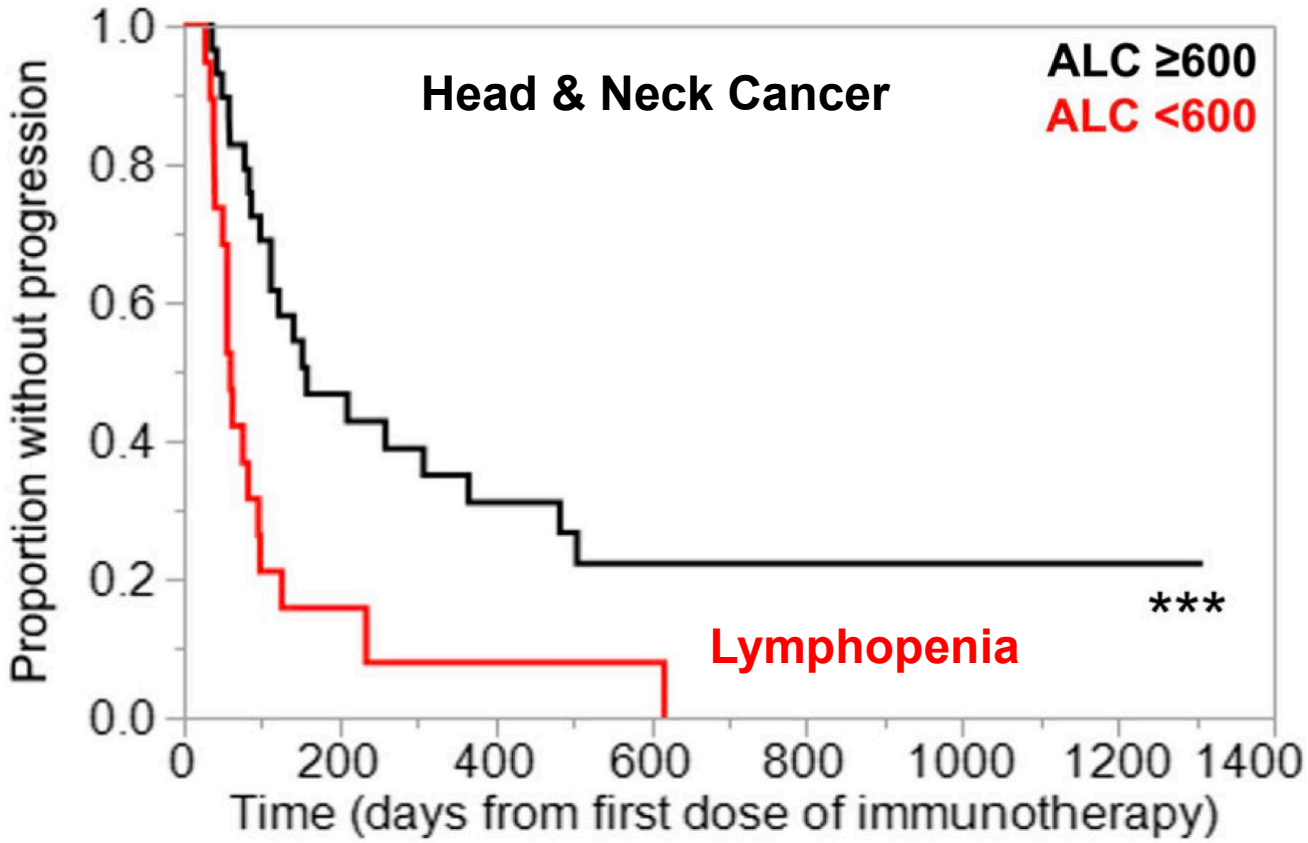
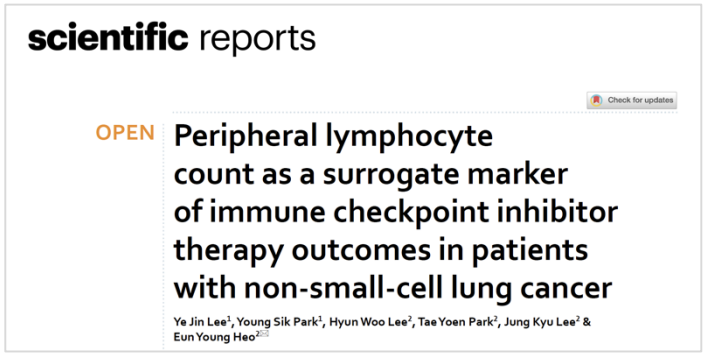


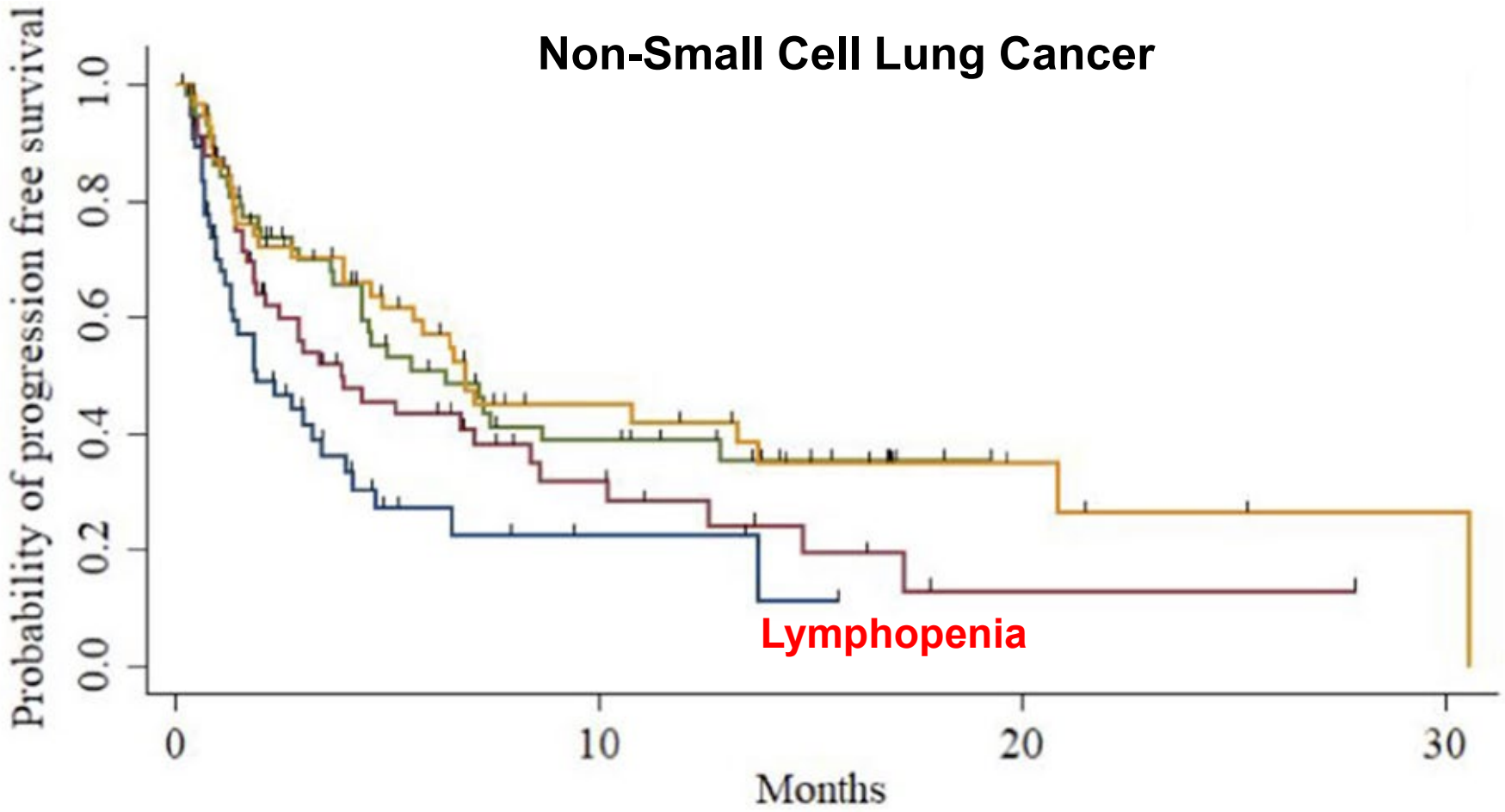
Fig. 3 An expanded cohort time-to-progression analysis was performed by including additional patients who have received other checkpoint inhibitor regimens. Patients with ALC < 600 cells/μl were associated with significantly shorter PFS. ***$P < 0.005$ by Wilcoxon test

Lymphopenia as a Poor Prognostic Indicator Across All Tumor Types

Rapid Progression of Disease in Patients with Lymphopenia

2022





Lymphopenia as a Poor Prognostic Indicator Across All Tumor Types

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†]

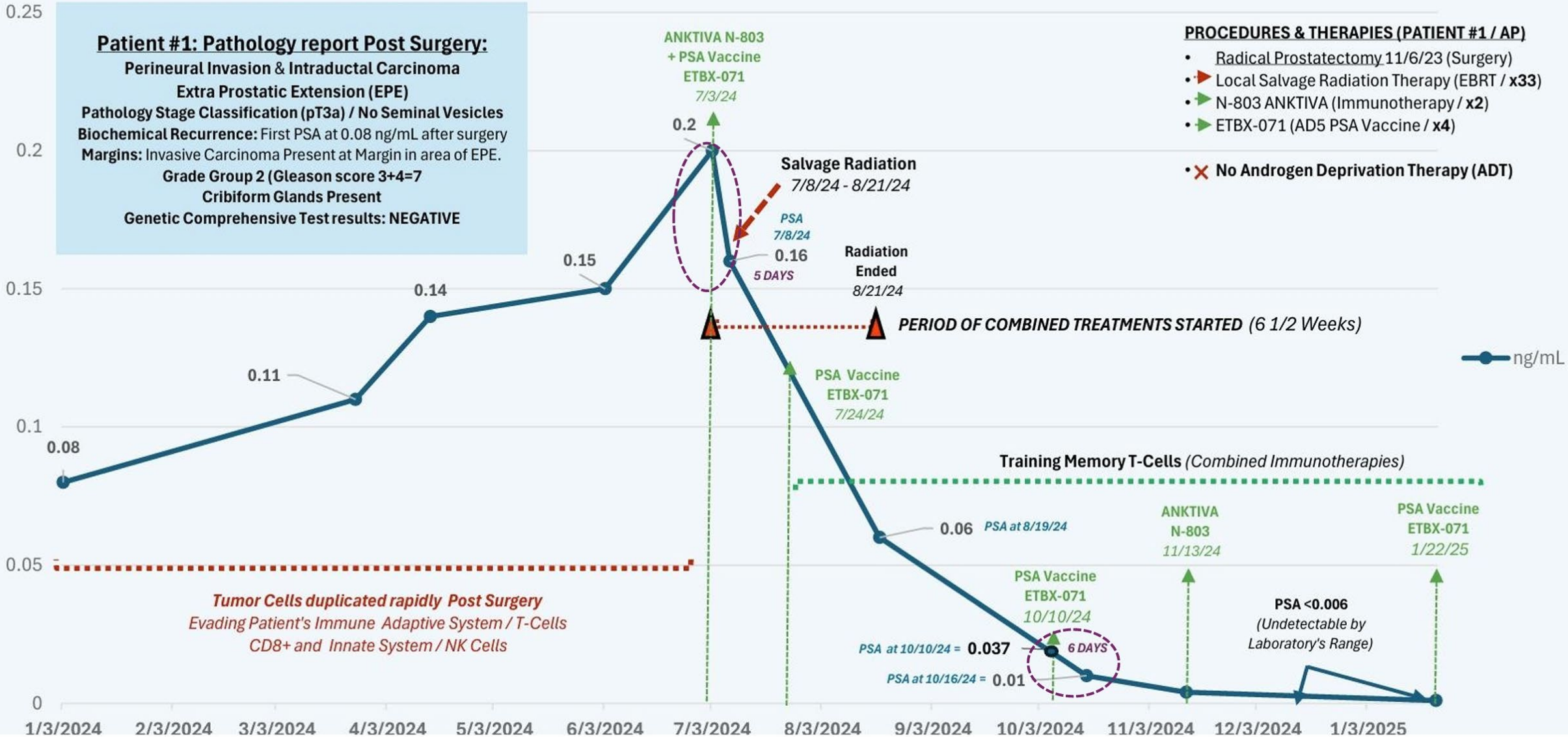
Table 1 Different published studies exploring the impact of the global lymphopenia or NK and T cell subsets on relapse-free survival (RFS) or overall survival (OS) in patients with solid tumors

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

PSA Velocity Post-Surgery, Radiation & Immunotherapies



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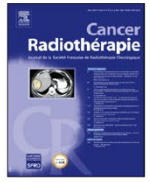
What is the Cause of Lymphopenia?

2023

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

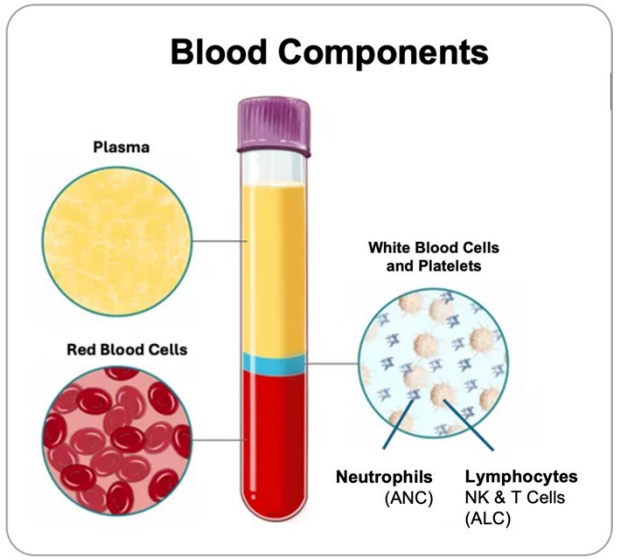
P.A. Laurent[a,b], É. Deutsch[a,b,*]

[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

The Unrecognized Absolute Lymphocyte Count (ALC) and Lymphopenia (Low ALC) in CBC

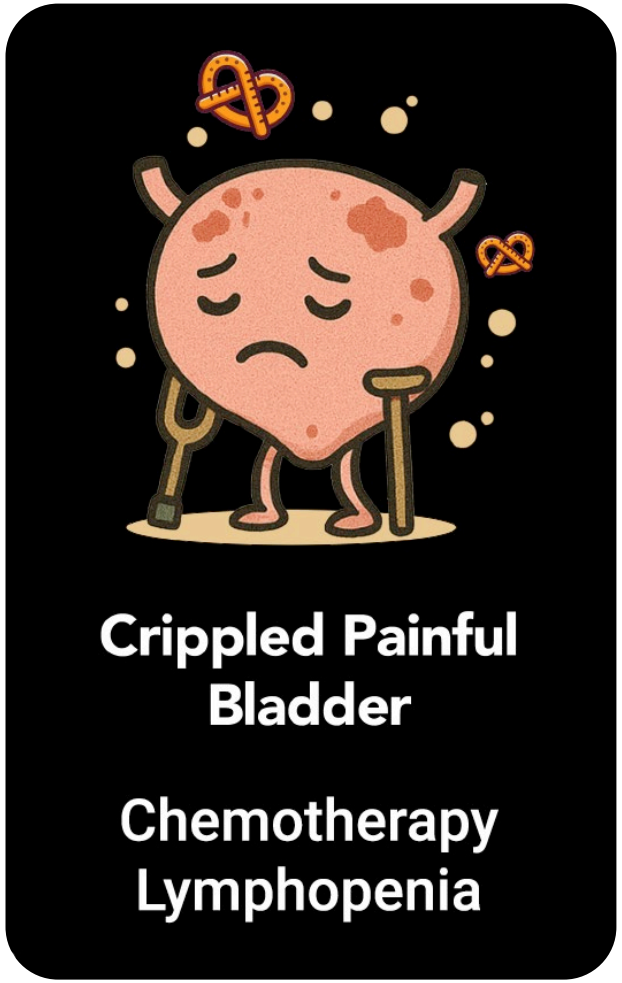


ANC: Absolute Neutrophil Count
ALC: Absolute Lymphocyte Count

ALC <1,000 Lymphocytes per Microliter = Lymphopenia

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

Chemotherapy & CPI Induced Lymphopenia

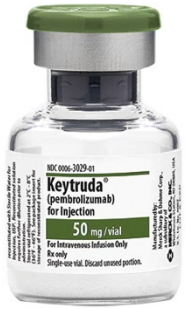


Lymphocyte Depleting Agents

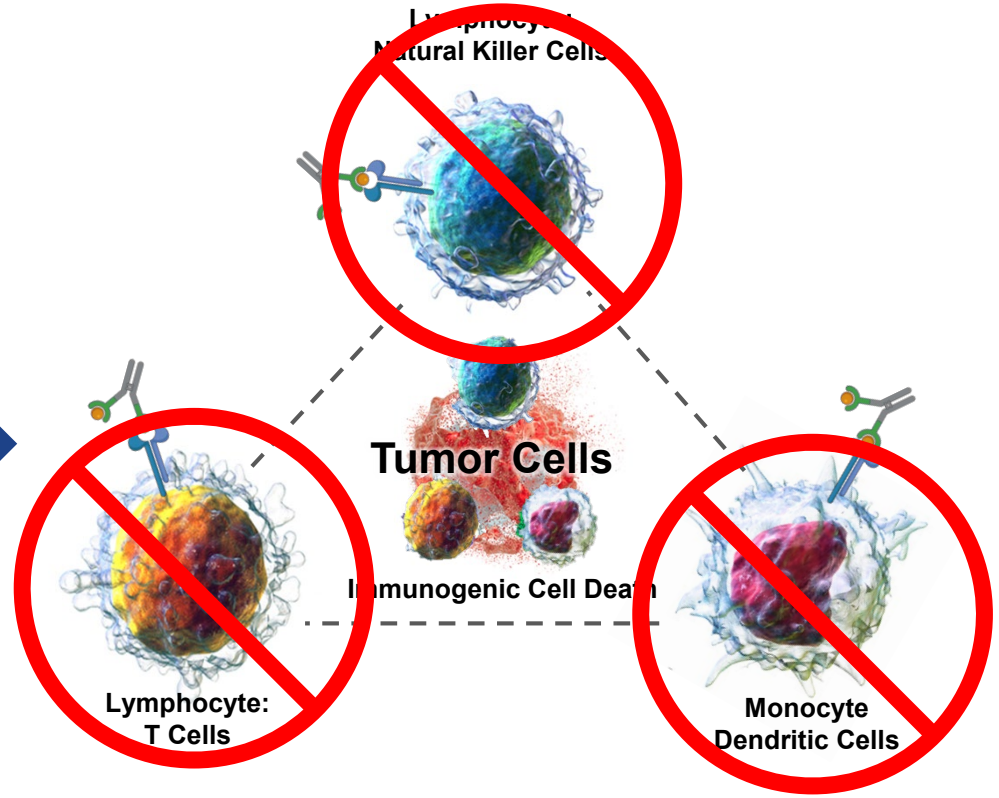
Absolute Lymphocyte Count (ALC) Ignored for 50 Years

Chemotherapies

Checkpoint Inhibitors



Chemo & Checkpoint Inhibitor Induced Lymphopenia



"Win the battle… Lose the war."

Proliferating Lymphocytes with ANKTIVA

2022

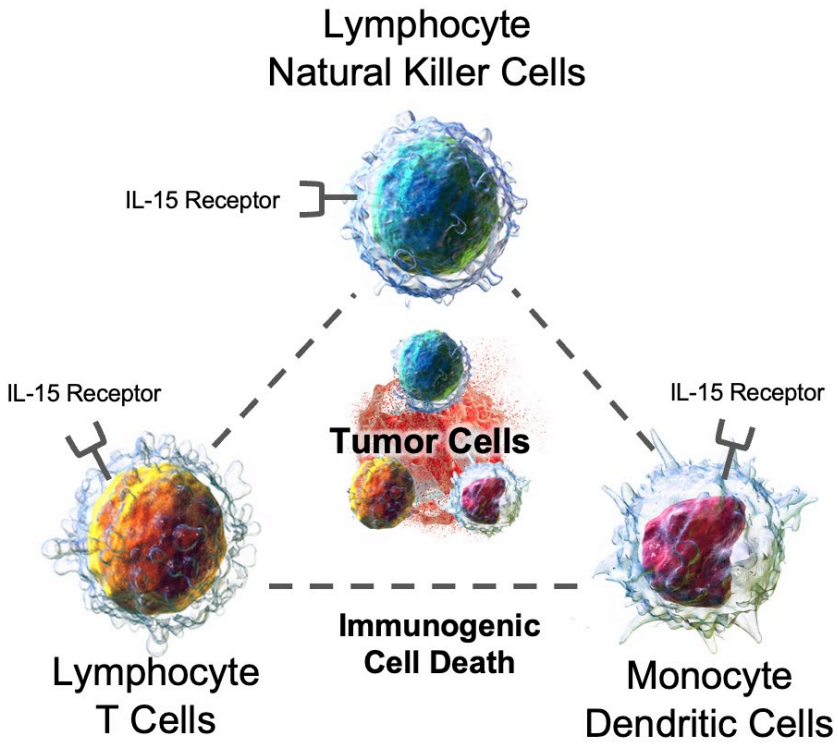
The Journal of Immunology

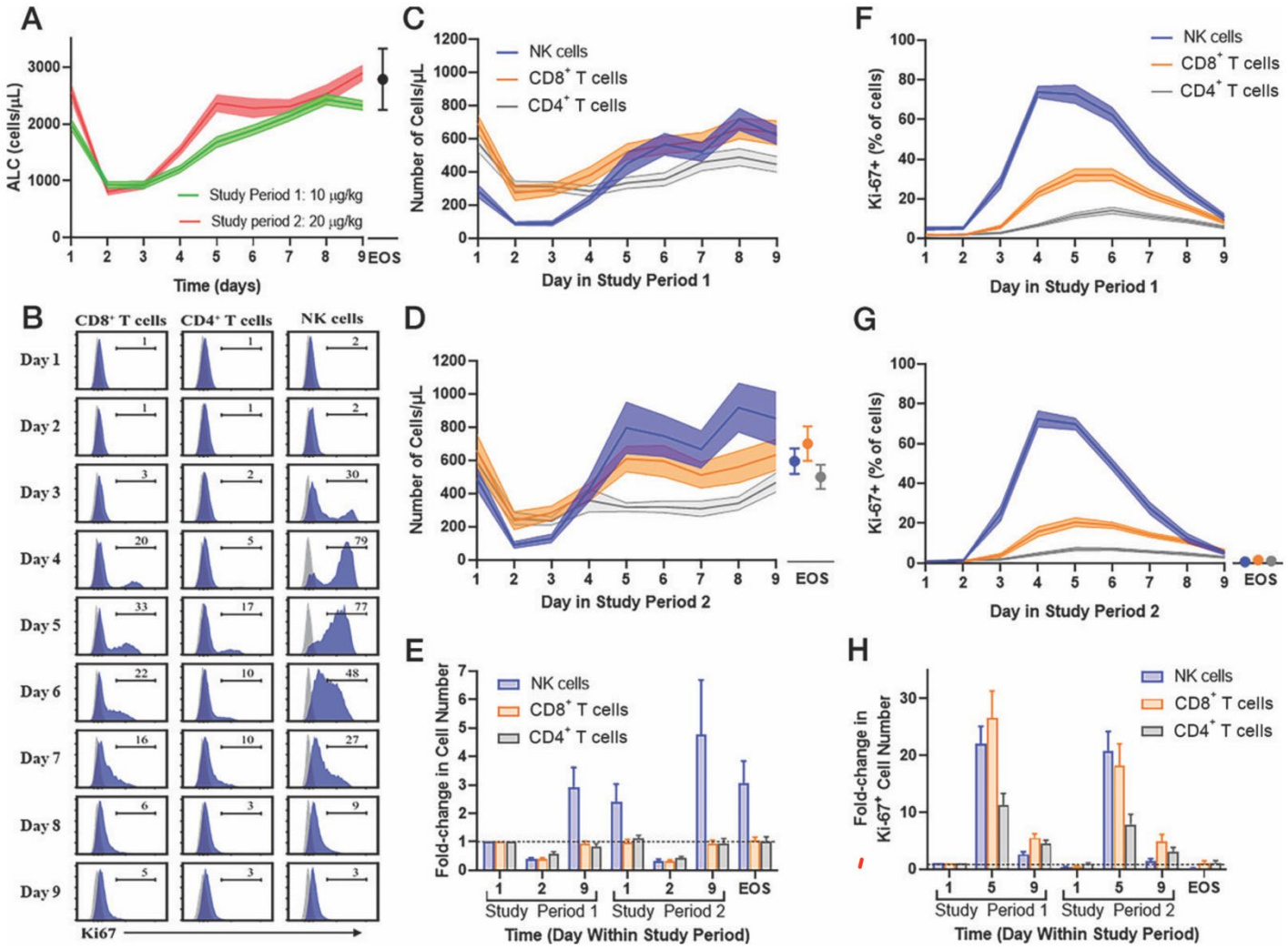
RESEARCH ARTICLE | MARCH 15 2022

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

Mark P. Rubinstein; ... et. al

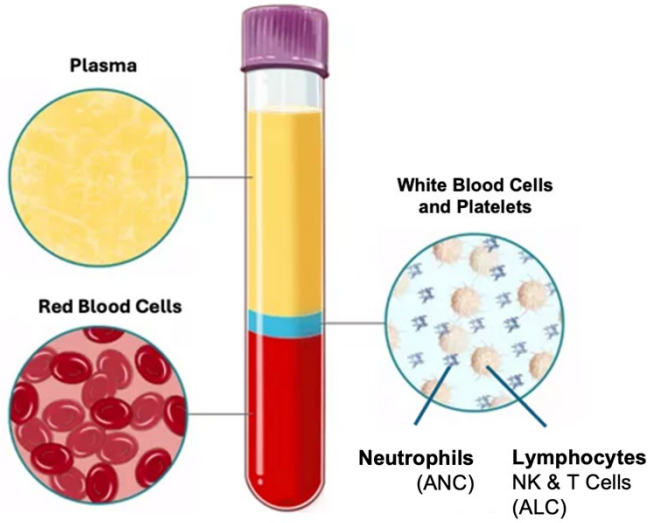
J Immunol (2022) 208 (6): 1362–1370.
https://doi.org/10.4049/jimmunol.2100066





Treatment of Lymphopenia: The Missing Link
IL-15 Superagonist Stimulating Lymphocytes

Complete Blood Count



ALC <1,000 Lymphocytes per Microliter =
Lymphopenia

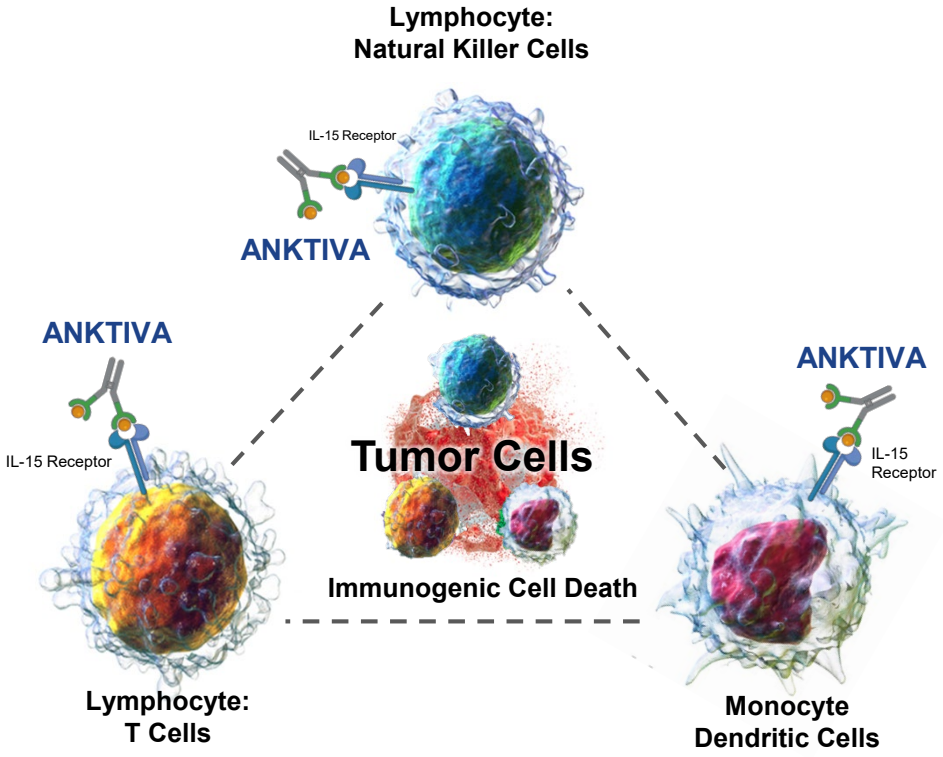
ALC 1,000 to 4,000 Lymphocytes per Microliter =
Normal ALC

The Missing Link

Nogapendekin alfa inbakicept (NAI)

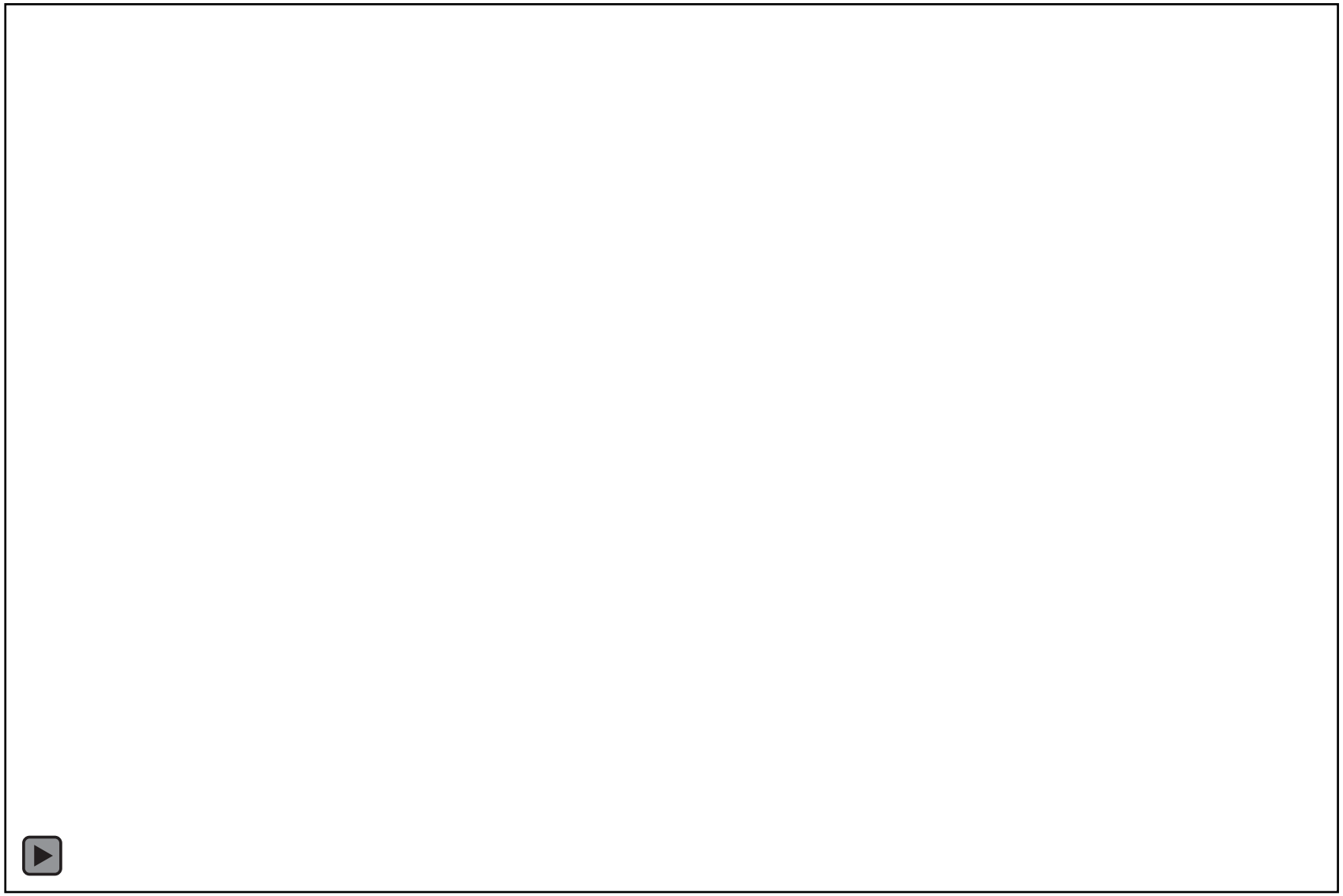
The Cancer BioShield

Lymphocyte Stimulating Agent



Mechanism of Action Per Package Insert:
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.

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



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V. Awaiting FDA Review & NCCN Guideline Update on NMIBC Papillary Disease

Prolonged Disease-Free Response Cystectomy Avoidance >36 Months in BCG Unresponsive Papillary Disease

Win The Battle But Lose The War… Lose the Bladder Duration Matters

NMIBC BCG-Unresponsive
CIS +/- Papillary

Best in Disease of Cystectomy Avoidance and Duration of Response

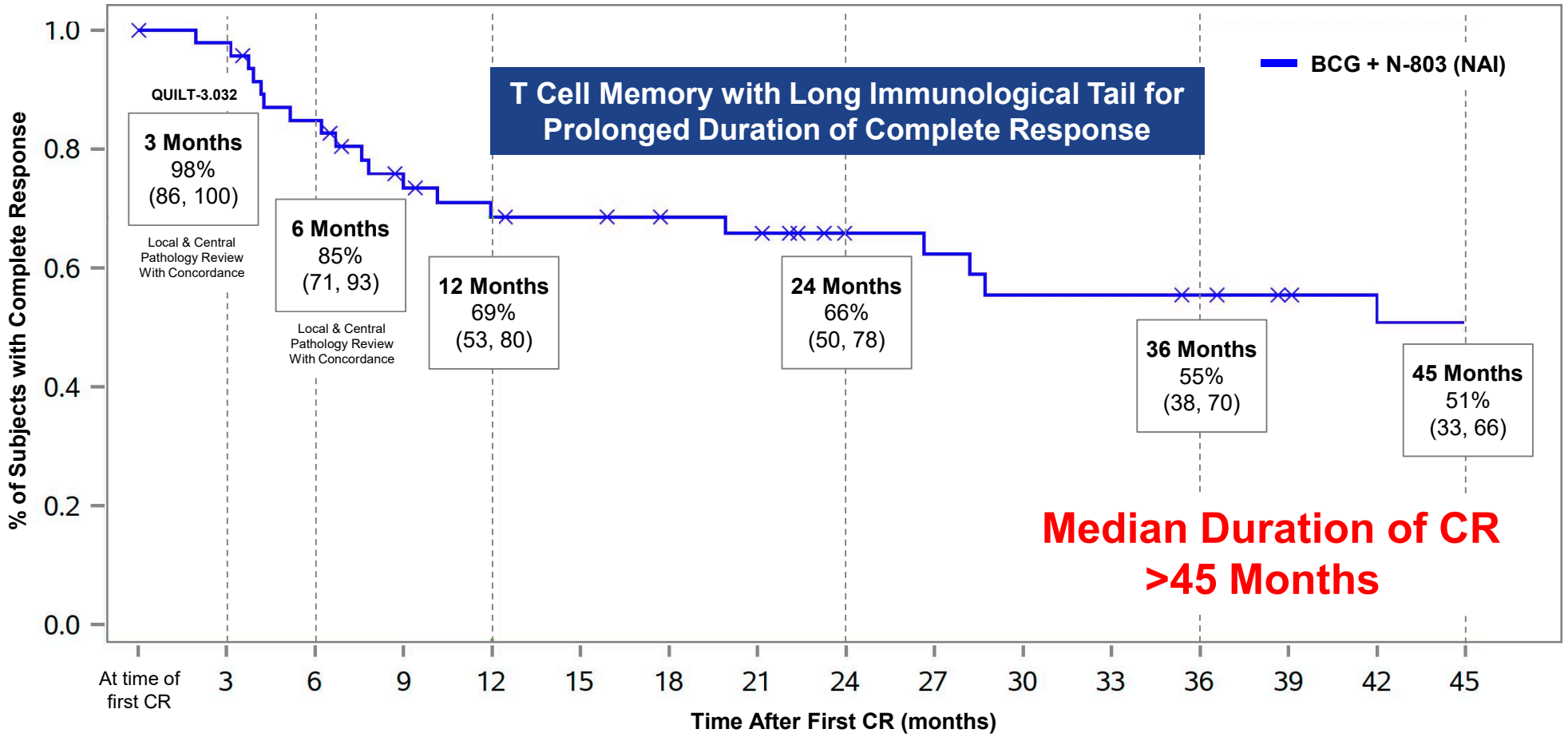
	TAR-200[3]	CG[2]	ANKTIVA[1]
CR Rate at Any Time (Primary Endpoint)	82%	76%	71%
Duration of Complete Response by K-M			
12 Months	56%	64%	69%
24 Months	52%	58%	66%
36 Months	***No Data***	***No Data***	55%
45 Months	***No Data***	***No Data***	51%
Median Duration of Response	25.8+ Months	27.9+ Months	**45+ Months**
Cystectomy Free Rate			
12 Months	87%	90%[4]	96%
24 Months	***No Data***	85%	90%
36 Months	***No Data***	***No Data***	84%
TRAE Grade ≥3	13.5%	0%	0-1%

References Accessed April 26, 2025

1. Sam Chang AUA 2025 “An Update on QUILT-3.032: Durable Complete Responses to NAI (ANKTIVA) Plus BCG Therapy in BCG-Unresponsive CIS With or Without Ta/T1 Papillary Disease and in Papillary Disease without CIS”
2. Mark Tyson, AUA 2025 "Trial in Progress: BOND-003 Cohort P- A Multi-national, Single-arm Study of Intravesical Cretostimogene Grenadenorepvec for the Treatment of High-Risk, Papillary Only, BCG-Unresponsive Non-Muscle Invasive Bladder Cancer
3. https://www.onclive.com/view/tar-200-produces-unprecedented-cr-rates-in-bcg-unresponsive-high-risk-nmibc
4. https://www.urologytimes.com/view/bond-003-cretostimogene-yields-high-cr-rate-is-well-tolerated-in-nmibc

The Only Data at AUA 2025 Showing a Median Duration of Complete Response for >45 Months Best-in-Class, Best-in-Disease

Median Duration of Complete Response >45 Months with 29.3 Months Median Follow-Up
QUILT-3.032, FDA Efficacy Population (N=77), Cohort A (CIS +/- Ta/T1)



Source: AUA 2025 Presentation Sam Chang

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Win The Battle But Lose The War… Lose the Bladder Duration Matters

NMIBC BCG-Unresponsive
Papillary without CIS

Best in Disease Duration of Response

	TAR-200[3]	CG[2]	ANKTIVA[1]
Disease Free Survival (DFS) Rate			
12 Months (Primary Endpoint)	*No Data*	*No Data*	58%
24 Months	*No Data*	*No Data*	52%
Median Disease-Free Survival Rate	Not Reached	*No Data*	25.3 Months
Cystectomy Avoidance Rate			
12 Months	*No Data*	*No Data*	92%
24 Months	*No Data*	*No Data*	88%
36 Months	*No Data*	*No Data*	82%
TRAE Grade ≥3	13.5%	0%	0-1%

References Accessed April 26, 2025

1. Sam Chang AUA 2025 “An Update on QUILT-3.032: Durable Complete Responses to NAI (ANKTIVA) Plus BCG Therapy in BCG-Unresponsive CIS With or Without Ta/T1 Papillary Disease and in Papillary Disease without CIS”
2. Mark Tyson, AUA 2025 "Trial in Progress: BOND-003 Cohort P- A Multi-national, Single-arm Study of Intravesical Cretostimogene Grenadenorepvec for the Treatment of High-Risk, Papillary Only, BCG-Unresponsive Non-Muscle Invasive Bladder Cancer
3. F Guerrero-Ramos, AUA 2025 “TAR-200 Monotherapy in Patients With Bacillus Calmette-Guérin–Unresponsive Papillary Disease–Only High-Risk Non–Muscle-Invasive Bladder Cancer: First Results From Cohort 4 of SunRISe-1”

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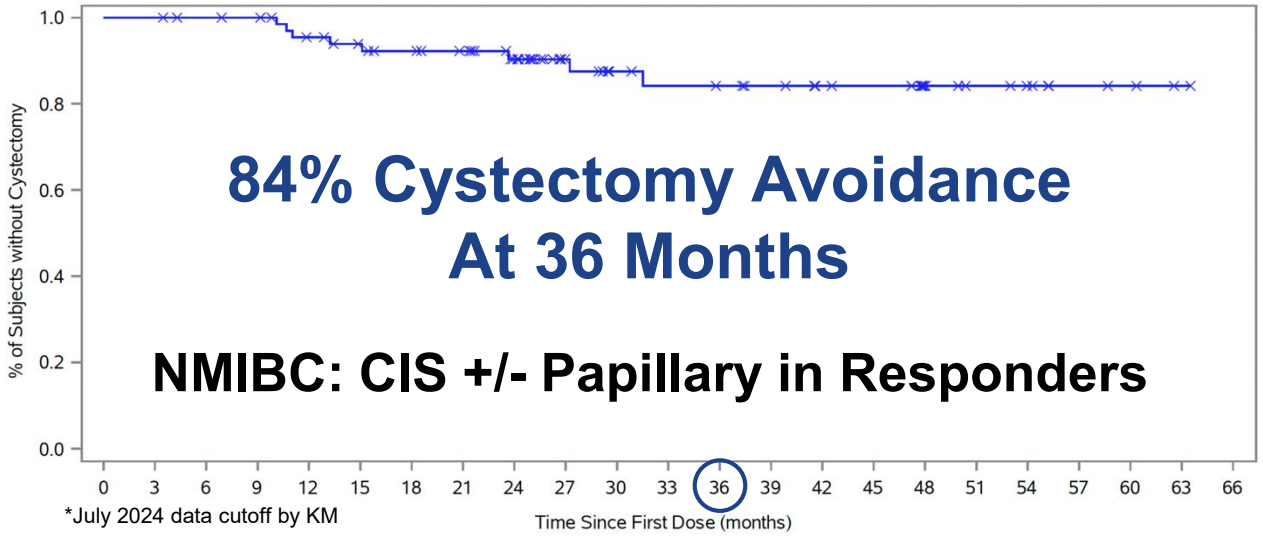
The Only Clinical Data at AUA 2025 in Both CIS and Papillary Disease with Five Year Follow Up and Bladder Sparing for 36 Months

FDA Approved 2024

Time to Cystectomy
Efficacy Population – Cohort A (CIS with or without Papillary)



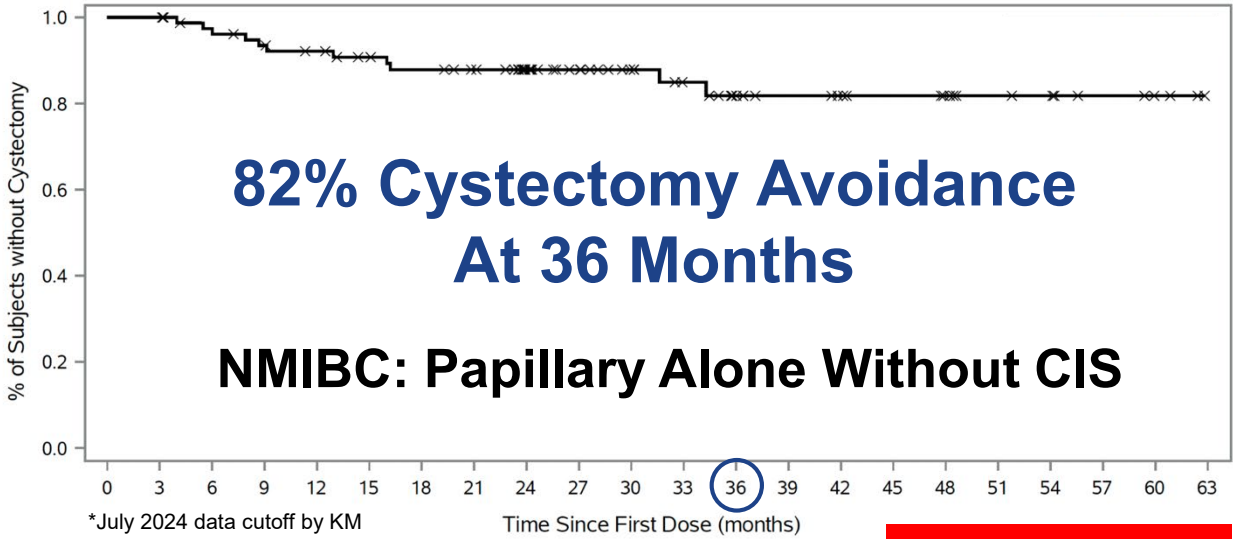
*July 2024 data cutoff by KM

84% Cystectomy Avoidance At 36 Months

NMIBC: CIS +/- Papillary in Responders

Supplemental BLA Filed 2025, Awaiting Approval

Time to Cystectomy
Efficacy Population – Cohort B (Papillary without CIS)



*July 2024 data cutoff by KM

82% Cystectomy Avoidance At 36 Months

NMIBC: Papillary Alone Without CIS

Awaiting NCCN Guidance Approval

Efficacy in **BOTH** CIS +/- Papillary and Papillary alone without CIS demonstrate **Cystectomy Avoidance ≥80%** and **Disease Specific Overall Survival ≥96% at 36-months**

Source: AUA 2025 Presentation Sam Chang

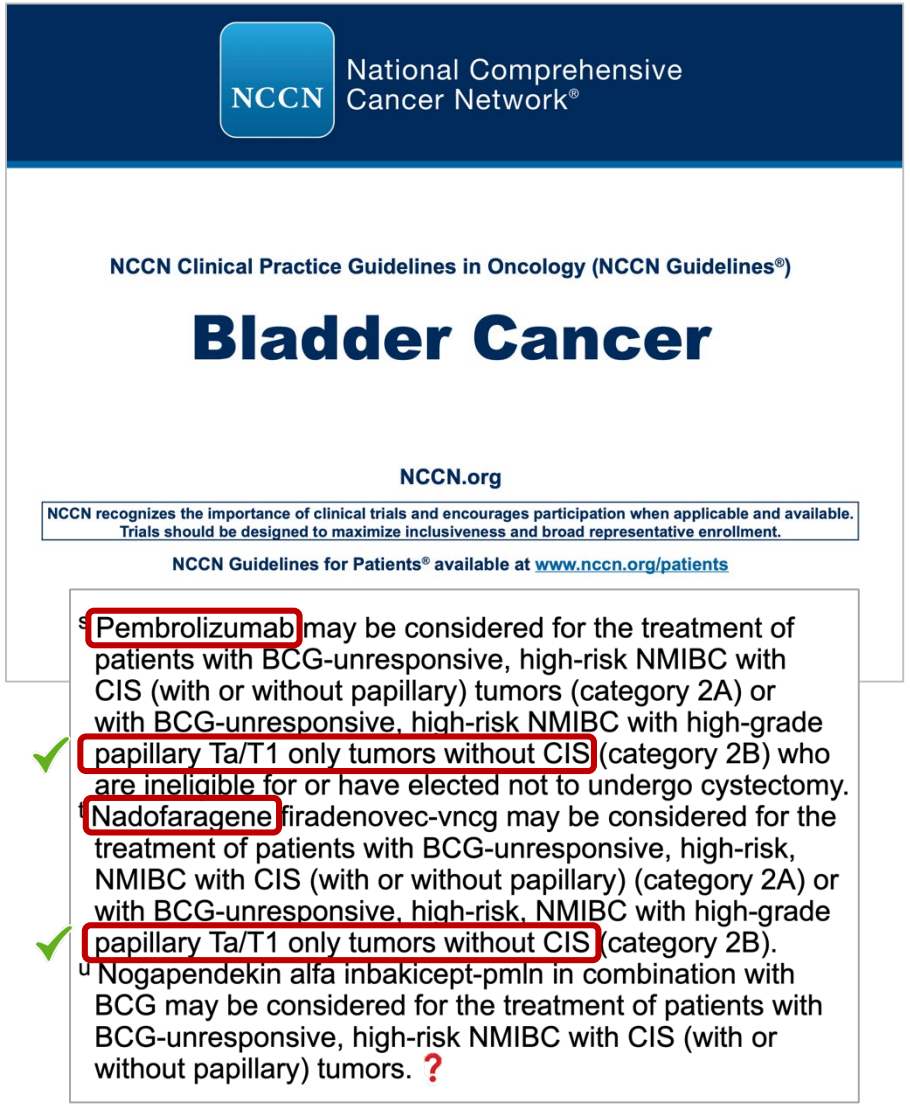
Win the Battle, Win the War, Save the Bladder

The Biological Mechanism of Action Determines Long-Term Memory, Duration of Response and Safety

Clinical Impact	IL-15 Superagonist Activating NK & T Cells without Upregulating T Reg Cells	Chemotherapy Inducing Lymphopenia and Suppressive MDSCs and T Reg Cells	GM-CSF Inducing Immuno-Suppressive Myeloid Derived Suppressor Cells (MDSC)	Checkpoint Inhibitor Inducing Lymphopenia and MHC-I Loss
Safety Consistent with BCG	✓	X	✓	X
Durable Complete Response at >48 Months	✓	X	X	X
Cystectomy Avoidance ≥80% at 36-Months	✓	X	X	X
Ease of Administration Consistent with BCG Alone	✓	X	X	X
Logistics of Administration (Timing in clinic) Consistent with BCG Alone	✓	X	X	X
Logistics of Storage of Drugs 2-8 C°	✓	✓	X	✓

Source: ImmunityBio

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

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.

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).

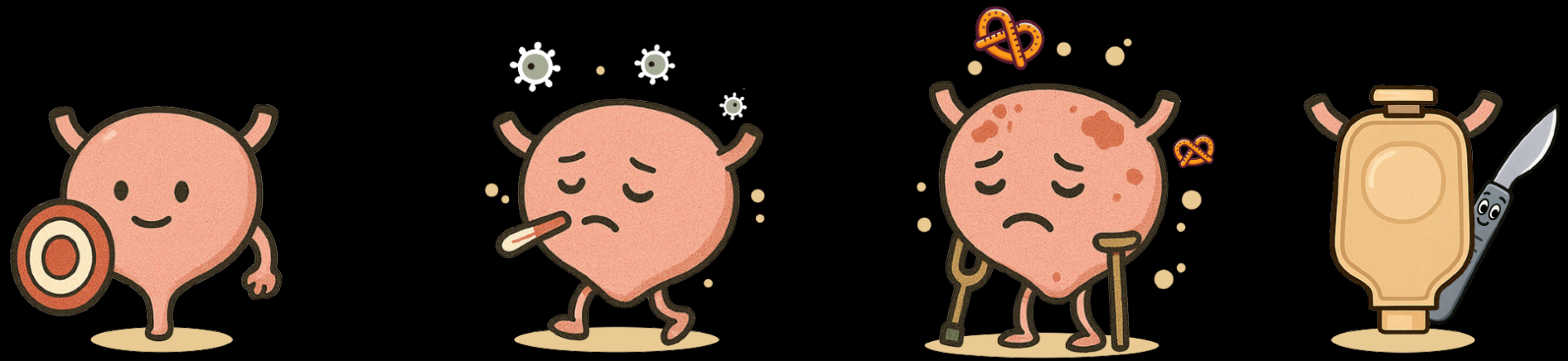
Nogapendekin alfa inbakicept-pmln in combination with BCG may be considered for the treatment of patients with BCG-unresponsive, high-risk NMIBC with CIS (with or without papillary) tumors. ?

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

Win the Battle, Win the War, Save the Bladder

The Bladder's Quantum State



Immune Protected Healthy Bladder

NK, T Cells, and Memory T Cells

Immune Compromised Bladder

GM-CSF Suppressor Neutrophils Myeloid Derived Suppressor Cells

Crippled Painful Bladder

Chemotherapy Lymphopenia

The Lost Bladder

Total Radical Cystectomy

Thank You

Patrick@ImmunityBio.com

The Power of ANKTIVA to Overcome Lymphopenia Through NK & Memory T Cells to Achieve Durable Responses in Urological Diseases - Duration Matters

Keynote Speaker:
Patrick Soon-Shiong, MBBCh, MSc, FRCS(C), FACS

ImmunityBio®