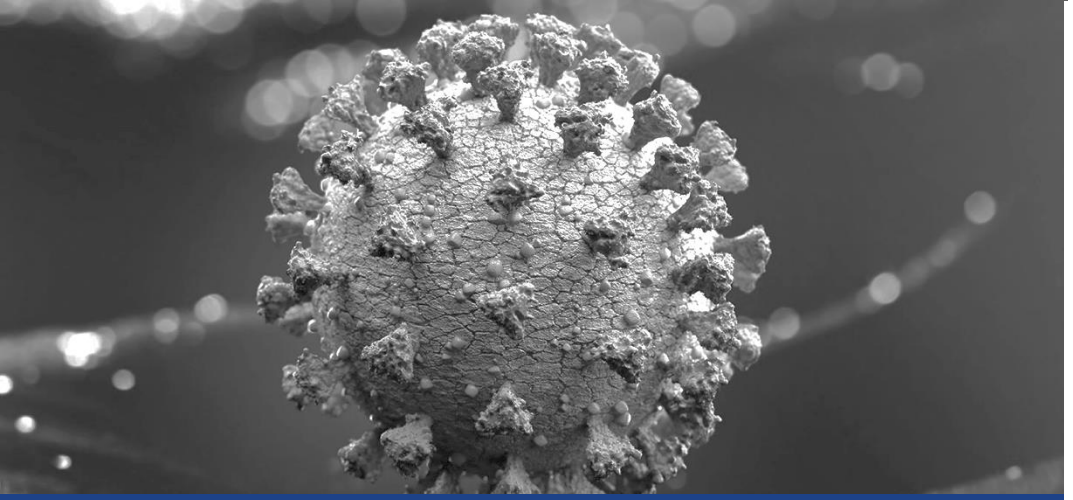
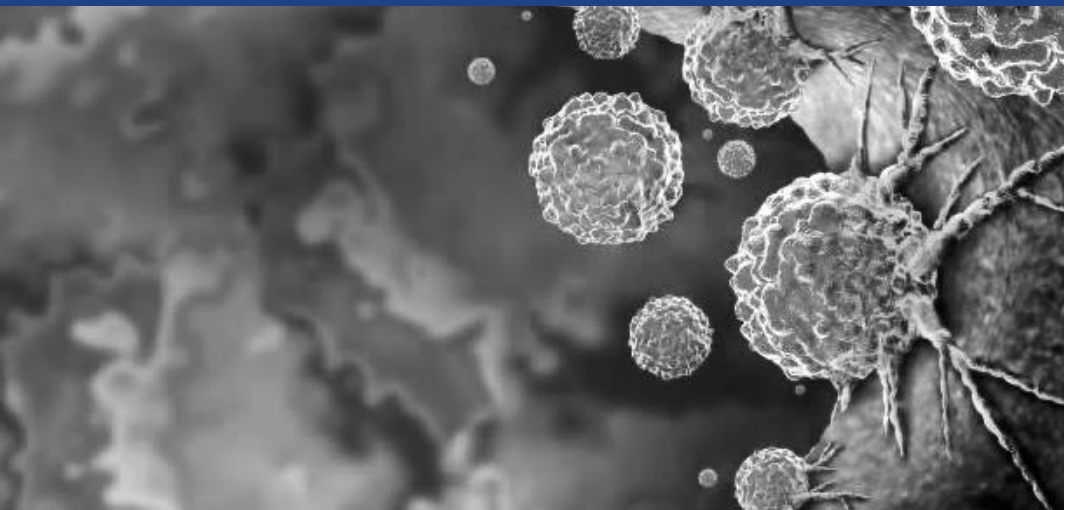


ImmunityBio®



ImmunityBio Investor Presentation

June 2024

Forward-Looking Statements and Intended Use

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 meetings, timelines and potential results therefrom, global expansion efforts, the collaboration between ImmunityBio and the Serum Institute of India 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 and review 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 the BG manufactured by Serum 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 19, 2024 and the Company's Form 10-Q filed with the SEC on May 9, 2024, 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.

This presentation is intended to provide a company overview and is intended for investor use only. It is not promotional and should not be used with patients or health care professionals.

Table of Contents

(nogapendekin alfa inbakicept-pmln)

ANKTIVA: FDA Approved
April 22, 2024

INDICATION AND USAGE

ANKTIVA is an interleukin-15 (IL-15) receptor agonist indicated with bacillus calmette-guérin (BCG) for the treatment of adult patients with BCG-unresponsive nonmuscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

IMPORTANT SAFETY INFORMATION

- **Warnings and precautions:** delaying cystectomy can lead to the development of metastatic bladder cancer, which can be lethal.
- **Contraindications:** none
- **Dosage and administration:** for intravesical use only. Instill intravesically only after dilution. Total time from vial puncture to the completion of the intravesical instillation should not exceed 2 hours.
- **Use in specific populations:** pregnancy: may cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.
- **Adverse reactions:** the most common (>15%) adverse reactions, including laboratory test abnormalities, are increased creatinine, dysuria, hematuria, urinary frequency, micturition urgency, urinary tract infection, increased potassium, musculoskeletal pain, chills and pyrexia.
- You are encouraged to report negative side effects of prescription drugs to FDA. Visit **www.Fda.Gov/medwatch** or call **1-800-332-1088.** You may also contact Immunitybio at **1-877-ANKTIVA (1-877-265-8482)**

ANKTIVA US Commercial Launch

ANKTIVA United States Commercial Launch

Commercial Product Readiness

- Labeling and Packaging Complete
- Shipping of First Commercial Product May 6th less than 2 weeks after approval
- Sufficient Inventory for 12 months

Distribution Readiness

- All three major Specialty Distributors, Contracts Executed and EDI Implemented Covering 99% of the US Market
  - Cardinal Health
  - Cencora (former AmerisourceBergen)
  - McKesson (Commercial and Government)

Ordering Readiness

- No Change in Ordering Practice
- Direct Drop Ship to Practice Location
- Stored Normal 2-8°C, no special freezers

ANKTIVA United States Commercial Launch (Contd.)

Commercial Salesforce Readiness

- 50+ Sales and Market Access Team hired, trained and certified
- 5 Regional Sales Area Business Directors with Seasoned Sales Experience in place

Marketing Events Readiness

- Launch with large booth presence at AUA conference San Antonio May 3-6, 2024
- Launch with large booth presence at ASCO conference Chicago May 31-June 4, 2024
- ThAnktiva Branding

Medical Education

- Chief Medical Officer and Global Chief Medical Officer
- 4 Medical Science Liaisons with seasoned experience in place

ANKTIVA United States Commercial Launch (Contd.)

Concentrated Urology Practices

- Discussions Initiated in the Past Year and Ongoing
- Key Opinion Leaders (KOLs) Discussions

Urology Practice Clinical Workflow

- Identical Schedule of dosing to BCG
- Identical Ordering as for BCG
- Simple Admixture of ANKTIVA and BCG with no special equipment or processes different from BCG administration
- Administration for up to 37 months

Urology Backoffice Ordering and Workflow

- Coding and Reimbursement Consistent with Current Workflow
- Pricing $35,800 per dose

No Change to Urology Practice Required

ANKTIVA United States Commercial Launch (Contd.)

No Change in Urology Order & BCG Administration Workflow

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

Specialty Distributors Readiness:

- ✓ Cencora (former AmerisourceBergen)
- ✓ Cardinal Health
- ✓ McKesson (Commercial and Government)

Patient Assistance Program

- ✓ Hub, Commercial Copay, Assistance Program
  ANKTIVA.com 1-877-ANKTIVA

ANKTIVA United States Commercial Launch (Contd.)

NCCN Guidelines in NMIBC – ANKTIVA Now Added

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2024
Non-Muscle Invasive Bladder Cancer

NCCN Guidelines Index
Table of Contents
Discussion

MANAGEMENT PER NMIBC RISK GROUP

AUA RISK GROUP (SEE BL-2)	INITIAL MANAGEMENT	FOLLOW-UP
Low	Surveillance[o]	Follow-up (BL-E) If prior BCG, maintenance BCG[p] (preferred)
Intermediate	Intravesical therapy[p,q] (preferred) or Surveillance	• Cytology positive • Imaging negative • Cystoscopy negative → BL-4
High: Bacillus Calmette-Guérin (BCG) naïve — Very-high-risk features[n]	Cystectomy (preferred) or BCG[p]	
High: Bacillus Calmette-Guérin (BCG) naïve — No very-high-risk features	BCG[p] (category 1, preferred) or Cystectomy	Cystoscopy positive → Reclassify AUA Risk Group and manage accordingly
High: BCG unresponsive or BCG intolerant	Cystectomy[r] (preferred) or Intravesical chemotherapy[p,s] or Pembrolizumab (select patients)[t] or Nadofaragene firadenovec-vncg (select patients)[u] or **Nogapendekin alfa inbakicept-pmln + BCG[v] (select patients)**	

May 15, 2024

Accessed: May 21, 2024
https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf

ANKTIVA United States Commercial Launch (Contd.)

Market Access and Reimbursement Readiness

- Compendia filing completed and accepted
- NCCN Guidelines updated to include ANKTIVA
- Payor discussions initiated and in progress
- Large healthcare groups discussions initiated and in progress

ImmunityBio Cares Patient Assistance Program Implemented

- Assist Patients and Practices to navigate their benefits
- Team of fully staff health care professionals, including nurses and case manager to support patients and Urology Practices
- Assistance with benefits question and process, including Benefits and Preauthorization
- Deploying ANKTIVA Co-Pay Assistance and Patient Assistance Program
  - Co-Pay Assistance can be as low as $100/dose
  - Patient Assistance Program offers free drug for patients based on their individual financial situation
- **ImmunityBio Cares Available 24/7 at 1 (877) ANKTIVA or ANKTIVA.com**

ANKTIVA United States Commercial Launch (Contd.)

Strong Cash Position

- $100 MM Non-dilutive Cash Infusion May 2024
- $240 MM Cash on Hand (as reported on investor call April 26, 2024)
- Commercial Launch on May 6th, 2024

ANKTIVA Global Regulatory Filing Status

Initiated Resources for Global Filing Utilizing FDA BLA Registration Documentation

Countries In Motion

- Canada
- United Kingdom
- Germany
- France
- Spain
- Italy

Anktiva®

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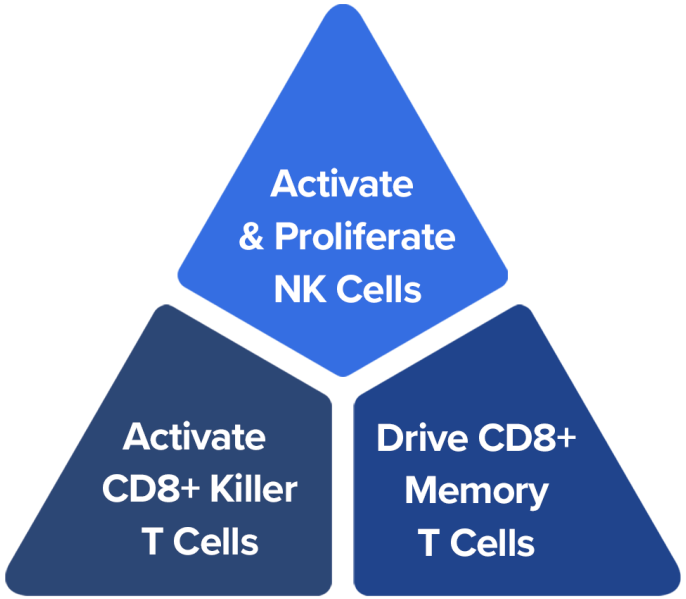


The Triangle Offense

Thank you to our patients, investigators and employees for their contributions

ANKTIVA Summary of Safety [1, 2, 3]

Safety and Tolerability Consistent with BCG Alone [2]

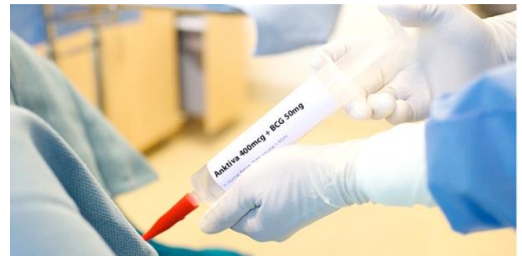
Anktiva®
(nogapendekin alfa inbakicept-pmln)

0% - 3.4%
Grade 3 & 4 Adverse Events [1]

0%
Grades 3 & 4* Dysuria, Urinary Frequency and Micturition Urgency [1]

0%
Treatment Related Grade 5 AEs [1, 3]

7%
Treatment Related Discontinuation [1]



The AE profile is consistent with PK results:
No systemic absorption with local intravesical administration [1]

Adverse reactions (≥5%) resulting in interruption with ANKTIVA plus BCG were UTI (10%), dysuria (8%), hematuria (6%), and bladder irritation (6%) [1]

The most common (≥15%) adverse reactions, including laboratory test abnormalities, were increased creatinine, dysuria, hematuria, urinary frequency, micturition urgency, urinary tract infection, increased potassium, musculoskeletal pain, chills and pyrexia. [1]

*Serious adverse reactions occurred in 16% of patients receiving Anktiva with BCG

1. ANKTIVA Package Insert. ImmunityBio, Inc. 2024. **2.** Chamie K, et al. IL-15 Superagonist NAI in BCG-Unresponsive Non-Muscle-Invasive Bladder Cancer. NEJM Evid. 2023 Jan;2(1): EVIDoa2200167. doi: 10.1056/EVIDoa2200167. **3.** One death reported due to a cardiac arrest that was unrelated to N-803 + BCG.

ANKTIVA Summary of Efficacy

BCG Unresponsive Non-Muscle Invasive Bladder Cancer

Duration of Complete Response

47+ Months and Ongoing[1]

Recommended Duration of Treatment

37 Months[1]

Maintenance Therapy

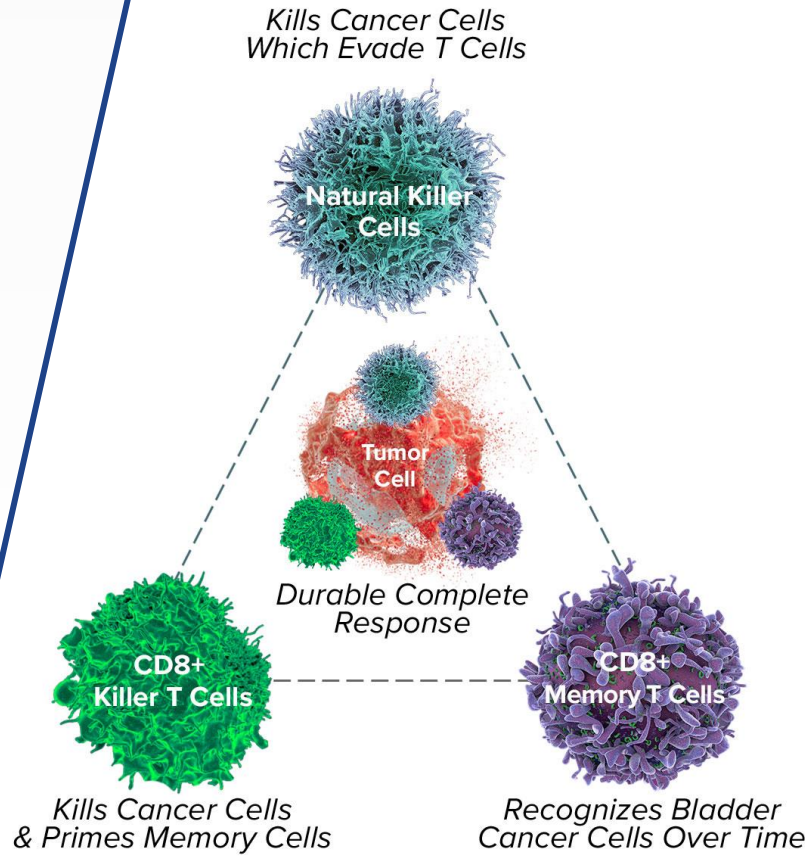
3 Years[1]

Complete Response

62%[1] N=77

72%[2] N=82

Ongoing N=100



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ANKTIVA Recommended Duration of Treatment 37 Months

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

For Intravesical Use Only. Do NOT administer by subcutaneous or intravenous or intramuscular routes.

- For induction: ANKTIVA is recommended at a dose of 400 mcg administered intravesically with BCG once a week for 6 weeks. A second induction course may be administered if complete response is not achieved at month 3.
- For maintenance: After BCG and ANKTIVA induction therapy, ANKTIVA is recommended at a dose of 400 mcg administered intravesically with BCG once a week for 3 weeks at months 4, 7, 10, 13 and 19 (for a total of 15 doses). For patients with an ongoing complete response at month 25 and later, maintenance instillations with BCG may be administered once a week for 3 weeks at months 25, 31, and 37 for a maximum of 9 additional instillations.

The recommended duration of treatment is until disease persistence after second induction, disease recurrence or progression, unacceptable toxicity, or a maximum of 37 months.

1. ANKTIVA Package insert. ImmunityBio, Inc.; 2024

ANKTIVA Durability of Response

Efficacy Profile

Complete Response [1, 2]

62% n=77 [1] (FDA Efficacy Population)

71% n=82 [2] (NEJM)

Cystectomy Free Rate at 24 Months [3, 4]

81% n=77 [3, 4]

Overall Survival at 24 Months [3, 4]

94% n=77 [3, 4]

Prolonged Duration of Response

Range of Duration of Response [1]

47+ Months & Ongoing n=77 [1]

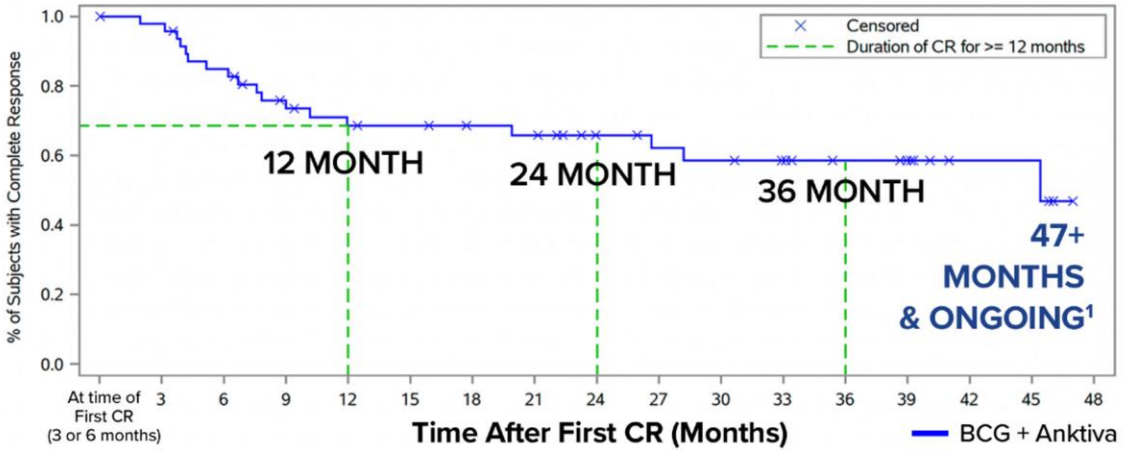
% with duration ≥ 12 months [1]

58% Of Responders [1]

% with duration ≥ 24months [1]

40% Of Responders [1]

Kaplan Meier (KM) Duration of Complete Response (N=77) [3, 4]



KM Duration of Complete Response [3, 4]

12 Month DoR 69%
95% CI: (53, 80)

24 Month DoR 66%
95% CI: (50, 78)

36 Month DoR 59%
95% CI: (41, 72)

Median Duration of Complete Response Not Determined to Date With Range of Duration of CR of 47+ Months Still Ongoing [1, 3, 4]

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(nogapendekin alfa inbakicept-pmln)

Maintenance Doses Approved for Responders [1]
3 Years

Intravesical Administration

Administration of ANKTIVA with BCG maintains the same favorable workflow and schedule as that of BCG in the urology practice environment.

1. ANKTIVA Package insert. ImmunityBio, Inc.; 2024. **2.** Chamie K, et al. IL-15 Superagonist NAI in BCG-Unresponsive Non-Muscle-Invasive Bladder Cancer. NEJM Evid. 2023 Jan;2(1): EVIDoa2200167. doi: 10.1056/EVIDoa2200167. **3.** Data on File, Supplemental Sponsor Data. **4.** P. Soon-Shiong, Oral Presentation (MP16-03) AUA May 2024 Presentation.

ANKTIVA Quality of Life

UROLOGY PRACTICE®
www.auajournals.org/journal/urpr

UPJ Insight

Quality of Life in the Phase 2/3 Trial of N-803 Plus Bacillus Calmette-Guérin in Bacillus Calmette-Guérin–Unresponsive Nonmuscle-Invasive Bladder Cancer

Karim Chamie, Sam S. Chang, Eugene V. Kramolowsky, et al.

Correspondence: Patrick Soon-Shiong (Patrick@immunitybio.com).

Full-length article available at https://doi.org/10.1097/UPJ.0000000000000517.

Study Need and Importance: To address the need for safe, efficacious, standard of care therapy for bacillus Calmette-Guérin (BCG)–unresponsive nonmuscle-invasive bladder cancer (NMIBC), the phase 2/3 study QUILT-3.032 was conducted to assess the ability of the investigational IL-15RαFc superagonist N-803 plus BCG to elicit complete responses (CRs) in this patient population. We previously reported a CR rate of 71% in cohort A patients with carcinoma in situ with or without Ta/T1 disease, with a median duration of 26.6 months and a disease-free survival rate of 55.4% at 12 months for cohort B patients with high-grade Ta/T1 papillary NMIBC.

What We Found: Here, we describe patient-reported outcomes based on EORTC (European Organization for Research and Treatment of Cancer) Core 30 and Quality of Life (QoL) NMIBC-Specific 24 questionnaires, revealing the stability of participant QoL on study, including both global health (GH) and physical function summary scores from the EORTC Core 30. Not unexpectedly, patients who achieved a CR maintained higher GH and physical function summary scores, and a greater number (>3) of transurethral resections of bladder tumor was associated with lower GH scores as compared with ≤ 3 transurethral resections of bladder tumor (Figure). Answers to the NMIBC-specific questions in the QoL NMIBC-Specific 24 questionnaire suggest a difference in concerns in patients with less advanced disease in cohort A, who reported changes in sexual function and activity, as compared to those with the more progressed high-grade papillary disease in cohort B, who appeared to focus more on future worries and intravesical treatment issues.

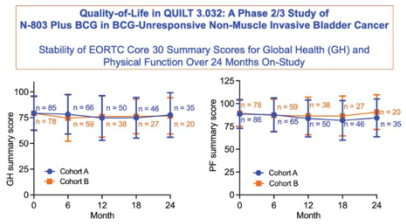
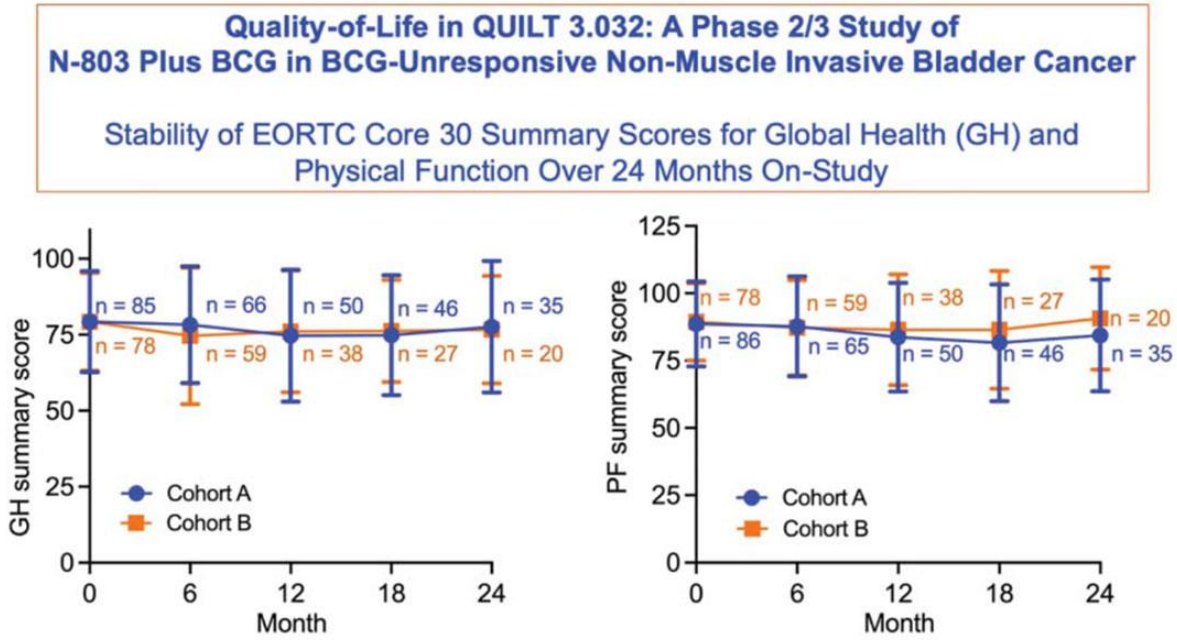


Figure. Global health (GH) and physical function (PF) summary scores. GH (A) and PF (B) 390 summary scores for all participants in cohorts A and B. N numbers at each time point are color-coded. Data are graphed as mean and SD. BCG indicates bacillus Calmette-Guérin; EORTC, European Organization for Research and Treatment of Cancer.

Limitations: The single-arm design of QUILT-3.032, used based on the known futility of BCG monotherapy in BCG-unresponsive patients, might be considered a limitation.

Interpretation for Patient Care: The favorable risk-benefit ratio for this novel combination therapy, including a CR rate in cohort A that is higher than those for other currently Food and Drug Administration–approved therapies for this indication and reasonable safety, suggests intravesical N-803 plus BCG has potential to provide an efficacious therapeutic option for BCG-unresponsive NMIBC patients.



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Chamie K, Chang SS, Kramolowsky EV, Gonzalgo ML, Huang M, Bhar P, Spilman P, Sender L, Reddy SK, Soon-Shiong P. Quality of Life in the Phase 2/3 Trial of N-803 Plus Bacillus Calmette-Guérin in Bacillus Calmette-Guérin–Unresponsive Nonmuscle-Invasive Bladder Cancer. Urol Pract. 2024 Mar;11(2):367-375. doi: 10.1097/UPJ.0000000000000517. Epub 2024 Jan 16. PMID: 38226931.

ANKTIVA Mechanism of Action

How ANKTIVA Converts a Cold MHC-I Negative Bladder Cancer Cell to a Hot MHC-I Positive Tumor and Rescues Killer T Cells and Memory T Cells[1,2]

1. Modified From: Garrido F, Aptsiauri N. Cancer immune escape: MHC expression in primary tumors versus metastases. Immunology. 2019 Dec;158(4):255-266. doi: 10.1111/imm.13114. Epub 2019 Oct 1. PMID: 31509607; PMCID: PMC6856929.
2. ANKTIVA Package insert. ImmunityBio, Inc.; 2024

ANKTIVA Mechanism of Action

Activation and Proliferation of NK, CD4+, CD8+ Killer & Memory T Cells, Without Proliferation of Immuno-Suppressive T Regulatory Cells

12 CLINICAL PHARMACOLOGY

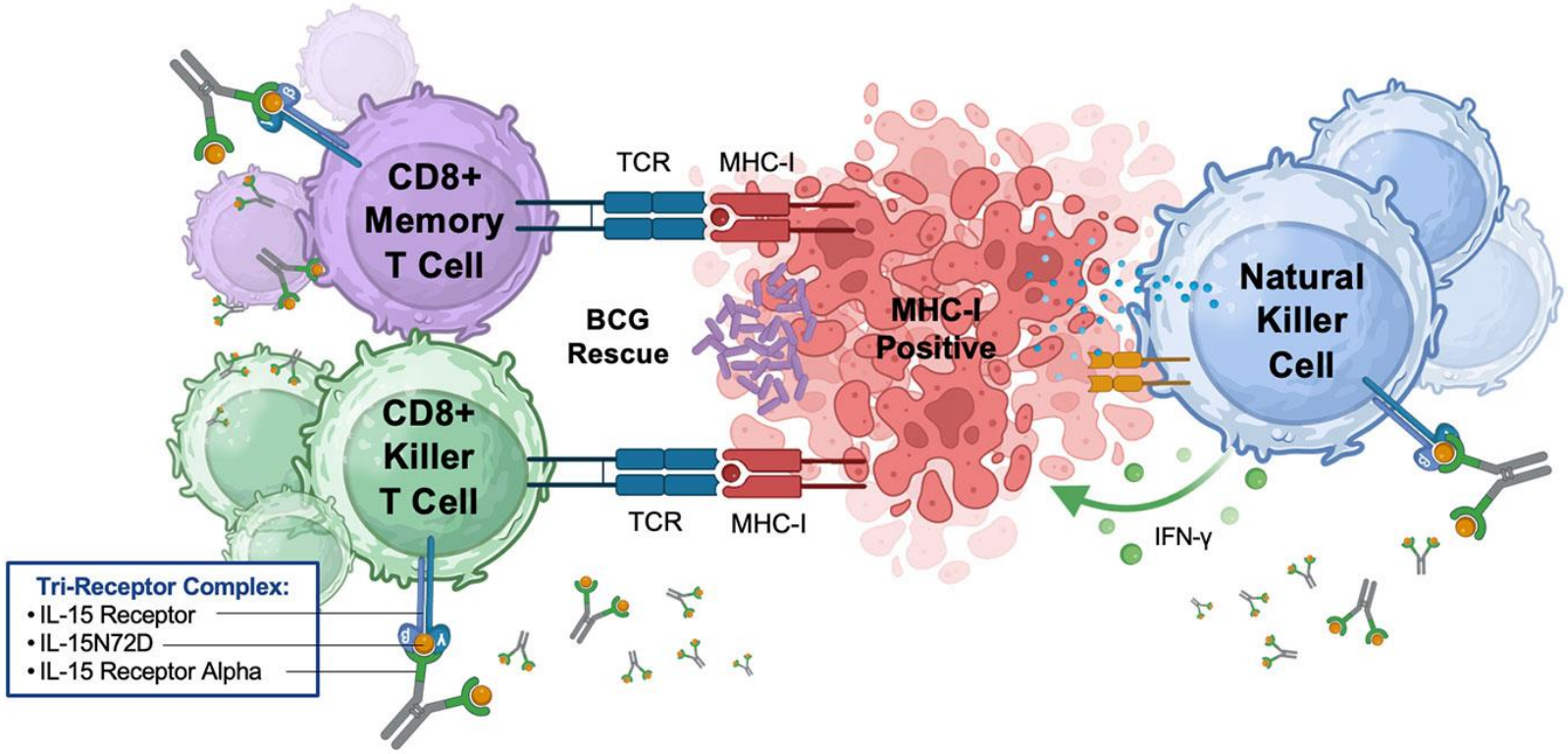
12.1 Mechanism of Action

Nogapendekin alfa inbakicept-pmln is an IL-15 receptor agonist. IL-15 signals through a heterotrimeric receptor that is composed of the common gamma chain (γc) subunit, the beta chain (βc) subunit, and the IL-15-specific alpha subunit, IL-15 receptor α. IL-15 is *trans*-presented by the IL-15 receptor α to the shared IL-2/IL-15 receptor (βc and γc) on the surface of $CD4^+$ and $CD8^+$ T cells and NK cells.

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. In vivo, intravesicular nogapendekin alfa inbakicept-pmln alone or in combination with BCG showed anti-tumor activity when compared to BCG alone, in a carcinogen-induced model of bladder cancer in immunocompetent rats.

1. ANKTIVA Package insert. ImmunityBio, Inc.; 2024

ANKTIVA Mechanism of Action
Rescue of BCG in NMIBC

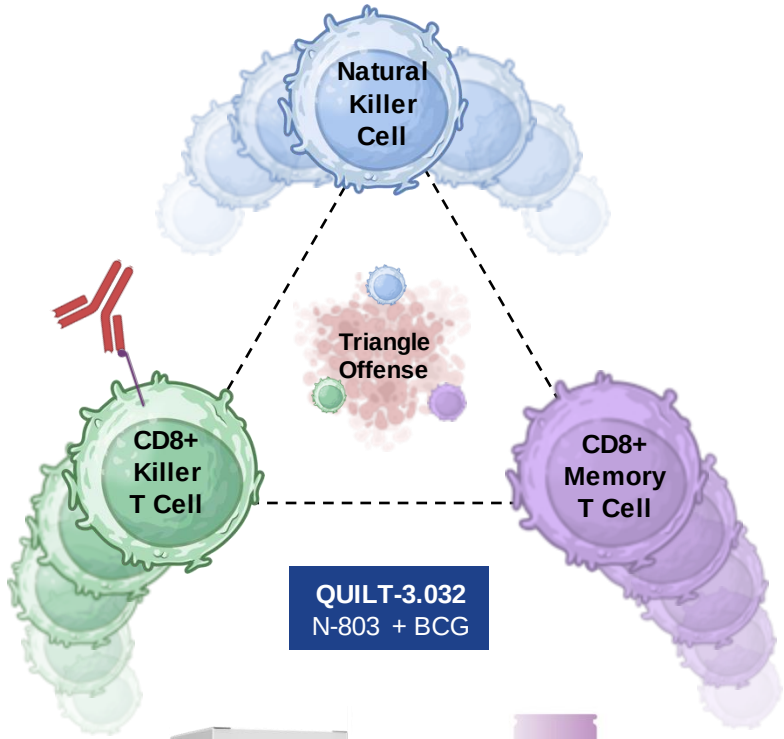


Immunogenic Cell Death by N-803 in the Triangle Offense: The Three Steps to Transforming the MHCscore™

- **Step 1:** Conversion of MHC Negative (Cold) to MHC Positive Tumor (Hot)
- **Step 2:** Activation of IL-15 Receptor in Killer NK and T Cells
- **Step 3:** Proliferation of NK, CD8+ Killer, and CD8+ Memory Cells

1. ANKTIVA Package insert. ImmunityBio, Inc.; 2024 **2.** Garrido F, Aptsiauri N. Cancer immune escape: MHC expression in primary tumors versus metastases. Immunology. 2019 Dec;158(4):255-266

Triangle Offense

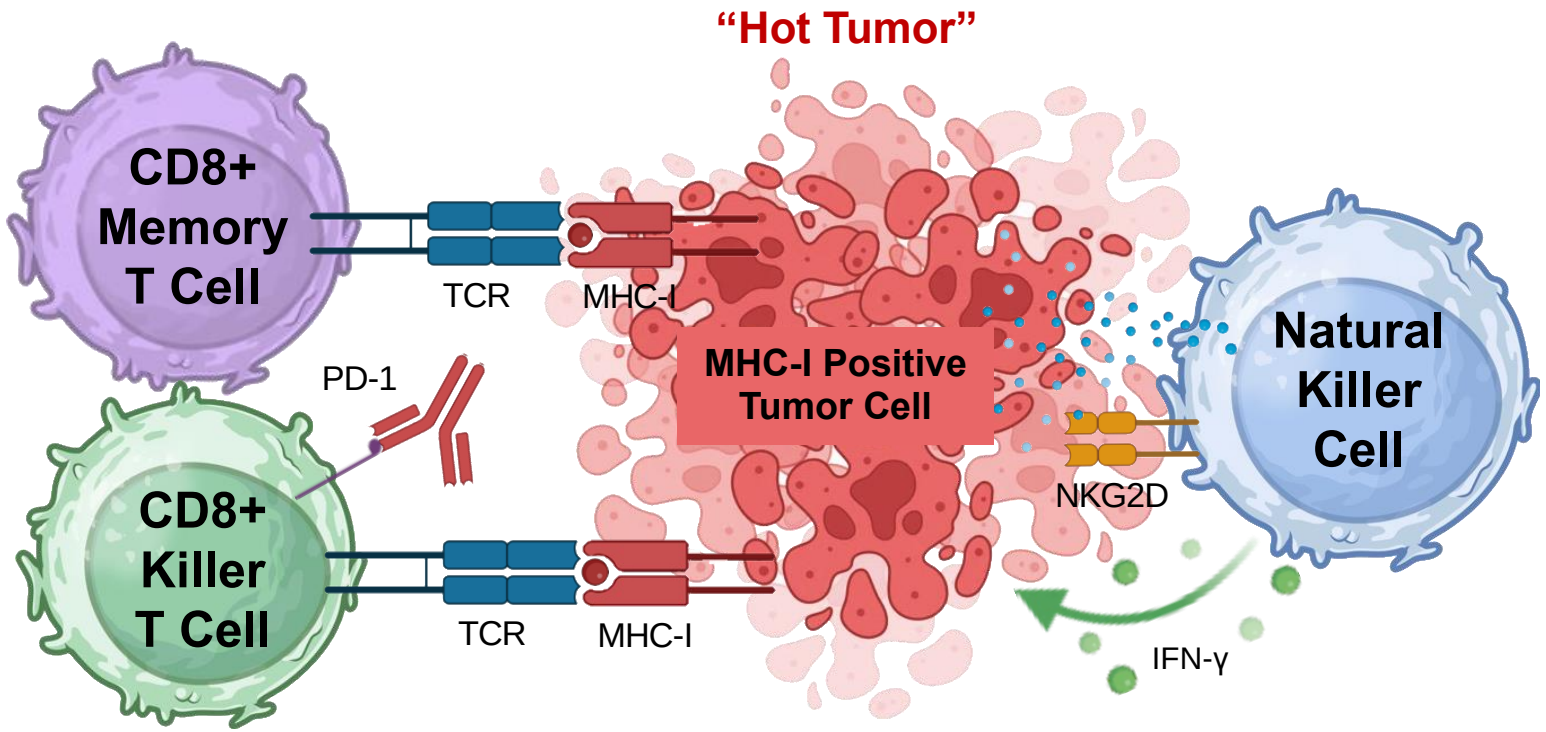


QUILT-3.032
N-803 + BCG

Long Term, Cancer Free Overall Survival
BCG Unresponsive in NMIBC: 47+ Months and Ongoing

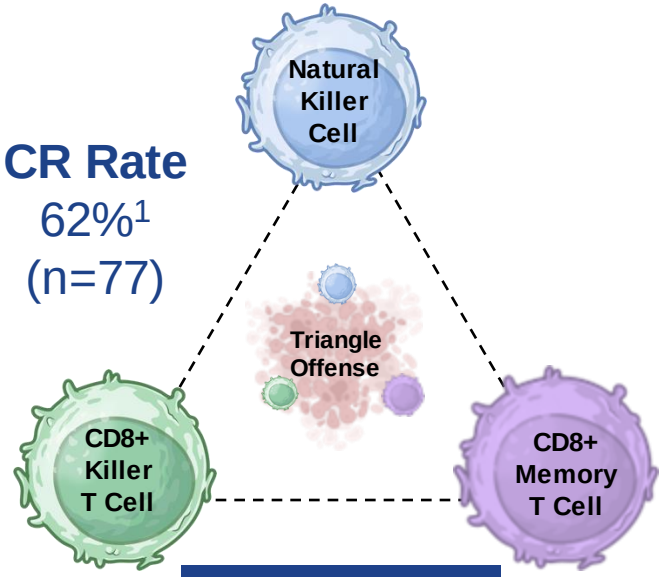
ANKTIVA Mechanism of Action (Contd.)
Rescue of BCG in NMIBC

CD8+ Killer T Cell and CD8+ Memory T Cell
Re-Activated and BCG / Checkpoint Inhibitor Rescued[1, 2, 3]



CD8+ Killer T Cell and CD8+ Memory Killer T Cells Re-Engages Tumor with Tumor Specific T Cells[1, 2]

Triangle Offense



QUILT-3.032
ANKTIVA + BCG

Long Term, Cancer Free Overall Survival
BCG Unresponsive in NMIBC: 47+ Months and Ongoing[1, 4]

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ANKTIVA Mechanism of Action (Contd.)

Power of IL-15 Receptor Alpha / IL-15 to Achieve Durable Complete Response

- **International Bladder Cancer Group (IBCG) Benchmark Expectations**
  - 30% at 12 Months[1]
  - 25% at 18 Months[1]
- **IBCG believed that this was a high bar for duration of response and unlikely to be achieved**
- **ANKTIVA duration of response exceeds this bar**
  - 58% at 12 months[2]
  - 40% at 24 months[2]
- **The mechanism of action to achieve a prolonged durable complete response is by activation of the IL-15 receptor on NK, Killer T and Memory T cells[2]**
- **The power of IL-15 receptor alpha / IL-15 from ANKTIVA (mimicking the dendritic cell) resulting in activation and proliferation of the killer and memory cells[2]**

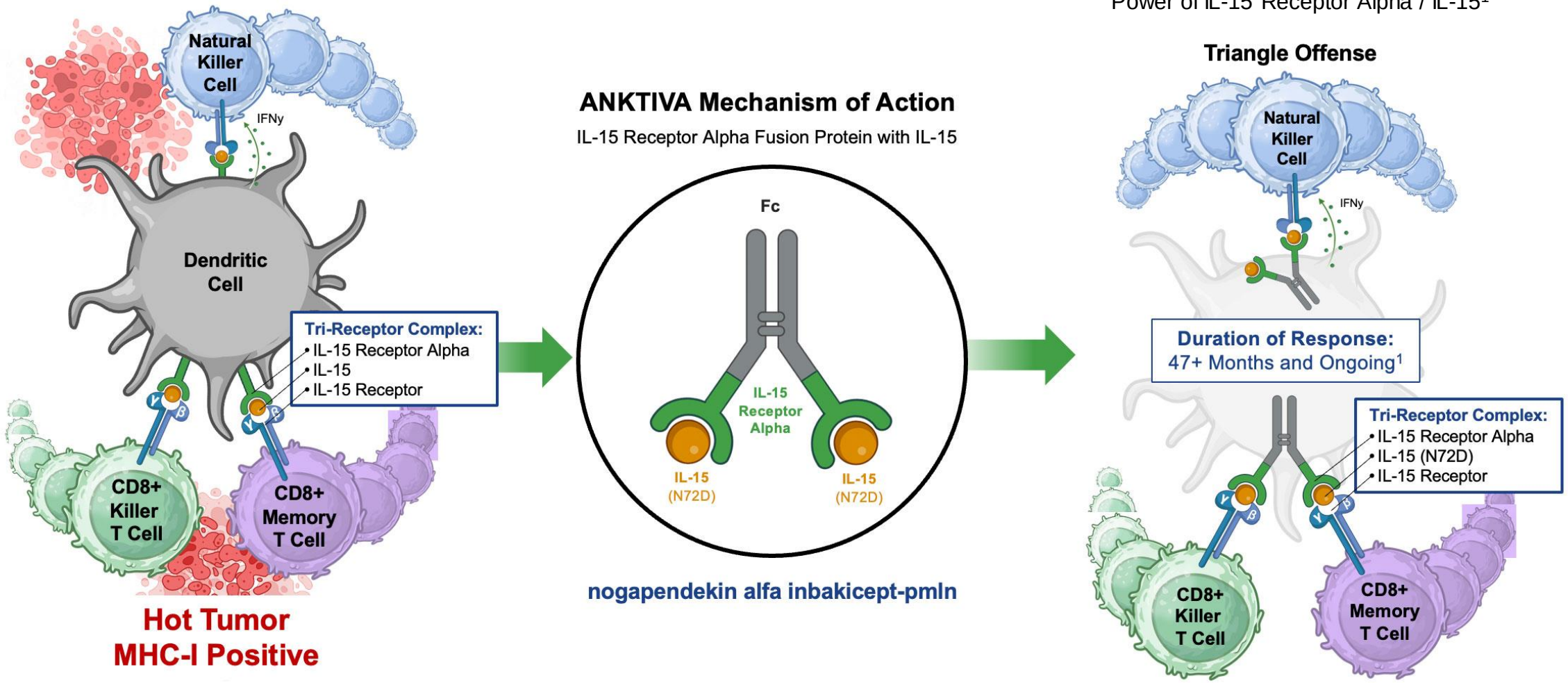
1. Kamat A, et al. Definitions, End Points, and Clinical Trial Designs for Non–Muscle-Invasive Bladder Cancer: Recommendations From the International Bladder Cancer Group. J Clin Oncol 34:1935-1944. **2.** ANKTIVA Package insert. ImmunityBio, Inc.; 2024

ANKTIVA Mechanism of Action (Contd.)

IL-15 Receptor Alpha / IL-15 Mimics a Dendritic Cell to Induce Proliferation of Immune Killer Cells[1]

IL-15 Receptor Alpha / IL-15 From a Dendritic Cell Proliferates NK, Killer and Memory T Cells via IL-15 Receptor[1]

ANKTIVA Mechanism of Action Mimicking the Activity of an Activated Dendritic Cell to Proliferate Killer Cells with the Power of IL-15 Receptor Alpha / IL-15[1]



1. ANKTIVA Package insert. ImmunityBio, Inc.; 2024 **2.** 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

ANKTIVA BCG Naïve Clinical Data

ANKTIVA in the NMIBC BCG Naïve Setting

Complete Responses in CIS and Papillary BCG Naïve NMIBC Patients

Duration of Complete Response and Disease Free in 9 out of 9 (100%) at Time of Publication with Follow-Up for 6 Years After Treatment

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

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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]

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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-naïve 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-naïve). 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

>6 Year Follow-Up

ANKTIVA in the NMIBC BCG Naïve Setting

QUILT-205 Trial: Long Term Follow-Up Beyond 6 Years in 6 out of 9 Evaluable Patients

QUILT-205 Findings[1, 2]

- 6 out of 9 were evaluable in 2023
- 2 subjects died of natural causes independent of bladder cancer
- 1 lost to follow up
- Quality of life high in all 6 subjects
- All 6 out of 6 (100%) remain in complete response (CIS) or disease free (Papillary) for >8.5 years
- All 6 patients avoided cystectomy for >8.5 years

As of 2023

6 out of 6 (100%) Remain Disease Free

≥8.5 Years

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

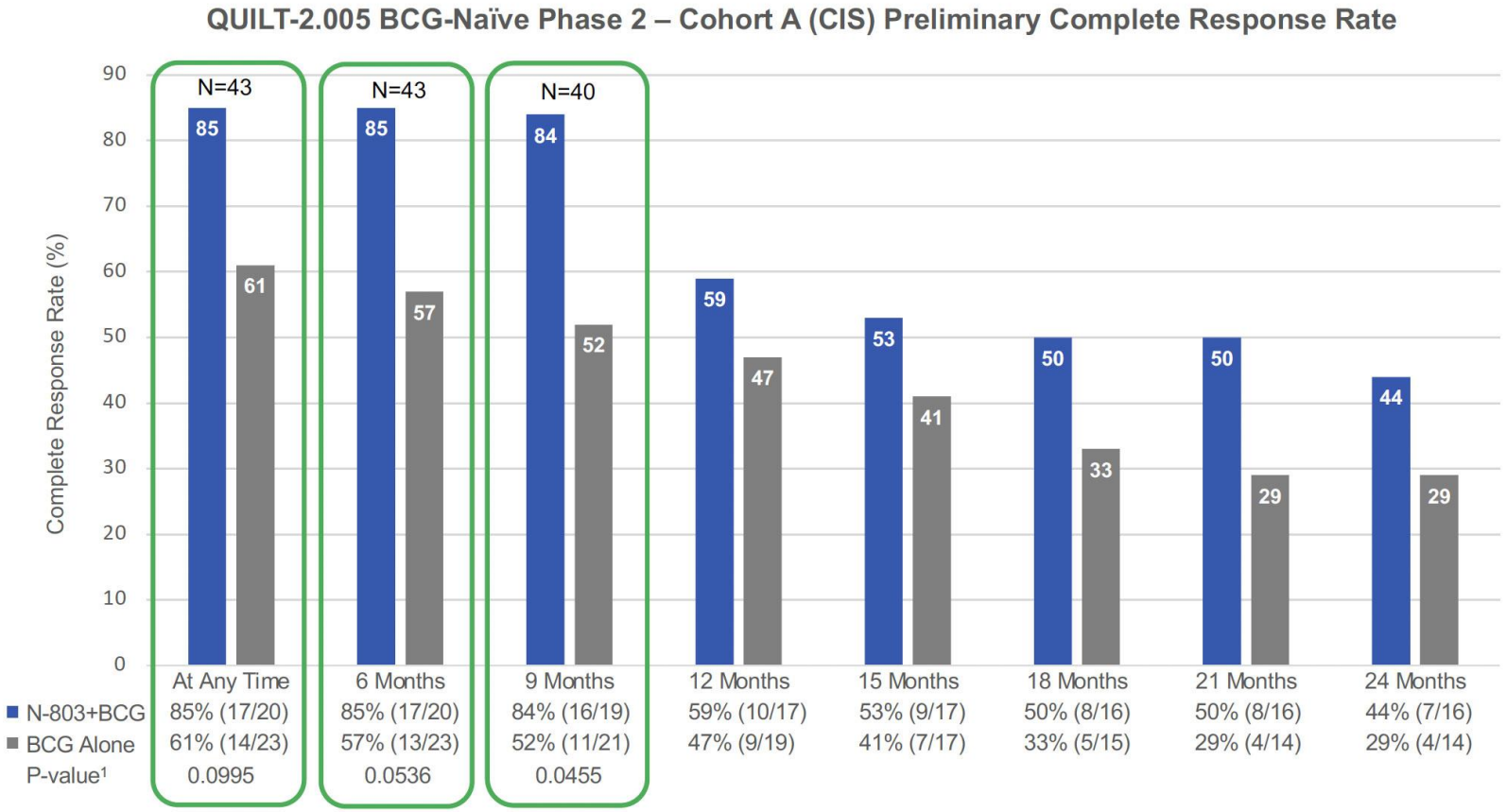
1. Adapted From Rosser CJ, et al., Safety, Tolerability, and Long-Term Clinical Outcomes of an IL-15 analogue (N-803) Admixed with Bacillus Calmette-Guérin (BCG) for the Treatment of Bladder Cancer. Oncoimmunology. 2021 May 2. Data on File

ANKTIVA in the NMIBC BCG Naïve Setting

- Complete response rate of 85% with BCG and ANKTIVA versus 61% at any time
- Duration of response statistically significant at 9 months at 84% versus 52%
- Continued trend of long duration of response at 12, 15, 18, 21 and 24 months when ANKTIVA is combined with BCG

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

Improvement of CR Rate Over Time and Contribution of Effect of N-803 Inducing Memory T Cells



[1] Based on Fisher's Exact Test.

1. BLA Submission on File 2024

BCG Supply - ImmunityBio-Serum Institute of India

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)

For More Information for Investigators:
QUILTBCG@ImmunityBio.com

ImmunityBio Pipeline

May 2024

Select Clinical Development Pipeline

ImmunityBio

Tumor	Indication	Regimen	Development Stage
Non-Muscle Invasive Bladder Cancer (NMIBC)	BCG Unresponsive NMIBC	ANKTIVA + BCG	**Approved[1]**
	BCG Naïve NMIBC	ANKTIVA + BCG	Pivotal Trial Recruiting
	BCG Replacement NMIBC	ANKTIVA + iBCG[2]	Planned
Prostate	Neoadjuvant & Adjuvant Post Prostatectomy Active Surveillance	ANKTIVA + M-ceNK + TELs	Phase I Planned
Lung	Non-Small Cell Lung Cancer (NSCLC) 2nd Line or Greater	ANKTIVA + PD1 CPI	Phase II Completed **FDA Type B Meeting June 2024**
	Non-Small Cell Lung Cancer (NSCLC) 1st Line	ANKTIVA + PD1 CPI	Phase III Ongoing
	Small Cell Lung Cancer (SCLC) 1st Line	ANKTIVA + M-ceNK	Phase II Planned
Colon	Lynch Syndrome: Prevention of Cancer (NIH/NCI)	ANKTIVA + TriAd	Phase II Recruiting
	3rd Line Colon Cancer	ANKTIVA + TriAd	Phase II Completed (Ad5 CEA Only) Phase II Planned (Combo)
Ovarian	2nd Line Platinum Resistant Ovarian Cancer	ANKTIVA + M-ceNK	Phase II Planned
Cervical	HPV+ 1st and 2nd Line Cervical Cancer	ANKTIVA + Ad5 HPV	Phase I Sites Initializing
Head & Neck	HPV+ / HPV- 2nd Line Head & Neck Cancer	ANKTIVA + Ad5 HPV	Phase I Sites Initializing
	HPV+ / HPV- 1st Line Head & Neck Cancer	ANKTIVA + Autologous M-ceNK + TELs	Phase I Planned
Brain	2nd Line Glioblastoma	ANKTIVA + PD-L1 t-haNK + Avastin	Phase I Sites Enrolling

1. FDA Approval of ANKTIVA with BCG for the treatment of adult patients with BCG-unresponsive NMIBC with carcinoma in situ with or without papillary tumors **2.** In Collaboration with Serum Institute of India (SII) & ImmunityBio

BCG: Bacillus Calmette-Guérin, **iBCG:** Recombinant BCG, **PD1**: Programmed-Cell Death Protein 1, **M-ceNK**: Memory Cytokine Enhanced Natural Killer, **TELs**: Tumor Educated Lymphocytes, **CPI**: Checkpoint Inhibitor, **TriAd**: Triple Antigen (CEA, MUC1, Brachyury) Adenovirus, **Ad5:** Adenovirus Type 5, **HPV:** Human Papillomavirus, **PD-L1 t-haNK:** Programmed Death-Ligand 1 Targeted High-Affinity Natural Killer Cell

Thank You

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Appendix

AUA 2024

ANK-00096-US

Click for Video

A Deep Dive with Patrick Soon-Shiong: Next-Generation Immunotherapy for NMIBC

AUA2024 San Antonio MAY 3-6

Friday, May 3, 2024

April 22, 2024

ImmunityBio Announces FDA Approval of ANKTIVA®, First-in-Class IL-15 Receptor Agonist for BCG-Unresponsive Non-Muscle Invasive Bladder Cancer

- Designated an FDA Breakthrough Therapy, the novel immunotherapy ANKTIVA activates the body's natural killer (NK) and killer T-cell immune system to attack tumor cells
- Therapy stimulates memory T cells, leading to long duration of complete response exceeding 47 months and ongoing to date, with a median duration of response yet to be determined
- The percentage of patients with durable responses at 12 and 24 months exceeded the benchmark for magnitude of clinically meaningful results established by experts at the International Bladder Cancer Group (IBCG)
- ANKTIVA in combination with BCG is approved for maintenance therapy for up to 37 months with tolerable side effects ranging from 0% to 3% Grade 3/4 adverse events
- ANKTIVA is expected to be available in the U.S. by mid-May 2024
- Conference call and webcast are expected to be held April 26 at 11:00 am EDT

May 7, 2024

ImmunityBio Completes GMP Drug Substance Manufacturing Sufficient for 170,000 Doses of ANKTIVA®

May 07, 2024 08:00 AM Eastern Daylight Time

- ANKTIVA® Drug Substance completed and released with two-year storage stability data sufficient for 170,000 doses of ANKTIVA product
- ImmunityBio's 400,000 square foot GMP fill-finish facility in Dunkirk, New York on track to be completed in 12-18 months with capacity to produce a million vials annually
- Coupled with a recent announcement of BCG availability in partnership with the Serum Institute of India (SII), ImmunityBio has large-scale inventory and capacity for BCG

Preparation and Administration

2.2 Preparation and Administration

Preparation of Agent

See BCG Prescribing Information for information on preparation and handling of BCG.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The solution is clear to slightly opalescent and colorless to slightly yellow. Discard the vial if visible particles are observed.

Draw 0.4 mL of ANKTIVA into a small syringe and using aseptic technique add to the saline containing the BCG suspension that has been prepared following the instructions provided in the Prescribing Information for BCG. Mix the suspension gently. Using a 60-mL syringe connected to an appropriate size needle, withdraw the ANKTIVA BCG mixture to a final volume of 50 mL.

If the admixture of ANKTIVA in combination with BCG is not used immediately, store refrigerated at 2°C to 8°C (36°F to 46°F) and use within 2 hours. Unused solution of admixture should be discarded after 2 hours.

Treatment

The admixture of ANKTIVA in combination with BCG is instilled into the bladder via a catheter. After instillation is complete, the catheter is removed. The ANKTIVA in combination with BCG admixture is retained in the bladder for 2 hours and then voided. Patients unable to retain the suspension for 2 hours should be allowed to void sooner, if necessary. Do not repeat the dose if the patient voids before 2 hours.

1. ANKTIVA Package insert. ImmunityBio, Inc.; 2024

ANKTIVA Efficacy Results with Duration of Response

47+ Months and Ongoing

Table 3: Efficacy Results in QUILT-3.032

	ANKTIVA with BCG (n=77)
Complete Response Rate (95% CI)	62% (51, 73)
Duration of Response[a]	
Range in months	0.0, 47.0+
% (n) with duration ≥ 12 months	58% (28)
% (n) with duration ≥ 24 months	40% (19)

+ Denotes ongoing response

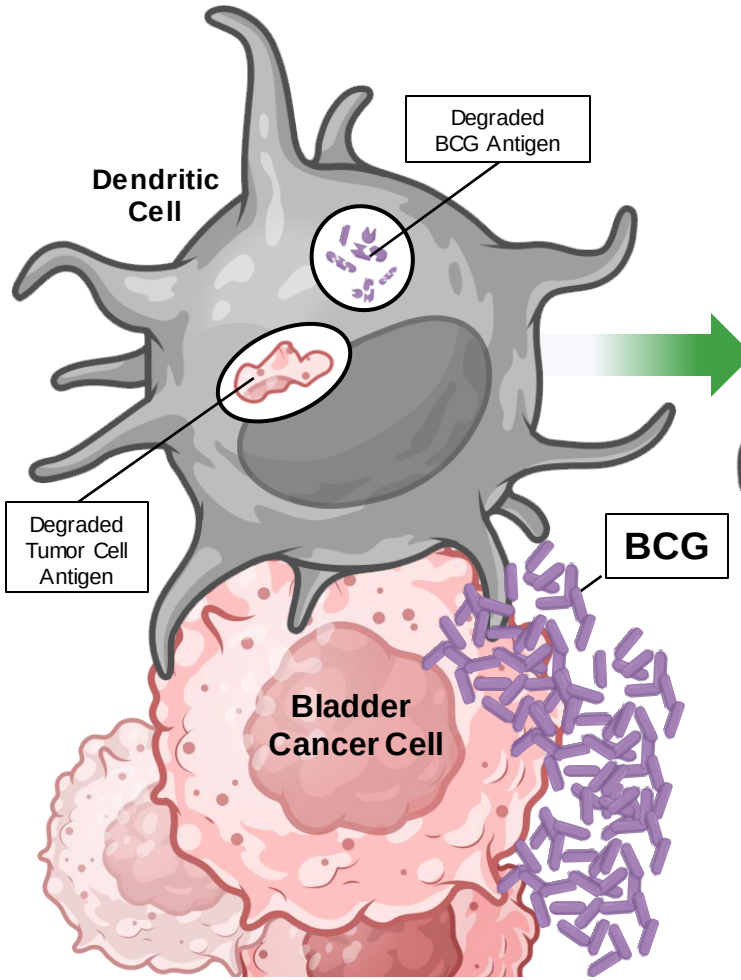
[a] Based on 48 patients that achieved a complete response at any time; reflects period from the time complete response was achieved.

1. ANKTIVA Package insert. ImmunityBio, Inc.; 2024

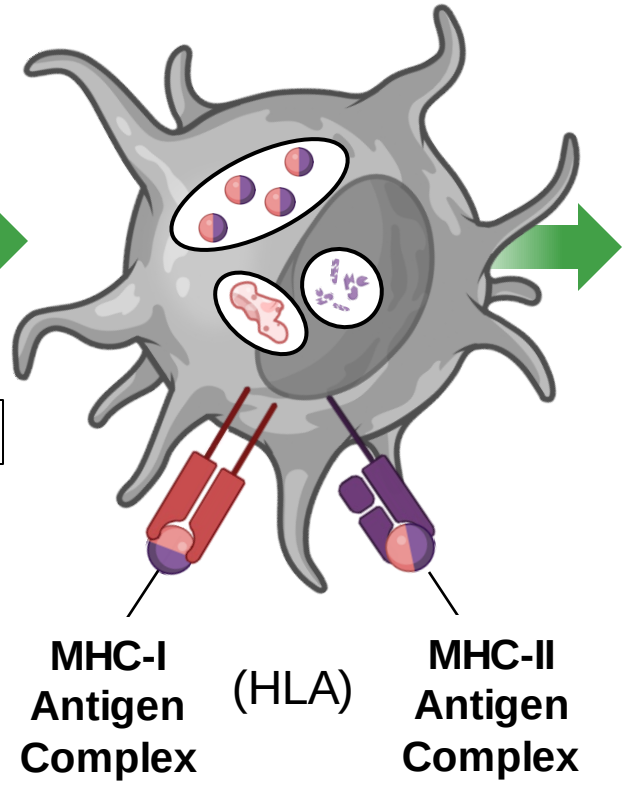
Bladder Cancer Specific Activation of Dendritic Cell for MHC-I and MHC-II Antigen Presentation

Activation of DC with PAMPs and DAMPs → **Presentation of Tumor Antigen via MHC-I and MHC-II Restriction** → **Cell-to-Cell Contact via MHC-I and MHC-II with T Cell Receptors**

Phagocytosis of BCG and Bladder Tumor Cell by DC[1]

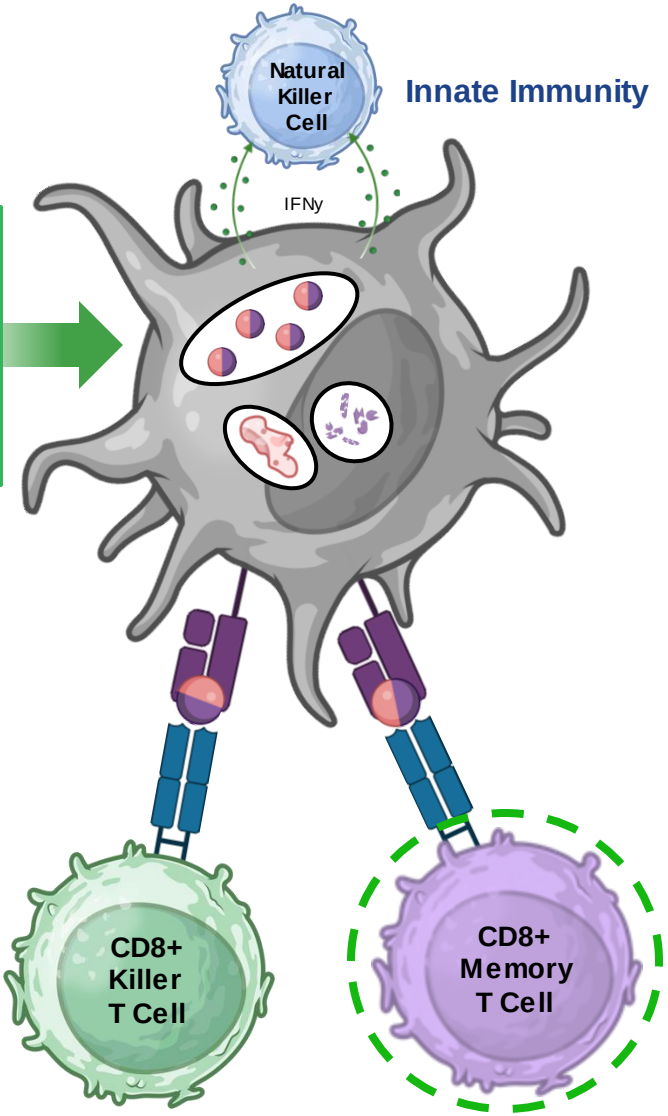


MHC-I and MHC-II Presentation of Tumor Antigens and Activation of NK Cells[2, 3, 4, 5]



Trained Immune Memory of CD8+ Killer T Cell to BCG Infected Bladder Cancer Cell[1]

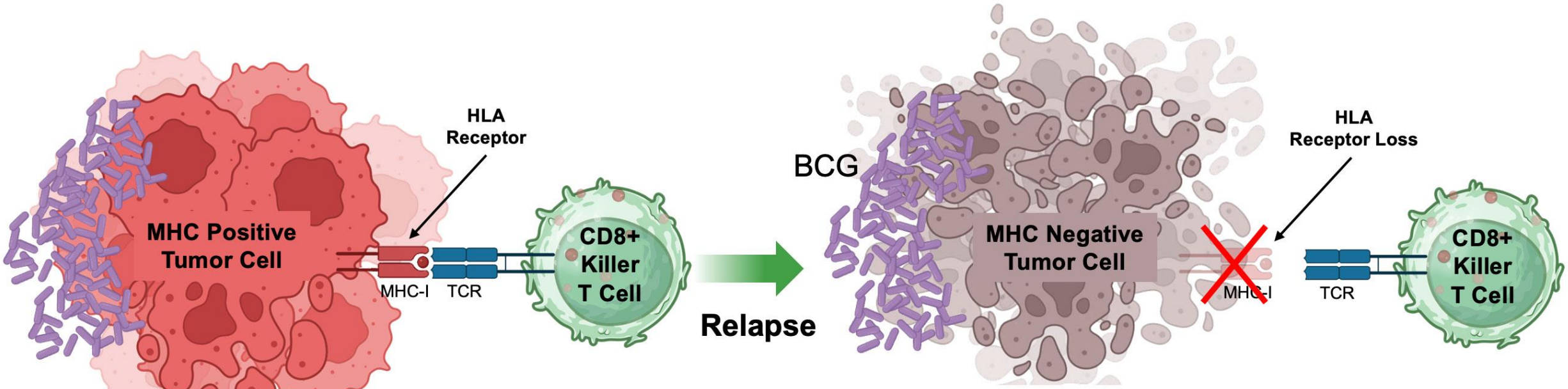
Education of CD8+ CD4+ T cells and Activation of NK Cells[1, 2, 6]



1. Van Puffelen et al, Trained Immunity as a Molecular Mechanism for BCG Immunotherapy in Bladder Cancer. Nat Rev Urol. 2020 2. ANKTIVA Package insert. ImmunityBio, Inc.; 2024 3. Gil-Julio H et al, Tumor Escape Phenotype in Bladder Cancer Is Associated with Loss of HLA Class I Expression, T-Cell Exclusion and Stromal Changes. Int J Mol Sci. 2021 4. Tsuji S et al, Maturation of human dendritic cells by cell wall skeleton of Mycobacterium bovis bacillus Calmette-Guérin: involvement of toll-like receptors. Infect Immun. 2000 5. ten Broeke T et al, MHC class II antigen presentation by dendritic cells regulated through endosomal sorting. Cold Spring Harb Perspect Biol. 2013 Dec 1;5(12):a016873. 6. Mace EM. Human natural killer cells: Form, function, and development. J Allergy Clin Immunol. 2023

BCG & Checkpoint Failure

Tumor Evasion by MHC-I Positive Converting to MHC-I Negative



Hot Tumor
MHC+

Trained CD8 Killer T Cell to Recognize Bladder Cancer Cell Infected with BCG[1, 2, 3]

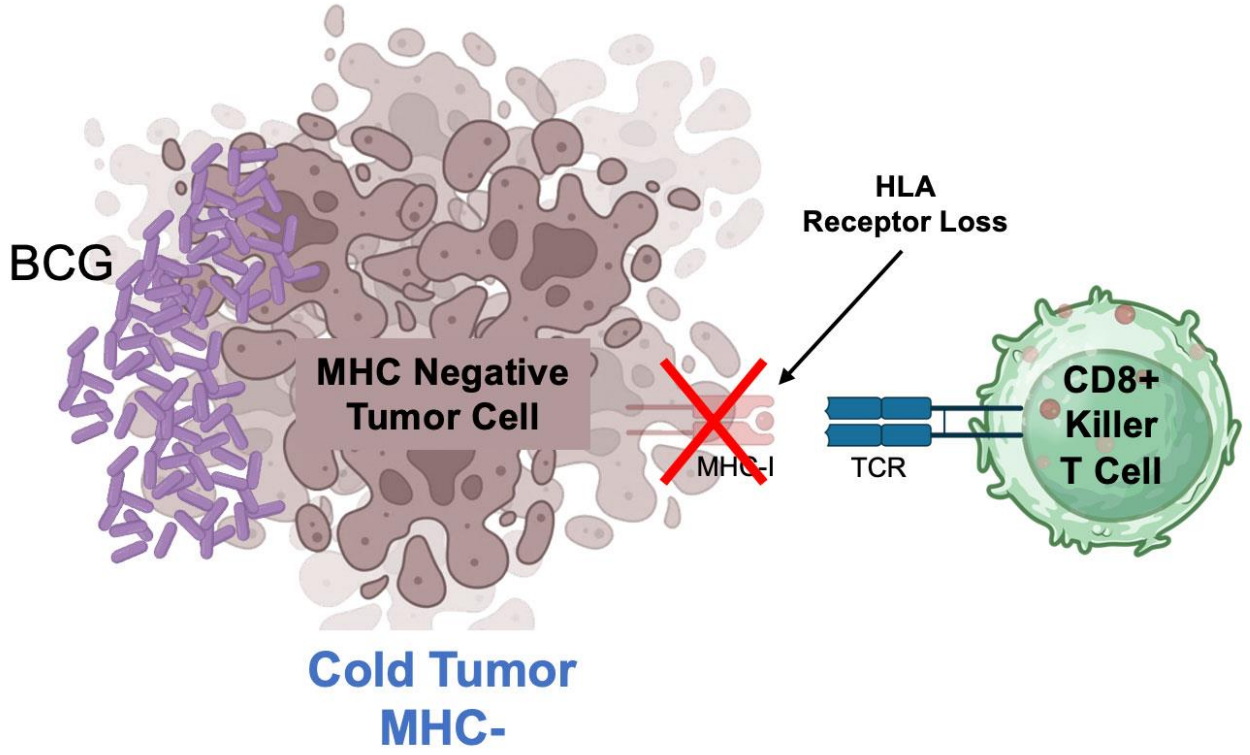
Cold Tumor
MHC-

Tumor Evasion by Not Expressing MHC With Loss of Activity of Killer T Cells[1, 4, 5]

1. ANKTIVA Package insert. ImmunityBio, Inc.; 2024 **2.** Tsuji S et al, Maturation of human dendritic cells by cell w all skeleton of Mycobacterium bovis bacillus Calmette-Guérin: involvement of toll-like receptors. Infect Immun. 2000 **3.** Van Puffelen et al, Trained Immunity as a Molecular Mechanism for BCG Immunotherapy in Bladder Cancer. Nat Rev Urol. 2020 Sep;17(9):513-525 4. Gil-Julio H et al, Tumor Escape Phenotype in Bladder Cancer Is Associated with Loss of HLA Class I Expression, T-Cell Exclusion and Stromal Changes. Int J Mol Sci. 2021 Jul 6;22(14):7248.

BCG & Checkpoint Failure

Tumor Evasion by MHC-I Positive Converting to MHC-I Negative



MHC Negative Tumor (Cold) is a Universal Target for All BCG, Checkpoint and Chemo Failures in Bladder Cancer to NK Cells[1, 2]

1. Rouanne M., et al. BCG Therapy Downregulates HLA-I on Malignant Cells to Subvert Antitumor Immune Responses in Bladder Cancer. J Clin Invest. 2022;132(12):e145666 **2**. Gil-Julio H et al, Tumor Escape Phenotype in Bladder Cancer Is Associated with Loss of HLA Class I Expression, T-Cell Exclusion and Stromal Changes. Int J Mol Sci. 2021 Jul 6;22(14):7248

Why BCG Duration of Response is Short Lived

MHC Negative Clonal Selection with T Cell Immune Evasion

2021

International Journal of
Molecular Sciences

MDPI

Article

Tumor Escape Phenotype in Bladder Cancer Is Associated with Loss of HLA Class I Expression, T-Cell Exclusion and Stromal Changes

Hernani Gil-Julio [1,†], Francisco Perea [2,3,†], Antonio Rodriguez-Nicolas [2,3], Jose Manuel Cozar [1,3,4], Amanda Rocío González-Ramirez [3,5,6], Angel Concha [7], Federico Garrido [2,3,8], Natalia Aptsiauri [2,3,8,*] and Francisco Ruiz-Cabello [2,3,8,*]

Gil-Julio H et al, Tumor Escape Phenotype in Bladder Cancer Is Associated with Loss of HLA Class I Expression, T-Cell Exclusion and Stromal Changes. Int J Mol Sci. 2021 Jul 6;22(14):7248

Why BCG Duration of Response is Short Lived

MHC Negative Clonal Selection with T Cell Immune Evasion

2022

The Journal of Clinical Investigation

RESEARCH ARTICLE

BCG therapy downregulates HLA-I on malignant cells to subvert antitumor immune responses in bladder cancer

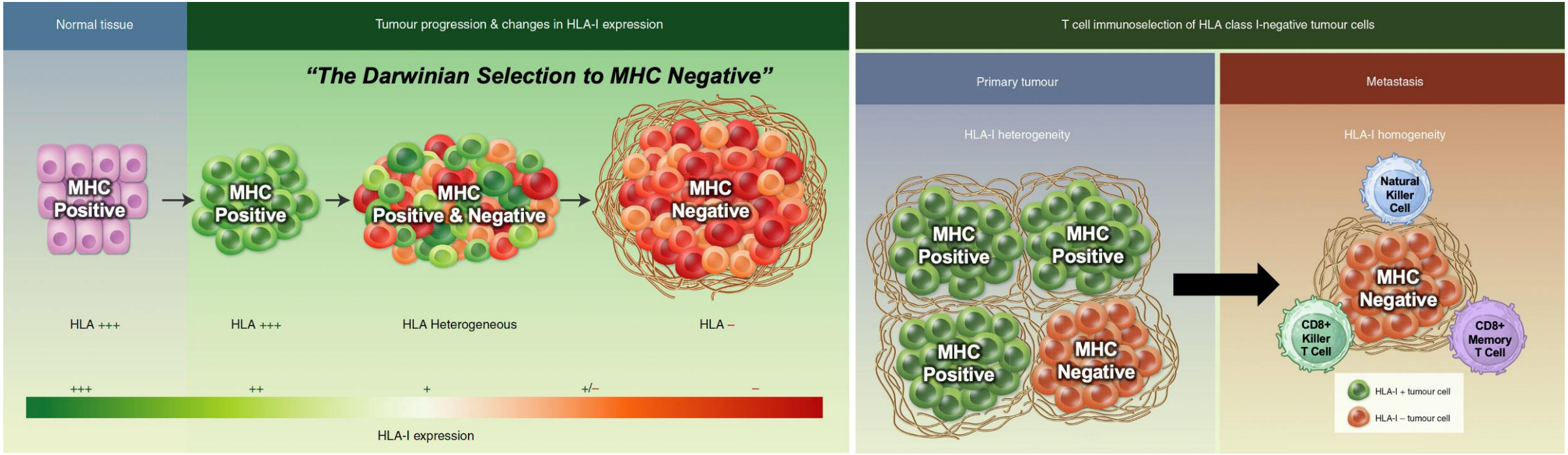
Mathieu Rouanne,[1,2,3] Julien Adam,[4,5] Camélia Radulescu,[6] Diane Letourneur,[1,7] Delphine Bredel,[1] Séverine Mouraud,[1] Anne-Gaëlle Goubet,[1] Marion Leduc,[8,9] Noah Chen,[2] Tuan Zea Tan,[10] Nicolas Signolle,[11] Amélie Bigorgne,[12,13] Michael Dussiot,[12] Lambros Tselikas,[1] Sandrine Susini,[1] François-Xavier Danlos,[1] Anna K. Schneider,[11] Roman Chabanon,[14,15] Sophie Vacher,[16] Ivan Bièche,[16] Thierry Lebret,[3] Yves Allory,[6,17,18] Jean-Charles Soria,[9,12] Nicholas Arpaia,[2,19] Guido Kroemer,[8,9,20,21] Oliver Kepp,[8,9] Jean Paul Thiery,[11,22] Laurence Zitvogel,[1,23] and Aurélien Marabelle[1,13,23]

Rouanne M., et al. BCG Therapy Downregulates HLA-I on Malignant Cells to Subvert Antitumor Immune Responses in Bladder Cancer. J Clin Invest. 2022;132(12):e145666

ANKTIVA: Next Generation Immunotherapy Beyond T Cells For All MHC-I Negative Tumors

Immunogenic Cell Death by ANKTIVA in the Triangle Offense:
The Three Steps to Transforming the "MHCscore" From a Cold Tumor (MHC-I Negative) to Hot (MHC-I Positive) and to Rescue Killer T Cells and Memory T Cells with NK[1]

- **Step 1:** Conversion of MHC Negative (Cold) to MHC Positive Tumor (Hot)[1]
- **Step 2:** Activation of IL-15 Receptor on NK and Killer T Cells[2]
- **Step 3:** Proliferation of NK, CD8+ Killer, and CD8+ Memory Cells[2]

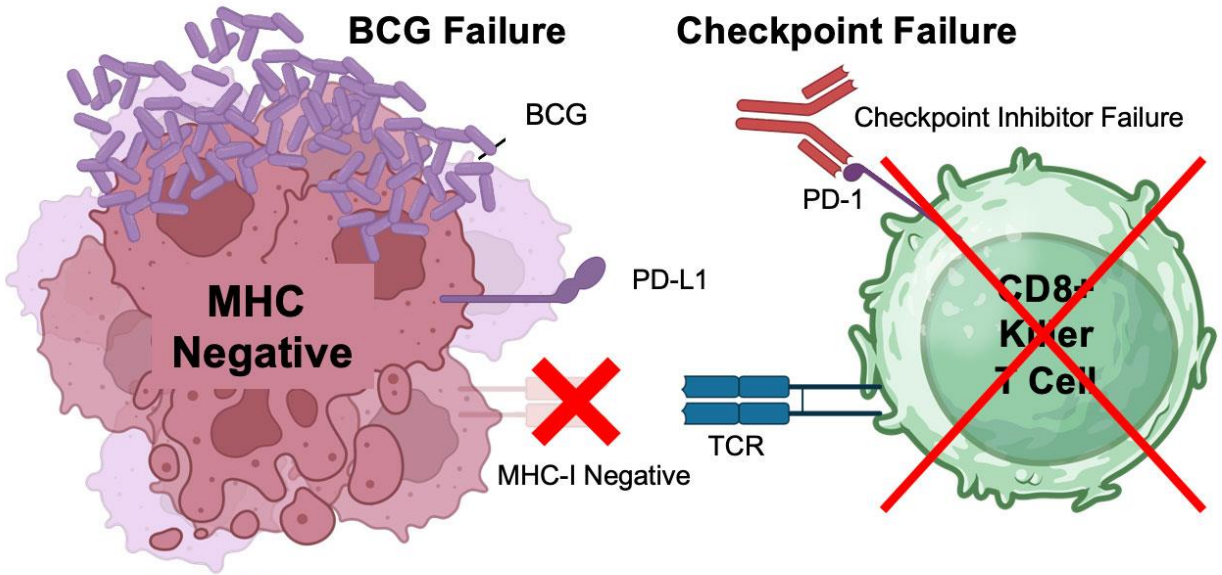


Transforming a Cold Tumor (MHC-Negative) to Hot (MHC-Positive) with ANKTIVA for Durable Complete Response[1, 2]

1. Adapted From: Garrido F, Aptsiauri N. Cancer immune escape: MHC expression in primary tumors versus metastases. Immunology. 2019 Dec;158(4):255-266 **2.** ANKTIVA Package insert. ImmunityBio, Inc.; 2024

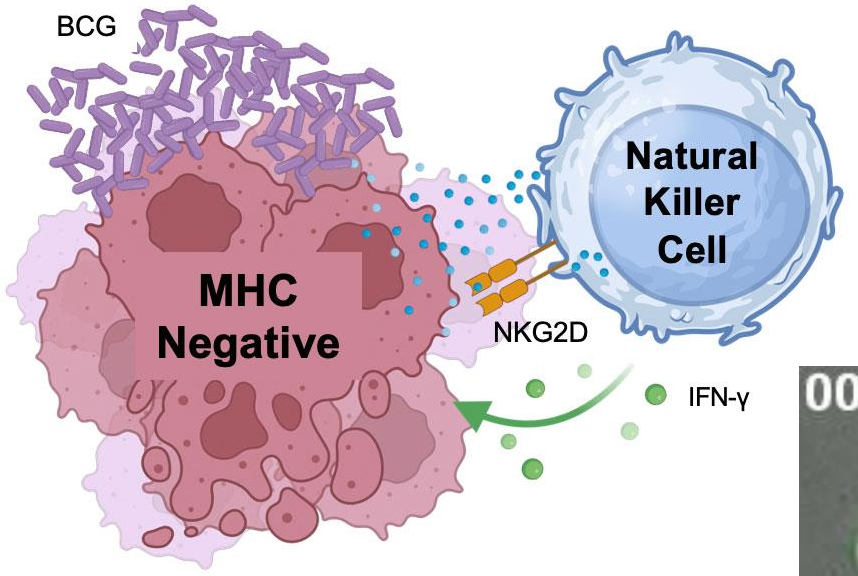
MHC Negative Tumor Cells Are a Target for Natural Killer Cells Across All MHC Negative Tumor Types[1, 2, 3, 4]

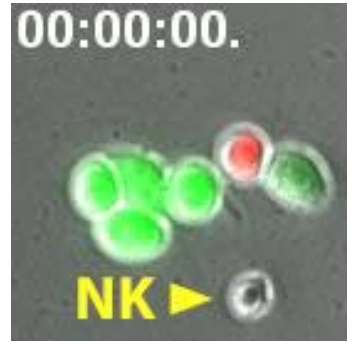
Tumor Evasion to T Cells: MHC Negative and Acquired Resistance to Checkpoint Inhibitors & BCG[4]



Cold Tumor MHC-

MHC Negative Tumor Cell is a Target for Natural Killer Cells (Missing-Self)[3, 4]





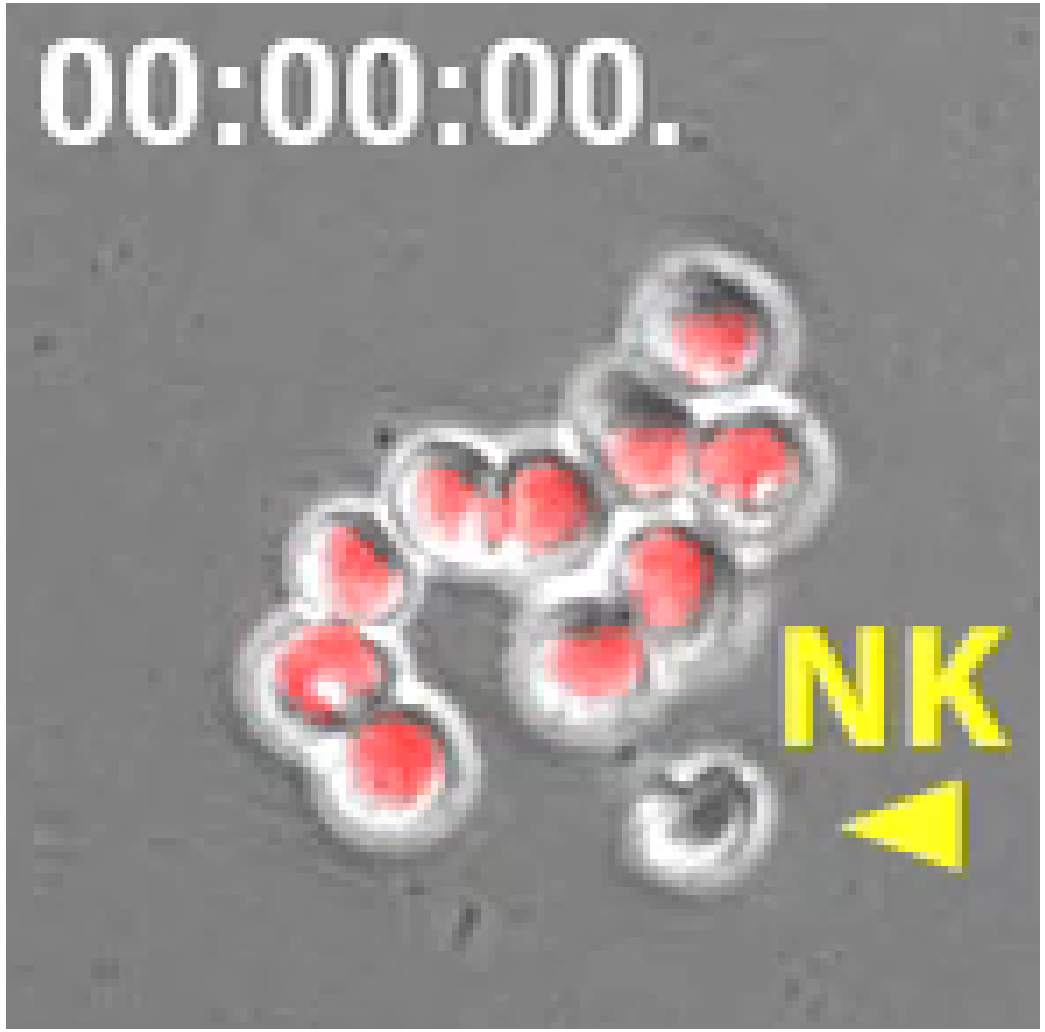
Cold Tumor as a Target for NK MHC-

MHC Negative as a Universal Target for All BCG, Chemo, and Checkpoint Failures Across all Tumor Types[3,4]

MHC Negative as a Universal Target for Natural Killer Cells Converting Cold Tumors to Hot[3,4]

1. ANKTIVA Package insert. ImmunityBio, Inc.; 2024 **2.** Rouanne M., et al. BCG Therapy Downregulates HLA-I on Malignant Cells to Subvert Antitumor Immune Responses in Bladder Cancer. J Clin Invest. 2022;132(12):e145666 https://doi.org/10.1172/JCI145666. **3.** Van Puffelen et al, Trained Immunity as a Molecular Mechanism for BCG Immunotherapy in Bladder Cancer. Nat Rev Urol. 2020 Sep;17(9):513-525. **4.** Gil-Julio, H.; et al., Tumor Escape Phenotype in Bladder Cancer Is Associated with Loss of HLA Class I Expression, T-Cell Exclusion and Stromal Changes. Int. J. Mol. Sci. 2021, 22, 7248. https://doi.org/10.3390/ijms22147248

Natural Killer Cells Attacking MHC Negative Tumor Cells and Generating IFNy[1]

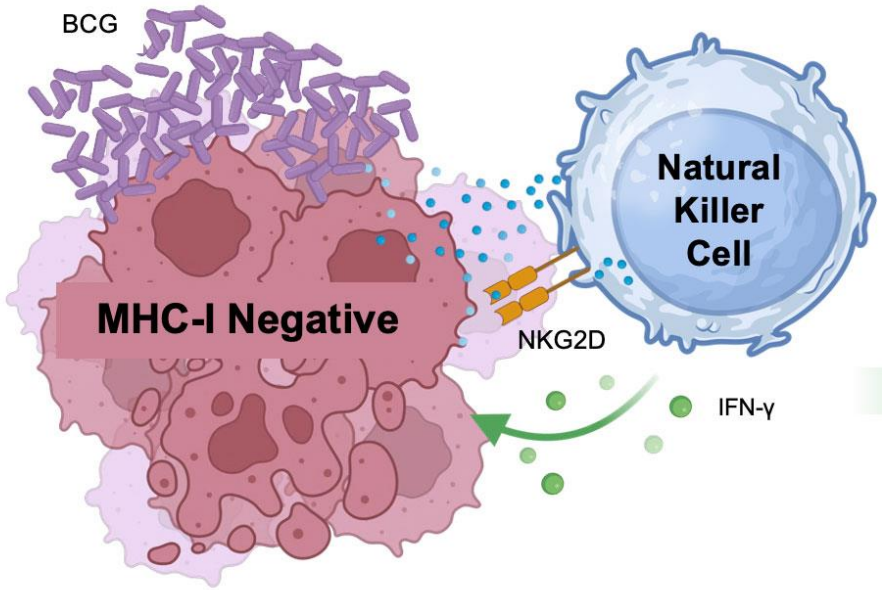


1. Rouanne M., et al. BCG Therapy Downregulates HLA-I on Malignant Cells to Subvert Antitumor Immune Responses in Bladder Cancer. J Clin Invest. 2022;132(12):e145666 https://doi.org/10.1172/JCI145666.

ANKTIVA Universal Capability of Converting a Cold Tumor to a Hot Tumor Via IFN-γ Stimulation and NK Cell Activation[1,2,3,4]

Cold Tumor: MHC Negative

MHC Negative Tumor Cell is a Target for Natural Killer Cells (Missing-Self)[2,3,4]

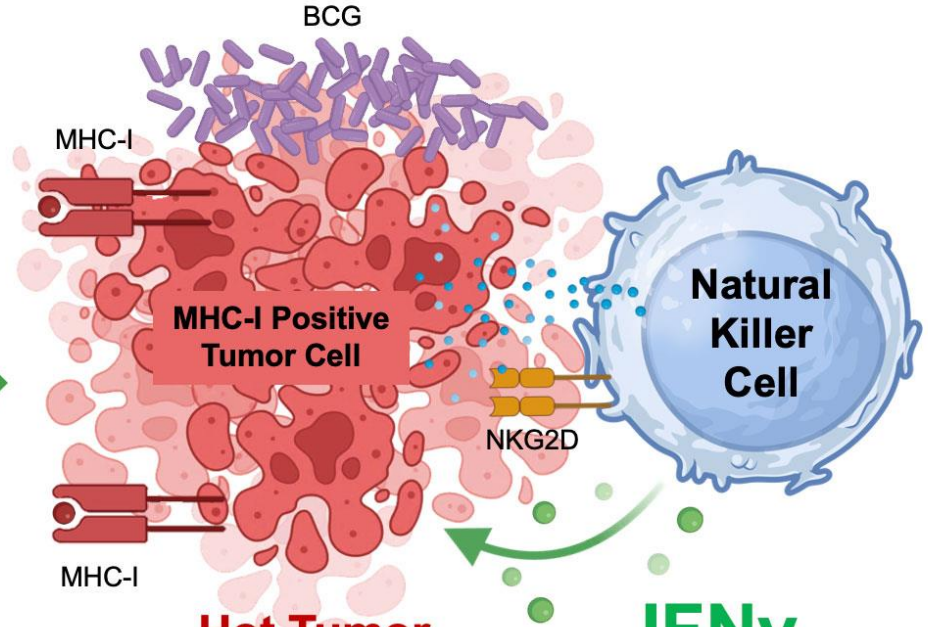


Cold Tumor
MHC-

Transformation by ANKTIVA From MHC- To MHC+ by Activating NK, CD8+ Killer and CD8+ Memory T Cells[1]

Hot Tumor: MHC Positive

Interferon Gamma (IFNγ) From NK Cells Reverses the Darwinian Selection from MHC Negative to MHC Positive[2,3,4]



Hot Tumor
MHC+

IFNγ

1. ANKTIVA Package insert. ImmunityBio, Inc.; 2024 **2.** Rouanne M., et al. BCG Therapy Downregulates HLA-I on Malignant Cells to Subvert Antitumor Immune Responses in Bladder Cancer. J Clin Invest. 2022;132(12):e145666 https://doi.org/10.1172/JCI145666. **3.** Van Puffelen et al, Trained Immunity as a Molecular Mechanism for BCG Immunotherapy in Bladder Cancer. Nat Rev Urol. 2020 Sep;17(9):513-525. **4.** Gil-Julio, H.; et al., Tumor Escape Phenotype in Bladder Cancer Is Associated with Loss of HLA Class I Expression, T-Cell Exclusion and Stromal Changes. Int. J. Mol. Sci. 2021, 22, 7248. https://doi.org/10.3390/ijms22147248