

Late Breaking Abstract, Annual BMUC meeting 2025 Urology

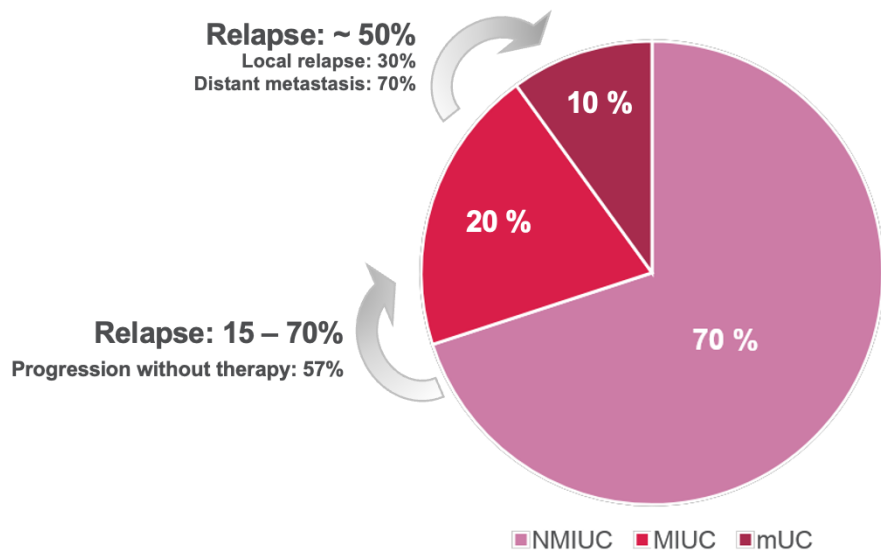
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Credentials and conflicts of interest

- Honoria as consultant/speaker : Astellas, Bayer, Bristol Myers-Squibb, Janssen, Sanofi, Ipsen, MSD.
- Honoria for scientific advisory Board: Janssen, Ipsen, MSD
- I have no potential conflict of interest related to this topic

Non muscle invasive bladder cancer - NMIBC

Incidence at diagnosis



5 Year - Survival



Risk groups stratification

Clinical risk factors:

- age > 70
- multiple papillary tumours
- tumour diameter > 3 cm.

Risk group	
Low Risk	• A primary, single, TaT1 LG/G1 tumour < 3 cm in diameter without CIS in a patient ≤ 70 years
	• A primary Ta LG/G1 tumour without CIS with at most ONE of the additional clinical risk factors
Intermediate Risk	Patients without CIS who are not included in either the low-, high-, or very high-risk groups
High Risk	• All T1 HG/G3 without CIS, EXCEPT those included in the very high-risk group • All CIS patients, EXCEPT those included in the very high-risk group
	Stage, grade with additional clinical risk factors: • Ta LG/G2 or T1G1, no CIS with all 3 risk factors • Ta HG/G3 or T1 LG, no CIS with at least 2 risk factors • T1G2 no CIS with at least 1 risk factor
Very High Risk	Stage, grade with additional clinical risk factors: • Ta HG/G3 and CIS with all 3 risk factors • T1G2 and CIS with at least 2 risk factors • T1 HG/G3 and CIS with at least 1 risk factor • T1 HG/G3 no CIS with all 3 risk factors

Probabilities of disease progression in 1, 5 and 10 year(s) for the new EAU NMIBC risk group

Risk group	Probability of Progression and 95% Confidence Interval (CI)		
	1 Year	5 Years	10 Years
New Risk Groups with WHO 2004/2016			
Low	0.06% (CI: 0.01%–0.43%)	0.93% (CI: 0.49%–1.7%)	3.7% (CI: 2.3%–5.9%)
Intermediate	1.0% (CI: 0.50%–2.0%)	4.9% (CI: 3.4%–7.0%)	8.5% (CI: 5.6%–13%)
High	3.5% (CI: 2.4%–5.2%)	9.6% (CI: 7.4%–12%)	14% (CI: 11%–18%)
Very High	16% (CI: 10%–26%)	40% (CI: 29%–54%)	53% (CI: 36%–73%)
New Risk Groups with WHO 1973			
Low	0.12% (CI: 0.02%–0.82%)	0.57% (CI: 0.21%–1.5%)	3.0% (CI: 1.5%–6.3%)
Intermediate	0.65% (CI: 0.36%–1.2%)	3.6% (CI: 2.7%–4.9%)	7.4% (CI: 5.5%–10%)
High	3.8% (CI: 2.6%–5.7%)	11% (CI: 8.1%–14%)	14% (CI: 10%–19%)
Very High	20% (CI: 12%–32%)	44% (CI: 30%–61%)	59% (CI: 39%–79%)

WHO = World Health Organization.

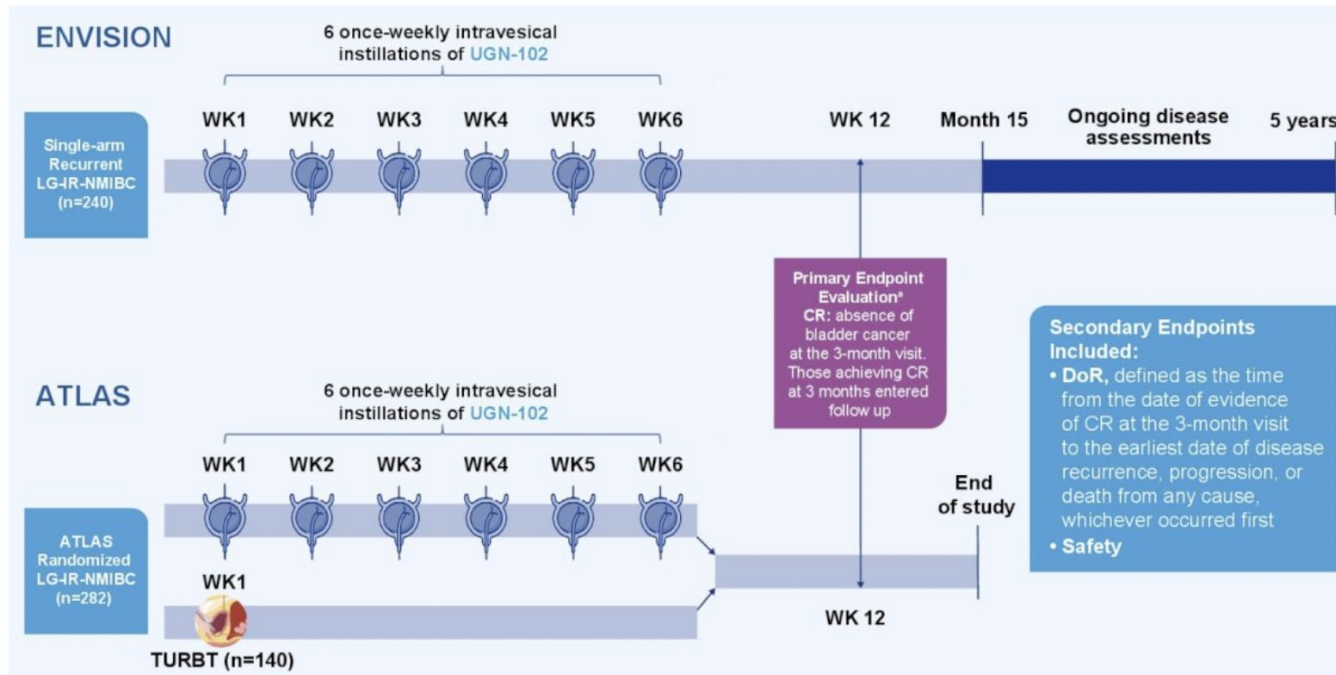
**Table 6.2 does not include patients with subtypes of urothelial carcinoma (variant histologies), LVI, CIS in the prostatic urethra, primary CIS or recurrent patients.*

Risk group stratification	Characteristics	Treatment
Low-risk	A primary, single, TaT1 LG/G1 tumour < 3 cm in diameter without CIS in a patient < 70 years A primary Ta LG/G1 tumour without CIS with at most ONE of the additional clinical risk factors	One immediate instillation of chemotherapy
Intermediate-risk	Patients without CIS who are not included in either the low-, high-, or very high-risk groups	One immediate instillation of chemotherapy followed by further instillations, either chemotherapy or BCG 1 year full-dose.
High-risk	All T1 HG/G3 without CIS, EXCEPT those included in the very high-risk group All CIS patients, EXCEPT those included in the very high-risk group Stage, grade with additional clinical risk factors: Ta LG/G2 or T1G1, no CIS with all 3 risk factors Ta HG/G3 or T1 LG, no CIS with at least 2 risk factors T1G2 no CIS with at least 1 risk factor	BCG full dose 1 to 3 years but discuss immediate cystectomy.
Very High risk	Stage, grade with additional clinical risk factors: Ta HG/G3 and CIS with all 3 risk factors T1G2 and CIS with at least 2 risk factors T1 HG/G3 and CIS with at least 1 risk factor T1 HG/G3 no CIS with all 3 risk factors	Immediate cystectomy or BCG full dose 1 to 3 years to those who refuse or are unfit for RC.

Clinical risk factors: age > 70; multiple papillary tumours; tumour diameter > 3 cm.

Treatment of Low-Grade Intermediate-Risk Non-Muscle-Invasive Bladder Cancer With UGN-102: Results of the Phase 3 ATLAS and ENVISION Studies

- UGN-102 is a reverse thermal gel containing mitomycin that can be delivered using a minimally invasive procedure in an ambulatory setting via a urethral catheter.



Treatment of Low-Grade Intermediate-Risk Non-Muscle-Invasive Bladder Cancer With UGN-102: Results of the Phase 3 ATLAS

- In ATLAS, UGN-102 was associated with a 54% reduction in risk of recurrence, progression, or death compared to TURBT
- UGN-102 may represent a valuable non-surgical treatment option for these patients

	ATLAS	
	UGN-102 ^a	TURBT
3-month CR rate, % (95% CI)	64.8 (56.3, 72.6)	63.6 (55.0, 71.5)
12-month DoR,^b % (95% CI)	79.7 (69.3, 86.9)	67.7 (55.8, 77.1)
Median DoR,^b (95% CI)	NE	NE
Median follow-up time for DoR,^b months (95% CI)	12.45 (12.02, 14.13)	12.16 (11.89, 12.75)
Any recurrence,^c n/N (%)	18/92 (19.6)	24/89 (27.0)
LG disease, n/N (%)	15/92 (16.3)	17/89 (19.1)
HG disease, n/N (%)	3/92 (3.3)	6/89 (6.7)
Death, n/N (%)	0	1/89 (1.1)

ENVISION: Primary Chemoablation of Recurrent Low-Grade Intermediate Risk NMIBC with UGN-102: A Single-Arm, Open-Label, Phase 3 Trial

Key inclusion criteria are as follows:

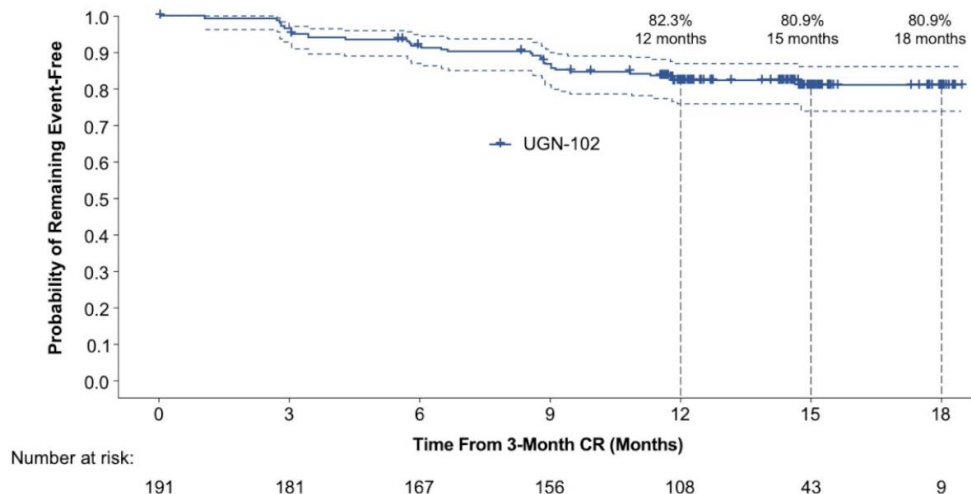
- History of ≥ 1 prior episodes of low grade non-muscle invasive bladder cancer requiring treatment with TURBT
- Low grade NMIBC (Ta) confirmed by cystoscopy + biopsy
- Negative voiding cytology for high grade disease
- Intermediate risk disease, defined as 1 or 2 of the following: multiple tumors, longest tumor diameter > 3 cm, early or frequent recurrence (ie, ≥ 1 episode within the previous year)

Characteristic		UGN-102 (N=240)
Mean age, years (SD)		68.8 (12)
Sex, n (%)		
	Male	147 (61)
	Female	93 (39)
Race, n (%)		
	Asian	2 (0.8)
	Black or African American	3 (1.3)
	White	234 (98)
Mean weight, kg (SD)		79.7 (16)
Tumor longest diameter pre-biopsy (cm)		
	≤ 3	216 (92)
	> 3	19 (8.1)
	Missing	5 (2.1)
Tumor burden pre-biopsy, aggregate (cm)		
	≤ 3	180 (81)
	> 3	41 (19)
	Missing	19 (7.9)
Tumor count		
	Single	41 (17)
	Multiple	198 (83)
	Missing	1 (0.41)

ENVISION: Primary Chemoablation of Recurrent Low-Grade Intermediate Risk NMIBC with UGN-102: A Single-Arm, Open-Label, Phase 3 Trial

	UGN-102 (N = 240)
	n (%)
Complete response	191 (80)
Non-complete response	49 (20)
Residual disease	35 (15)
Progression to HG disease	7 (2.9)
Indeterminate	2 (0.83)
Missing	5 (2.1)

**DURATION OF RESPONSE IN PATIENTS WITH A CR AT 3 MONTHS
(KAPLAN-MEIER PLOT)**



ENVISION: Primary Chemoablation of Recurrent Low-Grade Intermediate Risk NMIBC with UGN-102: A Single-Arm, Open-Label, Phase 3 Trial

UGN-102 (N=240)	
Patients with any TEAE(s), n (%)	137 (57)
Patients with any serious TEAE(s), n (%) ^a	29 (12)
TEAEs occurring in ≥5% of patients, n (%)	
Dysuria	54 (23)
Hematuria	20 (8.3)
Urinary tract infection	17 (7.1)
Pollakiuria	16 (6.7)
Fatigue	13 (5.4)
Urinary retention	12 (5)

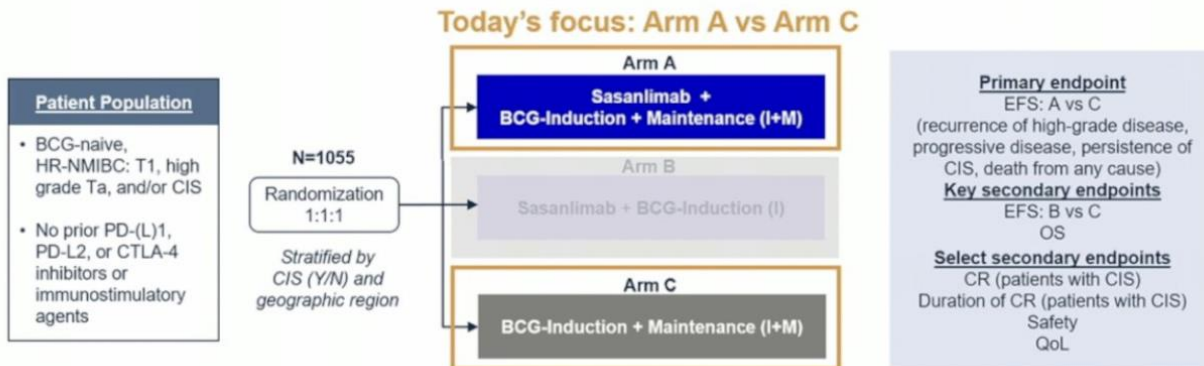
ENVISION: Primary Chemoablation of Recurrent Low-Grade Intermediate Risk NMIBC with UGN-102: A Single-Arm, Open-Label, Phase 3 Trial

- Results from ENVISION demonstrate that primary chemoablation using UGN-102 results in a high and clinically meaningful complete response rate in patients with recurrent low-grade intermediate-risk non-muscle invasive bladder cancer
- Furthermore, the durability of effect is robust, with trial participants who achieved an initial complete response having a high probability of remaining disease-free 12 months later
- These observations provide further evidence that UGN-102 may represent a well-tolerated and valuable alternative to TURBT for patients with low-grade intermediate-risk non-muscle invasive bladder cancer
- UGN-102 would potentially be the first approved medical therapy for this condition

Sasanlimab in Combination with BCG Improves Event-Free Survival vs BCG as Standard of Care in High-Risk Non-Muscle-Invasive Bladder Cancer: Phase 3 CREST Study Results

- Subcutaneous Sasanlimab : PD-1 inhibitor that has demonstrated durable anti-tumor activity and a manageable safety profile in patients with advanced or metastatic solid tumors.

CREST Study (NCT04165317)



Statistical Considerations:

- Data cutoff date Dec 2, 2024 (3 years after last randomized patient)
- EFS final analysis, significance threshold: 1-sided $\alpha = 0.025$
 - Interim OS analysis, nominal $\alpha = 0.0001$

BCG-I+M: BCG induction (6 doses)^a and maintenance (up to 2 years) therapy

BCG-I: BCG induction (6 doses)^a only

Sasanlimab: Administered SC for up to 25 four-week cycles

Sasanlimab in Combination with BCG Improves Event-Free Survival vs BCG as Standard of Care in High-Risk Non-Muscle-Invasive Bladder Cancer: Phase 3 CREST Study Results

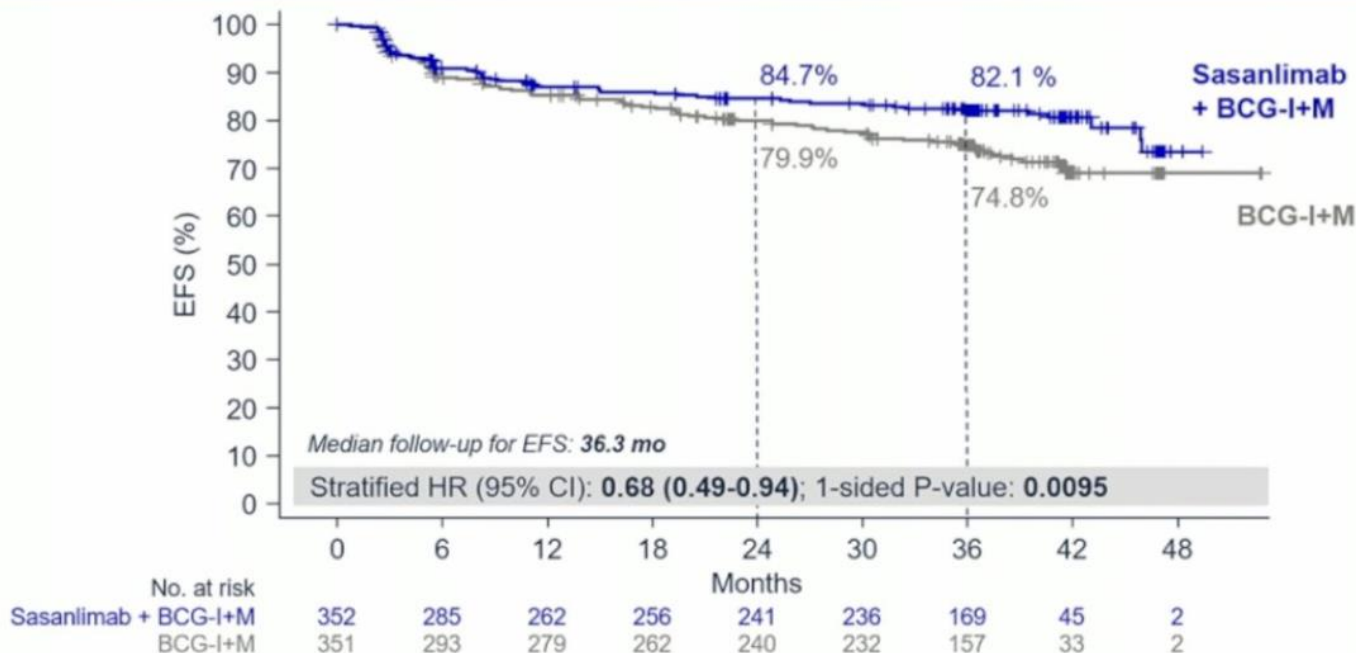
Baseline characteristics were balanced and representative of the HR-NMIBC population

	Sasanlimab + BCG-I+M (N=352)	BCG-I+M (N=351)
Median age, y (range)	67 (31–85)	67 (31–91)
Male, n (%)	280 (79.5)	284 (80.9)
Race, n (%)		
White	225 (63.9)	210 (59.8)
Asian	115 (32.7)	126 (35.9)
ECOG PS, n (%)		
0	298 (84.7)	291 (82.9)
1	54 (15.3)	59 (16.8)
Geographic region, n (%)		
US	49 (13.9)	47 (13.4)
Western Europe or Canada	85 (24.1)	86 (24.5)
Rest of world	218 (61.9)	218 (62.1)
Smoking history, n (%)		
Never smoker	127 (36.1)	126 (35.9)
Current smoker	71 (20.2)	54 (15.4)
Former smoker	154 (43.8)	171 (48.7)

	Sasanlimab + BCG-I+M (N=352)	BCG-I+M (N=351)
Histological classification, n (%)		
UC	339 (96.3)	332 (94.6)
Disease stage, n (%)		
Ta	96 (27.3)	107 (30.5)
T1	204 (58.0)	194 (55.3)
Pure CIS	52 (14.8)	50 (14.2)
CIS ± Ta or T1	88 (25.0)	88 (25.1)
Highest grade of tumor, n (%)		
High	319 (90.6)	316 (90.0)
Low	33 (9.4)	35 (10.0)
Number of tumors, n (%)		
Single	199 (56.5)	182 (51.9)
Multiple	136 (38.6)	146 (41.6)
Size of largest tumor, n (%)		
<3 cm	193 (54.8)	190 (54.1)
≥3 cm	94 (26.7)	95 (27.1)

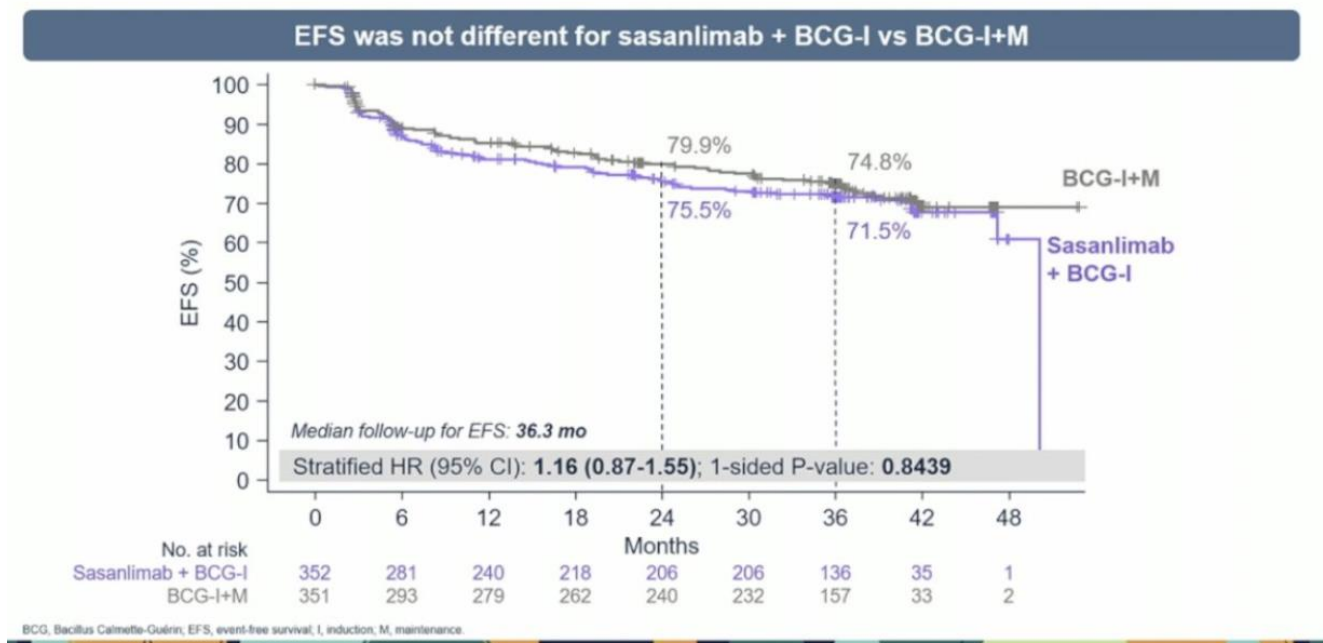
Sasanlimab in Combination with BCG Improves Event-Free Survival vs BCG as Standard of Care in High-Risk Non-Muscle-Invasive Bladder Cancer: Phase 3 CREST Study Results

The risk of experiencing an EFS event was 32% lower with sasanlimab + BCG-I+M vs BCG-I+M



Sasanlimab in Combination with BCG Improves Event-Free Survival vs BCG as Standard of Care in High-Risk Non-Muscle-Invasive Bladder Cancer: Phase 3 CREST Study Results

- When comparing Arm B versus Arm C, EFS was not significantly different between sasanlimab plus BCG induction and BCG induction plus maintenance, **underscoring the importance of BCG maintenance therapy in high-risk NMIBC**



Sasanlimab in Combination with BCG Improves Event-Free Survival vs BCG as Standard of Care in High-Risk Non-Muscle-Invasive Bladder Cancer: Phase 3 CREST Study Results

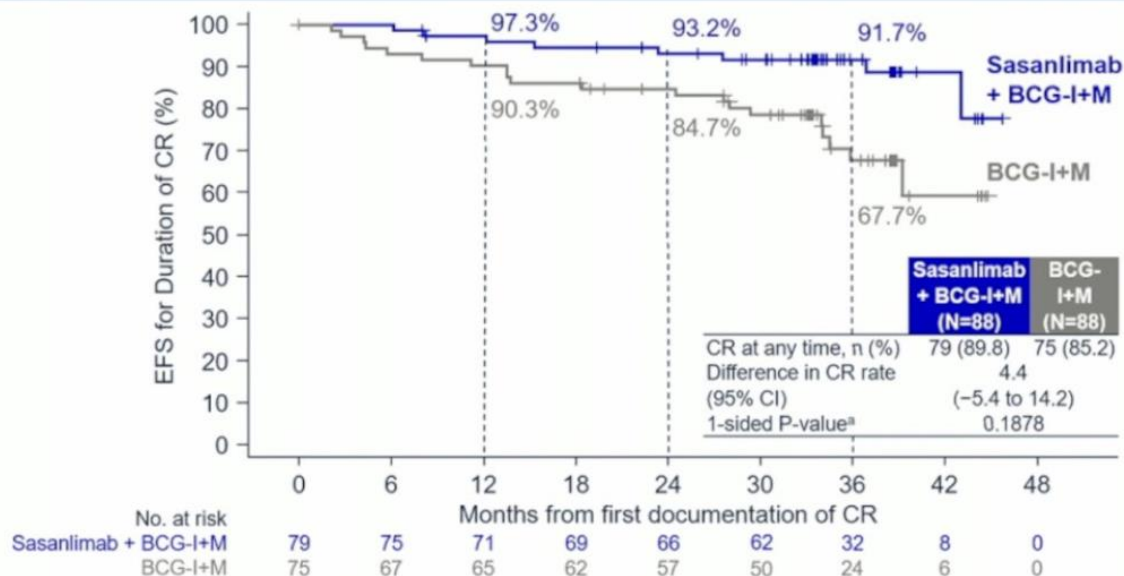
Rate of recurrence of high-grade disease was reduced by >50% with sasanlimab + BCG-I+M vs BCG-I+M

	Sasanlimab + BCG-I+M (N=352)	BCG-I+M (N=351)
Patients with EFS event, n (%)	61 (17.3)	89 (25.4)
Recurrence of high-grade disease	26 (7.4)	53 (15.1)
Persistence of CIS	1 (0.3)	1 (0.3)
Progressive disease	18 (5.1)	22 (6.3)
Progression to N+/M+, n	3	7
Progression to MIBC (≥T2), n	7	7
Stage Progression (high-grade Ta, T1), n	7	7
Unknown, n	1	1
Death	16 (4.5)	13 (3.7)

Sasanlimab in Combination with BCG Improves Event-Free Survival vs BCG as Standard of Care in High-Risk Non-Muscle-Invasive Bladder Cancer: Phase 3 CREST Study Results

CR and Duration of Response in **Patients With CIS**: Arm A vs Arm C

In patients with CIS, probability of continued CR at 36 months was 92% for sasanlimab + BCG-I+M



Sasanlimab in Combination with BCG Improves Event-Free Survival vs BCG as Standard of Care in High-Risk Non-Muscle-Invasive Bladder Cancer: Phase 3 CREST Study Results

- In Arm B and Arm A, which received sasanlimab, the rate of grade 3/4 adverse events was approximately 15%, with most cases resolving with thyroid hormone supplementation

Sasanlimab Immune-Mediated AEs: Arm A and Arm B

The combination with BCG did not substantially impact incidence and severity of imAEs

	Sasanlimab + BCG-I+M (N=350)		Sasanlimab + BCG-I (N=348)	
	Grades 1/2	Grades 3/4	Grades 1/2	Grades 3/4
Any imAE, n (%)	94 (26.9)	55 (15.7)	114 (32.8)	48 (13.8)
Thyroid disorders	60 (17.1)	2 (0.6)	70 (20.1)	1 (0.3)
Rash	36 (10.3)	10 (2.9)	40 (11.5)	8 (2.3)
Hepatitis	3 (0.9)	12 (3.4)	3 (0.9)	11 (3.2)
Pancreatitis	7 (2.0)	7 (2.0)	4 (1.1)	6 (1.7)
Adrenal insufficiency	6 (1.7)	6 (1.7)	7 (2.0)	5 (1.4)
Pneumonitis	6 (1.7)	4 (1.1)	3 (0.9)	1 (0.3)
Colitis	4 (1.1)	5 (1.4)	6 (1.7)	3 (0.9)
Hypophysitis/Hypopituitarism	4 (1.1)	4 (1.1)	6 (1.7)	3 (0.9)
Type 1 diabetes mellitus	1 (0.3)	6 (1.7)	0	4 (1.1)
Nephritis and renal dysfunction	2 (0.6)	4 (1.1)	2 (0.6)	7 (2.0)
Myasthenic syndrome/Myasthenia gravis	1 (0.3)	1 (0.3)	0	0
Myocarditis	0	1 (0.3)	1 (0.3)	1 (0.3)
Myositis	0	1 (0.3)	1 (0.3)	1 (0.3)
Uveitis	0	1 (0.3)	0	0
Other imAEs ^a	7 (2.0)	1 (0.3)	12 (3.4)	4 (1.1)

^a ImAEs leading to death were n=0 for Arm A and n=1 for Arm B (myocarditis)

Sasanlimab in Combination with BCG Improves Event-Free Survival vs BCG as Standard of Care in High-Risk Non-Muscle-Invasive Bladder Cancer: Phase 3 CREST Study Results

- CREST is the first study showing a significant EFS benefit with sasanlimab + BCG induction and maintenance vs BCG induction and maintenance alone (HR 0.68; 95% CI: 0.49–0.94).
- In CIS patients, the probability of continued CR at 36 months was higher with sasanlimab + BCG (92% vs 68%).
- The safety profile of sasanlimab + BCG was consistent with the known profiles of each agent individually.
- Subcutaneous sasanlimab + BCG may redefine treatment for HR-NMIBC, particularly for CIS and T1 disease.
- Multidisciplinary workflows are critical for monitoring and managing imAEs

Guidelines for the treatment of BCG failure

Category	Treatment options	Strength rating
BCG-unresponsive	1. Radical cystectomy (RC).	Strong
	2. Enrollment in clinical trials assessing new treatment strategies.	Weak
	3. Bladder-preserving strategies in patients unsuitable or refusing RC.	Weak
Late BCG relapsing: T1Ta/HG recurrence > 6 months or CIS > 12 months of last BCG exposure	1. Radical cystectomy or repeat BCG course according to individual situation.	Strong
	2. Bladder-preserving strategies.	Weak
LG recurrence after BCG for primary intermediate-risk tumour	1. Repeat BCG or intravesical chemotherapy.	Weak
	2. Radical cystectomy.	Weak

US FDA Guidance for BCG-unresponsive NMIBC: developing drugs and Biologics for Treatment

- **Study design:** Single arms trials are appropriate for assessment of therapies for BCG unresponsive disease (CIS with or without resected papillary disease)
- **Endpoints:** Complete Response (CR) rate in patients with CIS
- **FU:** Q3m 2y then Q6m 2y and then annually (cystoscopy, directed biopsy and urine cytology). Random biopsies at specific time points recommended but not required.
- **Clinically meaningful amplitude of effect:**

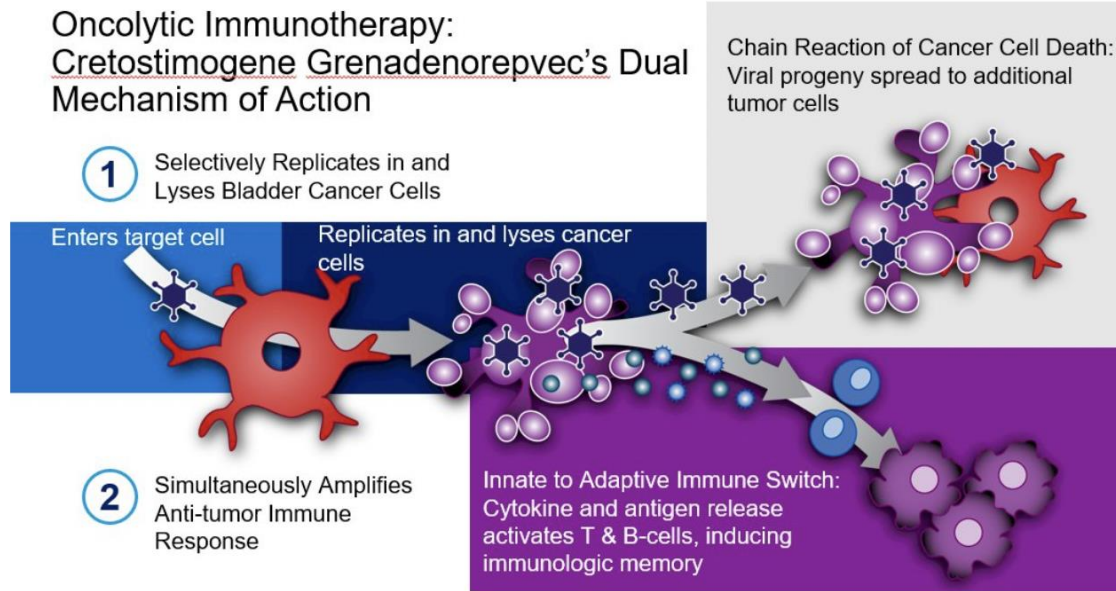
CR definition:

- Negative cystoscopy and negative (including atypical) urine cytology
- Positive cystoscopy with biopsy-proven benign or low-grade NMIBC and negative urine cytology

	6 months	12 months	18 months
CR	50%	30%	25%

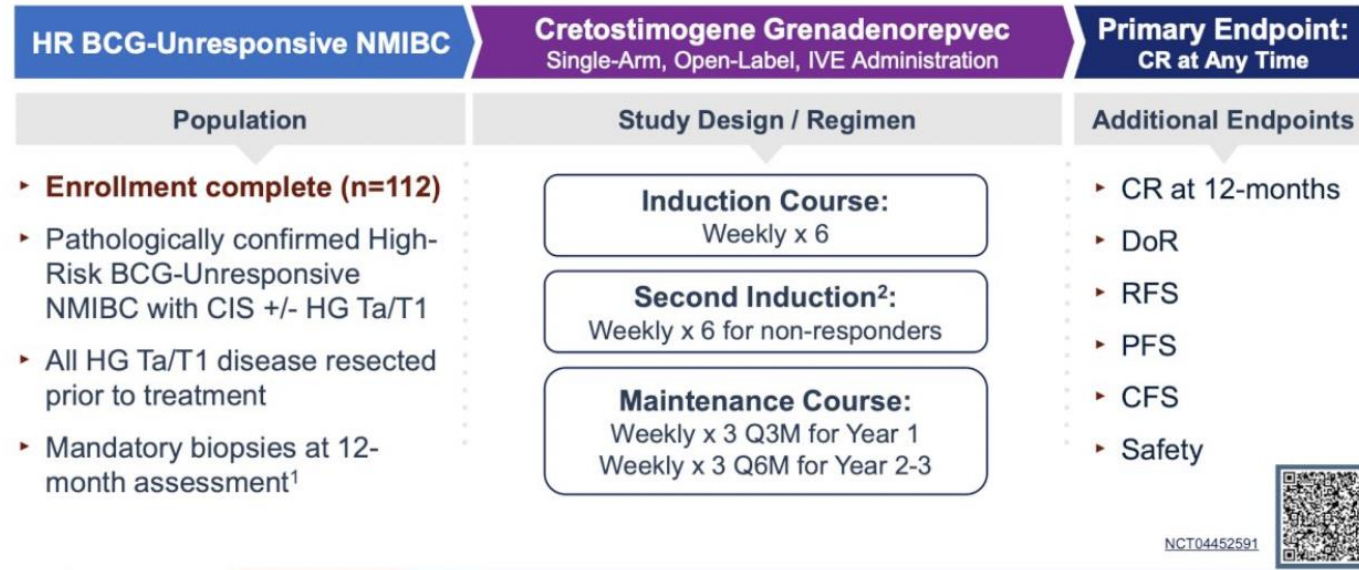
BOND-003 Cohort C – A Phase 3, Single-Arm Study of Intravesical Cretostimogene Grenadenorepvec for BCG-Unresponsive High-Risk NMIBC with CIS

- Cretostimogene grenadenorepvec selectively replicates inside tumor cells with RB-E2F alterations, causing tumor cell lysis and immunogenic cell death. The rupture of the cancer cells releases tumor-derived antigens, along with GM-CSF, that can stimulate a systemic anti-tumor immune response involving the body's immune system



BOND-003 Cohort C – A Phase 3, Single-Arm Study of Intravesical Cretostimogene Grenadenorepvec for BCG-Unresponsive High-Risk NMIBC with CIS

- Cretostimogene has received both US FDA Fast Track and Breakthrough Therapy Designations for the BCG-unresponsive high risk non-muscle invasive bladder cancer with CIS indication

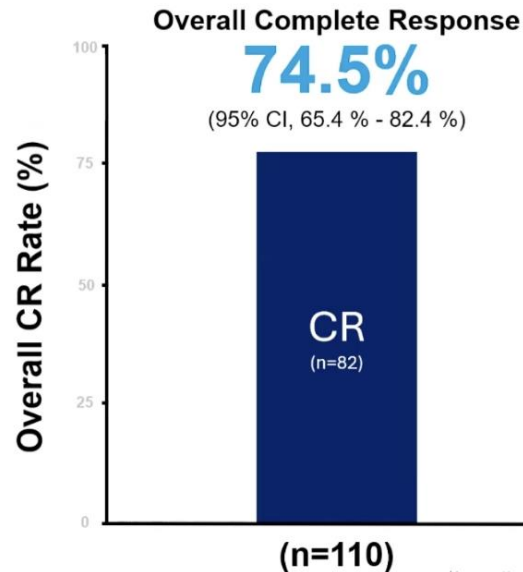


BOND-003 Cohort C – A Phase 3, Single-Arm Study of Intravesical Cretostimogene Grenadenorepvec for BCG-Unresponsive High-Risk NMIBC with CIS

Subjects in Safety Dataset	N=112	%
Gender		
Male	83	74.1
Female	29	25.9
Age (Years)		
Mean (SD)	72.9 (9.19)	
Median (Range)	74.0 (43-90)	
Age (Categories)		
< 65	19	17.0
≥ 65 and < 75	43	38.4
≥75	50	44.6
BCG History: Number of Prior Instillations		
Median (Range)	12 (7 – 66)	
High-Risk NMIBC T-Stage at Study Entry		
CIS with HG Ta/T1	22	19.6
CIS alone	90	80.4

BOND-003 Cohort C – A Phase 3, Single-Arm Study of Intravesical Cretostimogene Grenadenorepvec for BCG-Unresponsive High-Risk NMIBC with CIS

Compelling Efficacy & Durability Data



Other Orders

CR Landmark	CR Rate, % (95% CI)	CR by K-M Est, % (95% CI)
12-month	47% (36.9, 56.7) ¹ 49 out of 105 evaluable patients	50% (39.6, 58.9)
24-month	There are 25 confirmed CRs that have reached 24-month timepoint and beyond ²	41% (30.4, 50.8)

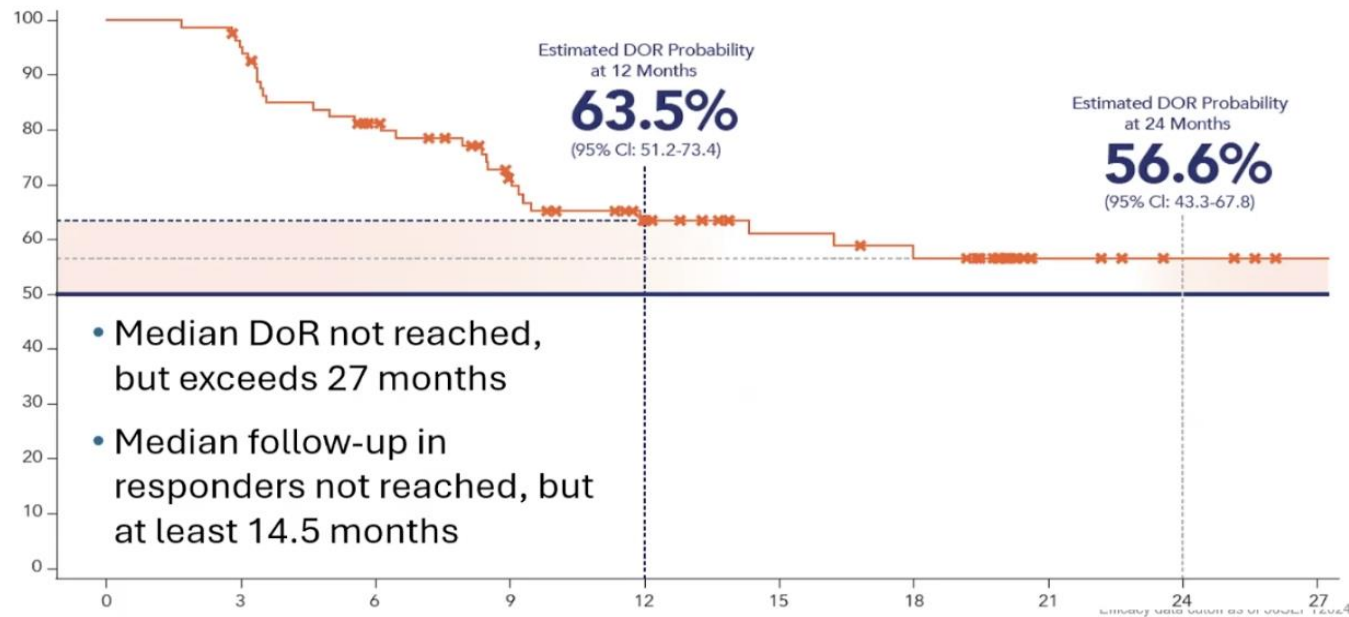
Analysis based on both landmark CR rate assessed in clinical trial and CR by Kaplan-Meier estimate.

- 97.3% free from progression to MIBC at 12 months
- 90.0% Cystectomy-Free Survival at 12 months
- CR rate consistent across patient subgroups
- All complete responses are centrally confirmed³

Efficacy analysis centrally confirmed. All patients have active disease at baseline prior to enrollment. Received adequate BCG per FDA 2018 guidance.
¹ Assessment based on evaluable patients that have reached 12-month evaluation timepoint. ² Based on centrally confirmed responders who have reached 24-month evaluation timepoint.
³ A CR is defined as having a negative cystoscopy, a negative urine cytology, and a negative biopsy. In addition, all patients at 12-month timepoint undergo mandatory, systematic bladder mapping of 5 locations, biopsy of the prostatic urethra, and upper tract imaging to confirm CR and detect potential occult disease in the bladder.



BOND-003 Cohort C – A Phase 3, Single-Arm Study of Intravesical Cretostimogene Grenadenorepvec for BCG-Unresponsive High-Risk NMIBC with CIS



- Median DoR not reached, but exceeds 27 months
- Median follow-up in responders not reached, but at least 14.5 months

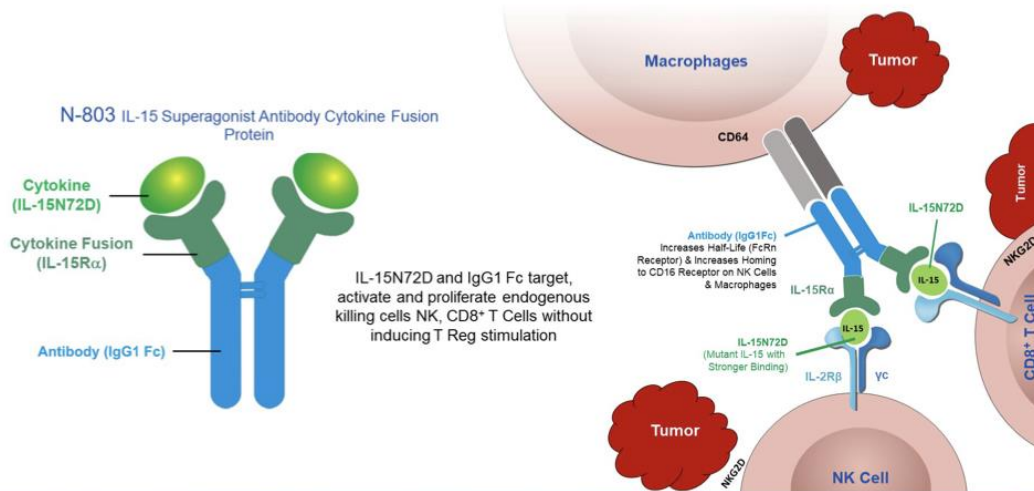
BOND-003 Cohort C – A Phase 3, Single-Arm Study of Intravesical Cretostimogene Grenadenorepvec for BCG-Unresponsive High-Risk NMIBC with CIS

- Cretostimogene grenadenorepvec provides a compelling complete response rate of 74.5%
- Durable responses include a median duration of response not reached, but exceeding 27 months, and 63.5% (95% CI 51.2%- 73.4%) remain in response at 12 months
- Cretostimogene is a very well-tolerated regimen, with no grade 3+ treatment related adverse events or discontinuations, and 97.3% completing all protocol defined treatments
- This regimen easily fits, and is scalable within existing clinic workflow, with treatment administered by MAs and RNs
- Future and ongoing clinical trials are evaluating cretostimogene monotherapy, and rational combinations, as a backbone therapy

ANKTIVA® Plus BCG in BCG-Unresponsive NMIBC CIS and Papillary Disease Alone

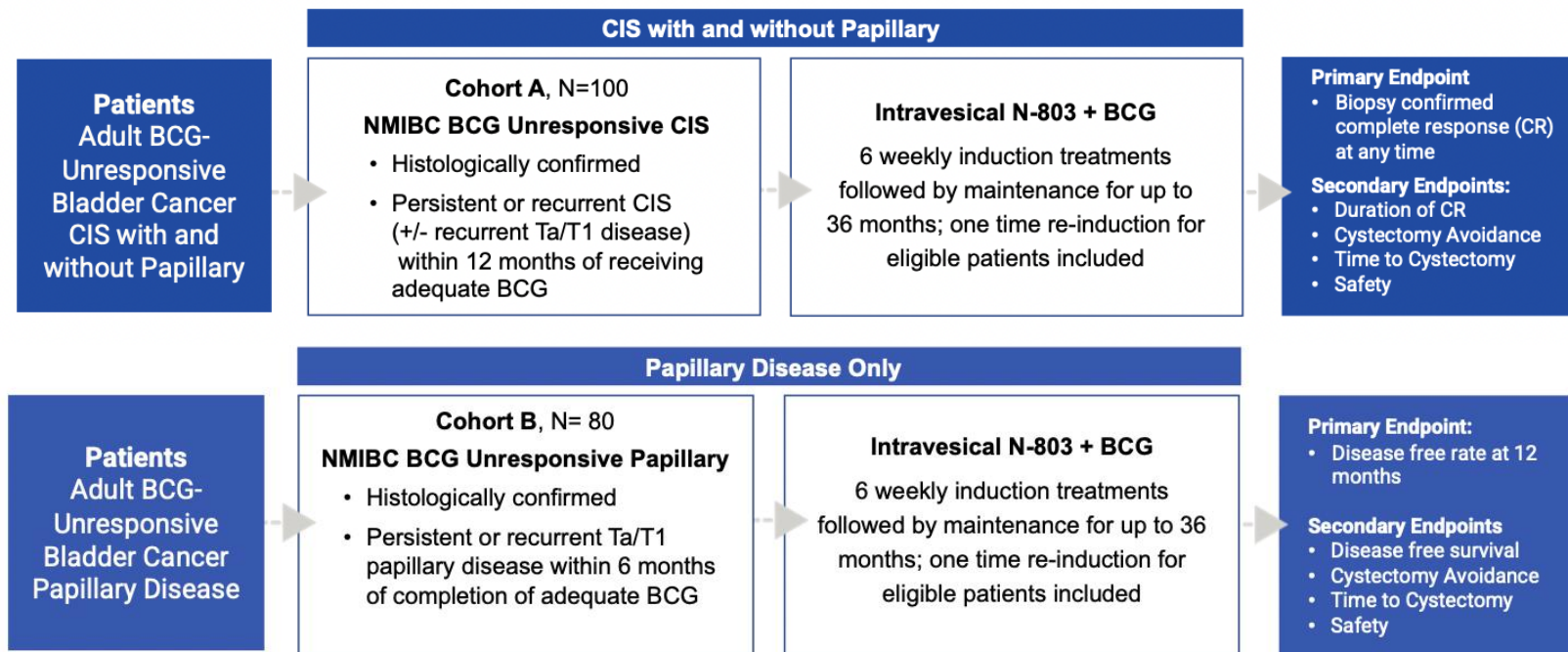
- ANKTIVA is a IL-15 receptor agonist IgG1 fusion complex, consisting of an IL-15 mutant (IL-15N72D) fused with an IL-15 receptor alpha, which binds with high affinity to IL-15 receptors on NK, CD4+, and CD8+ T cells
- ANKTIVA was approved by the FDA in 2024 with BCG for the treatment of adult patients with BCG-unresponsive nonmuscle invasive bladder cancer with CIS with or without papillary tumors

N-803 Mechanism of Action



ANKTIVA® Plus BCG in BCG-Unresponsive NMIBC CIS and Papillary Disease Alone

- **QUILT-3.032** is a Phase II/III, open-label, single-arm, multicenter study of intravesical BCG plus ANKTIVA or ANKTIVA only in patients with BCG unresponsive high grade non-muscle invasive bladder cancer (NMIBC)



ANKTIVA® Plus BCG in BCG-Unresponsive NMIBC CIS and Papillary Disease Alone

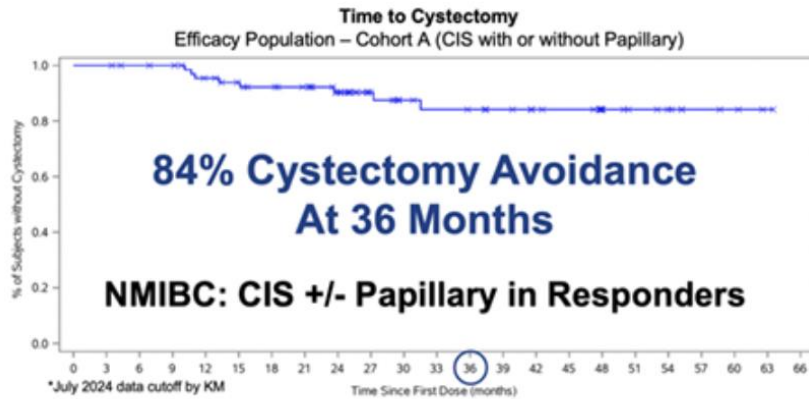
QUILT-3.032 Update Cohort A: NMIBC CIS		NAI + BCG Efficacy
Complete Response (CR) Rate % (95% CI) N=100		71% (61.1, 79.6)
Duration of Complete Response N=71 (Evaluable Responders)		53+ Months & Ongoing (>4 Years)
Disease Specific Survival % (N=100)		
12 Months		100%
24 Months		99%
36 Months		99%
July 2024 data cutoff by KM		

ANKTIVA® Plus BCG in BCG-Unresponsive NMIBC CIS and Papillary Disease Alone

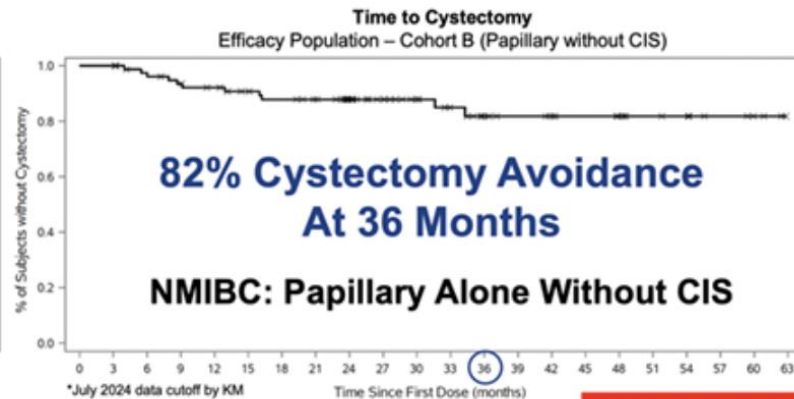
QUILT-3.032 Cohort B: NMIBC Papillary Without CIS NAI + BCG Efficacy, N=80	
Disease-Free Survival (DFS)	
12 Months (Primary Endpoint)	58% (46.6, 68.2)
24 Months	52% (40.3, 62.7)
Median Disease-Free Survival, Mo (95% CI)	25.3 Mo (9.8 - 40.1)

ANKTIVA® Plus BCG in BCG-Unresponsive NMIBC CIS and Papillary Disease Alone

FDA Approved 2024



Supplemental BLA Filed 2025, Awaiting Approval



Awaiting NCCN
Guidance Approval

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

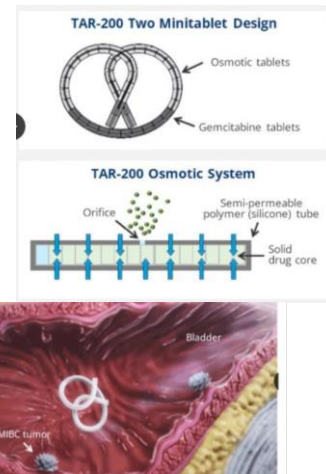
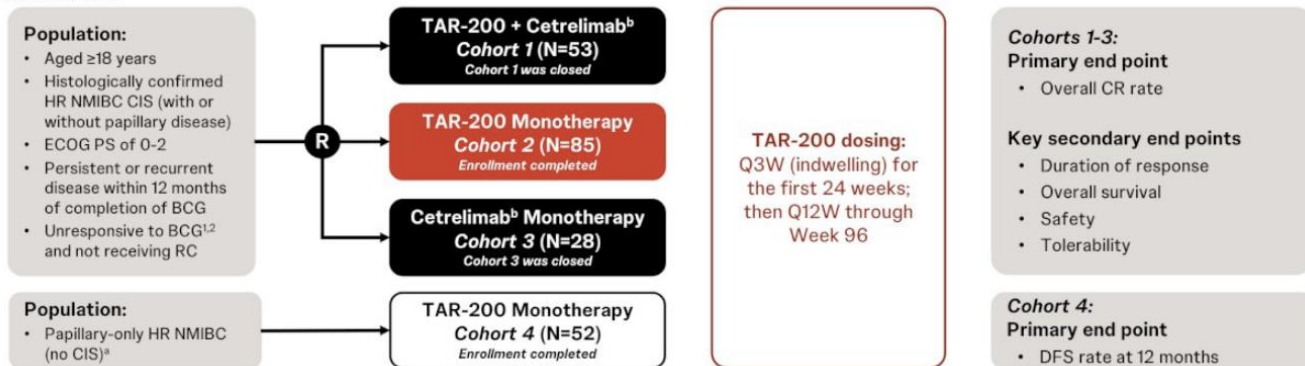
ANKTIVA® Plus BCG in BCG-Unresponsive NMIBC CIS and Papillary Disease Alone – Best in Disease and Best in Class with 5 Year Follow-Up

- In BCG-unresponsive CIS +/- papillary disease (Cohort A):
 - CR was 71%, with a CR maintained in 51% of patients with >45 months follow-up
 - Among responders, the 36 months cystectomy-free rate was 84%
 - The overall disease-specific survival in Cohort A (responders + non-responders) was 99%
- In BCG-unresponsive papillary-only disease (Cohort B):
 - The 36 months cystectomy-free rate was 82%
 - The 36 months disease-specific survival was 96%
- Currently, the combination of NAI (ANKTIVA) + BCG is approved by the FDA for BCG-unresponsive CIS +/- papillary NMIBC.
- An application for a supplemental approval in BCG-unresponsive papillary-only disease has been submitted to the FDA

TAR-200 +/- Cetrelimab and Cetrelimab Alone in Patients with BCG-Unresponsive High-Risk NMIBC: Updated Results from SunRISe-1

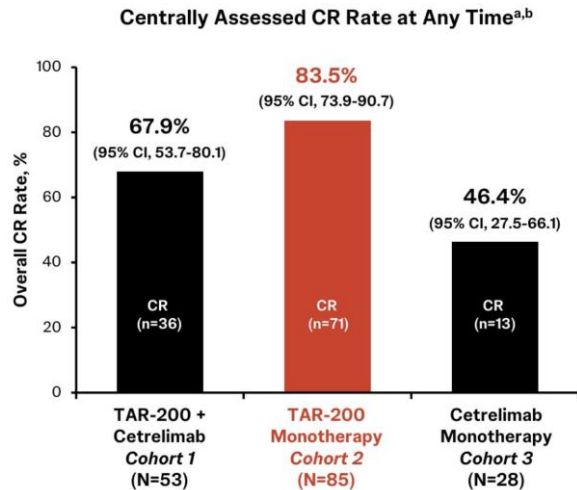
- TAR-200 is a novel drug delivery system for sustained, local release of gemcitabine in the bladder
- Cetrelimab (CET) is a novel investigational PD-1 inhibitor

NCT04640623



TAR-200 +/- Cetrelimab and Cetrelimab Alone in Patients with BCG-Unresponsive High-Risk NMIBC: Updated Results from SunRISe-1

- Centrally confirmed complete response rates in Cohort 1, Cohort 2, and Cohort 3 were 68%, 84%, and 46%, respectively.
- In Cohort 2, the estimated 12-month complete response rate was 57.4%, estimated 12-month duration of response rate was 65.7%, median follow-up in responders was 9.2 months (range: 3.7-36.6), and patients remaining in response was 81.6%.



	TAR-200 + Cetrelimab <i>Cohort 1</i> (N=53)	TAR-200 Monotherapy <i>Cohort 2</i> (N=85)	Cetrelimab Monotherapy <i>Cohort 3</i> (N=28)
Estimated 12-month CR rate ^c , % (95% CI)	56.7 (41.2-69.6)	57.4 (40.6-71.0)	22.8 (8.6-41.1)
Estimated 12-month DOR rate ^c , % (95% CI)	75.9 (57.5-87.2)	65.7 (45.2-80.1)	48.5 (17.9-73.7)
Median follow-up in responders, months (range)	21.8 (9.2-35.9)	9.2 (3.7-36.6)	18.2 (11.3-33.1)
Patients remaining in response, % (n/N)	75.0 (27/36)	81.6 (58/71)	53.8 (7/13)

TAR-200 Monotherapy in Patients with BCG–unresponsive Papillary Disease–only High-Risk Non–muscle-Invasive Bladder Cancer: First Results from Cohort 4 of SunRISe-1

NCT04640623



- Response is determined by quarterly cystoscopy, quarterly central cytology, local imaging Q24W, and bladder biopsy by central assessment as clinically indicated
- The **study protocol did not allow re-induction for nonresponders**, consistent with US FDA guidance²

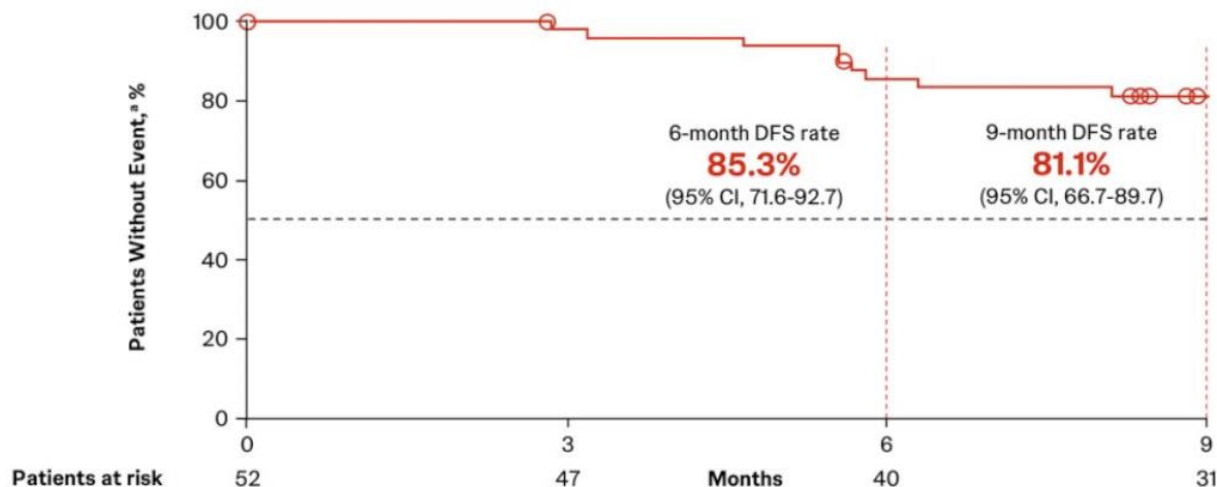
TAR-200 Monotherapy in Patients with BCG–unresponsive Papillary Disease–only High-Risk Non–muscle-Invasive Bladder Cancer: First Results from Cohort 4 of SunRISe-1

Characteristics	TAR-200 Monotherapy Cohort 4 (N=52) ^a
Age, years, median (range)	71.0 (42-88)
Sex, male, %	71.2
Race, %	
White	86.5
Asian	11.5
Black or African American	1.9
Nicotine use, %	
Current	13.5
Former	55.8
Never	30.8
ECOG PS 0, %	94.2

Characteristics	TAR-200 Monotherapy Cohort 4 (N=52) ^a
Tumor stage, % ^b	
Papillary disease	100.0
Ta	59.6
T1	40.4
Total doses of prior BCG, n, median (range)	12 (8-45)
Time from last BCG to high-grade papillary disease diagnosis, months, median (range)	2.8 (0.3-9.9)
Reason for not receiving RC, % ^c	
Declined	82.4
Ineligible	17.6

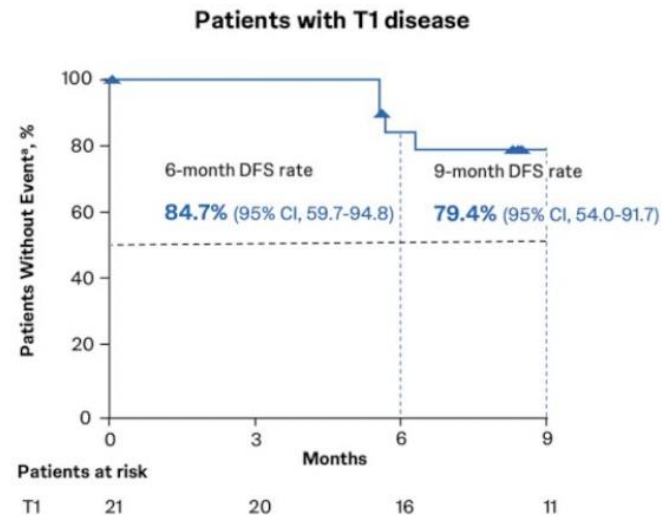
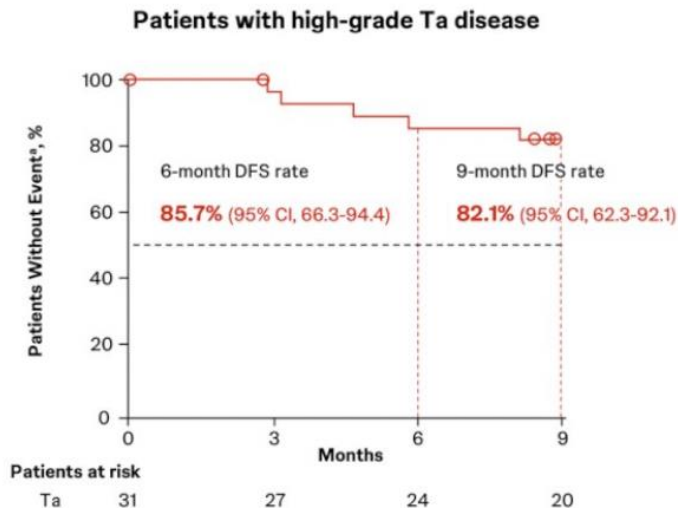
TAR-200 Monotherapy in Patients with BCG-unresponsive Papillary Disease-only High-Risk Non-muscle-Invasive Bladder Cancer: First Results from Cohort 4 of SunRISe-1

6- and 9-Month DFS Rates With TAR-200 Monotherapy in Papillary Disease-Only HR NMIBC



TAR-200 Monotherapy in Patients with BCG-unresponsive Papillary Disease—only High-Risk Non-muscle-Invasive Bladder Cancer: First Results from Cohort 4 of SunRISe-1

Consistently High DFS Rates With TAR-200 Monotherapy Across High-Grade Ta and T1 Disease



TAR-200 Monotherapy in Patients with BCG–unresponsive Papillary Disease–only High-Risk Non–muscle-Invasive Bladder Cancer: First Results from Cohort 4 of SunRISe-1

- Serious treatment-related adverse events (TRAEs) occurred in 3 patients (5.8%), and 4 patients (7.7%) discontinued treatment due to TRAEs.
- No treatment-related deaths were reported.

Patients With Events, n (%)	TAR-200 Monotherapy Cohort 4 (N=52) ^c	
	Any Grade	Grade ≥3
≥1 TRAE ^d	42 (80.8)	7 (13.5)
Most frequent TRAEs ^{e,f}		
Dysuria	21 (40.4)	0
Pollakiuria	16 (30.8)	0
Micturition urgency	14 (26.9)	0
Urinary tract infection	12 (23.1)	1 (1.9)
Hematuria	7 (13.5)	0
Bladder pain	5 (9.6)	2 (3.8)
Nocturia	5 (9.6)	0
Bladder spasm	4 (7.7)	0
Noninfective cystitis	4 (7.7)	0
Pruritus	4 (7.7)	0
Asthenia	3 (5.8)	0
Bladder irritation	3 (5.8)	0
Pelvic pain	3 (5.8)	1 (1.9)
Urinary incontinence	3 (5.8)	1 (1.9)
Urinary tract pain	3 (5.8)	0

TAR-200 Monotherapy in Patients with BCG–unresponsive Papillary Disease–only High-Risk Non–muscle-Invasive Bladder Cancer: First Results from Cohort 4 of SunRISe-1

- The first results of TAR-200 monotherapy in SunRISe-1 Cohort 4 showed impressive DFS rates in patients with BCG-unresponsive papillary-only high-risk NMIBC.
- DFS rates at 6 and 9 months were 85.3% and 81.1%, respectively.
- DFS rates remained consistently high across both high-grade Ta and T1 disease, reflecting the sustained tissue penetration achieved with TAR-200 via the iDRS.
- **Only 5.8% of patients underwent subsequent radical cystectomy.**
- High overall survival (OS) and progression-free survival (PFS) rates were observed at 9 months (98.0% and 95.6%, respectively).
- No new safety signals were detected; most TEAEs were grade 1 or 2 lower urinary tract symptoms, with low rates of serious TRAEs and few discontinuations due to TRAEs.
- The ongoing **phase 3 SunRISe-5 study (NCT06211764)**, comparing TAR-200 monotherapy to intravesical chemotherapy in patients with BCG-unresponsive or BCG-experienced papillary-only high-risk NMIBC, will provide further evidence supporting TAR-200's potential in this setting

Imfinzi regimen demonstrated statistically significant and clinically meaningful improvement in disease-free survival for high-risk non-muscle-invasive bladder cancer in POTOMAC Phase III trial



PUBLISHED
9 May 2025

Positive high-level results from the POTOMAC Phase III trial showed one year of treatment with AstraZeneca's *Imfinzi* (durvalumab) plus standard-of-care BCG induction and maintenance therapy demonstrated a statistically significant and clinically meaningful improvement in disease-free survival (DFS) for patients with high-risk non-muscle-invasive bladder cancer (NMIBC) compared to BCG induction and maintenance therapy alone.

Thank You

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