Baptist Health

Advancement in Therapy Options for BCG Refractory Patients

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Background

- Bladder cancer is the sixth most common cancer in the U.S.
- Approximately 83,190 new cases of bladder cancer in the U.S. in 2024
  - 75% NMIBC
- Bladder cancer cost of inpatient and outpatient care in US was estimated to be $4.9 billion on 2020.
- The overall 5-year survival for bladder cancer is 78.4%
  - 97.2% for carcinoma in situ (CIS)
  - 71.7% for localized disease
  - 39.5% for regionally spread
  - 8.8% for distant metastasis

Burger et al, Eur Urol. 2013;63(2):234-41
Al Hussein et al, Curr Oncol Rep. 2023;25(2):83-91
Chamie et al,NEJM. 2023;2(1)

Risk stratification for Non-Muscle Invasive Bladder Cancer

Low Risk	Intermediate Risk	High Risk
Papillary urothelial neoplasm of low malignant potential	Low grade urothelial carcinoma • T1 or • >3 cm or • Multifocal or • Recurrence within 1 year	High grade urothelial carcinoma • CIS or • T1 or • >3 cm or • Multifocal **BCG preferred treatment*
Low Grade Urothelial Carcinoma • Ta and • ≤3 cm and • Solitary	High grade urothelial carcinoma • Ta and • ≤3 cm and • Solitary	Very high-risk features (any): • BCG unresponsive • Variant histologies • Lymphovascular invasion • Prostatic urethral invasion **Cystectomy preferred treatment*

Chamie et al,NEJM. 2023;2(1)
NCCN Guidelines® for Bladder Cancer V.1.2024

Background: NMIBC Treatment Options for High Risk

Bacillus Calmette-Guerin (BCG) vaccine

- Contains live attenuated Mycobacterium bovis and is the most effective intravesical therapy
- Complete response rates after induction
  - 55-65% for papillary tumors
  - 70-75% CIS
  - 30-45% fail BCG
- More than half of patients with an initial complete response, have recurrence and progression within the first year and some may develop BCG-unresponsiveness

BCG unresponsiveness

- BCG responsiveness involves humoral and cell-mediated mechanisms
- Evidence suggests impaired Th1 and cytotoxic cellular responses leading to BCG therapy failure
- Targeted immunotherapies are thought to potentiate the response
  - IFN-γ, IL-2, IL-12, and IL-15

Chamie et al,NEJM. 2023;2(1)
NCCN Guidelines® for Bladder Cancer V.1.2024

Treatment for BCG-Unresponsive or BCG-Intolerant NMIBC

Radical cystectomy (preferred)

- The most definitive treatment but carries high morbidity and many patients are not candidates for the procedure

Systemic pembrolizumab therapy

- Not an option for patients who are not candidates for immune checkpoint inhibitors
  - Category 2A: high-risk NMIBC with Tis (with or without papillary tumors)
  - Category 2B: high-risk NMIBC high-grade papillary Ta/T1 only tumors without Tis who are ineligible for cystectomy

Nadofaragene Firadenovec-vncg

- FDA approved on 12/2022 for adult patients with high-risk BCG unresponsive NMIBC with CIS with or without papillary tumors.
  - Category 2A: high-risk NMIBC with CIS (with or without papillary)
  - Category 2B: high-risk NMIBC with high-grade papillary Ta/T1 only tumors without CIS

Nogapendekin alfa inbakicept

- FDA approved for adult patients with high-risk BCG unresponsive, high risk NMIBC with CIS with or without papillary tumors.
  - Category 2A

Chamie et al,NEJM. 2023;2(1)
NCCN Guidelines® for Bladder Cancer V.1.2024

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Pembrolizumab

- Activation of PD-1-PD-L1 pathway is associated with resistance to BCG
- Increased PD-L1 expression was observed in tumors that relapsed after BCG treatment
- PD-L1 expression is associated with recurrence and progression
- KEYNOTE-057 hypothesized that pembrolizumab could induce a clinical complete response in BCG-unresponsive high risk NMIBC

Balar et al, Lancet Oncol. 2021;22(7)

Study Keynote-057

Pembrolizumab monotherapy for the treatment of high-risk non-muscle invasive bladder cancer unresponsive to BCG: an open-label, single arm, multicenter, phase 2 study

Design

- Phase 2 multicenter, single-arm, open-label clinical study

Intervention

- Pembrolizumab 200mg every 21days
  - Cohort A (n=101): patients with CIS with or without papillary tumors
  - Cohort B (n=47): BCG unresponsive high-grade Ta or any grade T1 papillary disease without carcinoma in situ

Procedure

- Treatment up to 24 months or until evidence of disease persistence, recurrence, or progression; unacceptable toxicity or withdrawing consent
  - Patients with evidence of high risk NMIBC at any efficacy evaluation, including at 3 months had to discontinue treatment without possibility of retreatment
  - Patients with low grade Ta recurrence could remain in the study after complete resection
  - After 18 months of treatment, if no evidence of disease on at least 2 consecutive evaluations, stopping treatment was allowed

Balar et al, Lancet Oncol. 2021;22(7)

Study Keynote-057

Pembrolizumab monotherapy for the treatment of high-risk non-muscle invasive bladder cancer unresponsive to BCG: an open-label, single arm, multicenter, phase 2 study

Primary objective:

- Complete response rate, defined as the absence of high-risk disease or progressive disease

Secondary objectives:

- Safety
- Complete rate of any disease (absence of low-grade Ta, high risk, and progressive disease)
- Duration of response for high risk and any disease (time from first documented evidence of complete response until centrally confirmed recurrence of high risk NMIBC or progressive disease or any disease)
- Progression free survival to worsening of grade or stage or death
- Progression free survival to muscle invasive or metastatic disease or death
- Overall Survival (time from enrollment to death from any cause)

Balar et al, Lancet Oncol. 2021;22(7)

Study Keynote-057: Results

Efficacy in Cohort A

Complete Response	**39 (41%, 30.7-51.1)**
Non-Complete Response	56 (58%, 47.8-68.3)
Persistent disease	40 (42%, 31.7-52.2)
Recurrent disease	6 (6%, 2.3-13.1)
NMIBC stage progression (CIS or Ta to T1 disease)	9 (9%, 4.4-17.1)
Non bladder malignancy (Pancreatic malignancy)	1 (1%, 0.0-5.7)
Progression to muscle invasive disease (T2)	0 (N/A-N/A)
Non evaluable (Discontinue from trial)	1 (1%, 0.0-5.7)

Balar et al, Lancet Oncol. 2021;22(7)

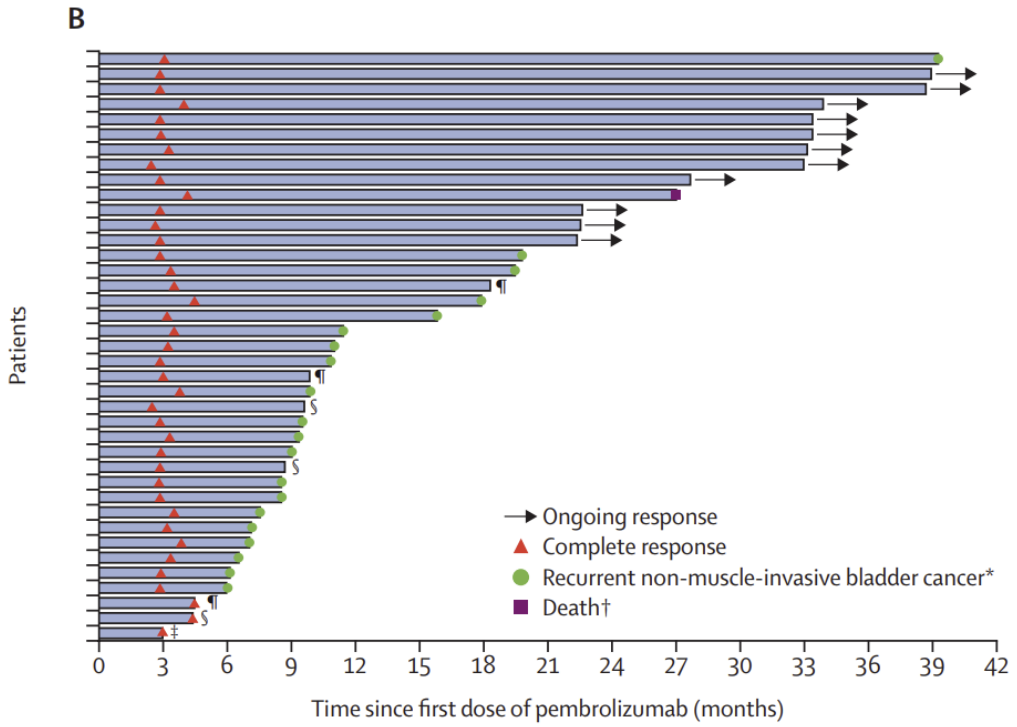
Study Keynote-057: Results

Cohort A

- Median duration of complete response: 16.2 months (95% CI 6.7-36.2)

Of 39 patients with complete response:

- 18 (46%) remained in complete response at 12 months
- 11 (28%) had an ongoing complete response at data cutoff
- 20 (51%) had recurrent disease after an initial complete response
- 1 (3%) recurred after 2 or more consecutive non-evaluable assessments
- 3 (8%) started new anticancer treatment before confirmed recurrence
- 3 (8%) withdrew consent
- 1 (3%) died from CHF (unrelated to treatment)



Balar et al, Lancet Oncol. 2021;22(7)

Study Keynote-057: Safety

Cohort A

	Grade 1 or 2	Grade 3*	Grade 4†
Any	54 (53%)	11 (11%)	2 (2%)
Diarrhoea	11 (11%)	0	0
Fatigue	11 (11%)	0	0
Pruritus	10 (10%)	1 (1%)	0
Hypothyroidism	7 (7%)	0	0
Rash maculo-papular	6 (6%)	0	0
Hyperthyroidism	5 (5%)	0	0
Rash	5 (5%)	0	0
Nausea	5 (5%)	0	0
Arthralgia	4 (4%)	2 (2%)	0
Dry mouth	3 (3%)	0	0
Pneumonitis	3 (3%)	0	0
Rash pruritic	3 (3%)	0	0
Abdominal pain	2 (2%)	0	0
Alanine aminotransferase increased	2 (2%)	0	0
Asthaenia	2 (2%)	0	0
Blood thyroid-stimulating hormone decreased	2 (2%)	0	0
Colitis	2 (2%)	0	0
Constipation	2 (2%)	0	0
Eczema	2 (2%)	0	0
Haematuria	2 (2%)	0	0
Influenza-like illness	2 (2%)	0	0
Malaise	2 (2%)	1 (1%)	0
Myalgia	2 (2%)	0	0
Neuropathy peripheral	2 (2%)	0	0
Pyrexia	2 (2%)	0	0
Dermatitis	1 (1%)	1 (1%)	0
Hyponatraemia	0	2 (2%)	1 (1%)

Balar et al, Lancet Oncol. 2021;22(7)

Study Keynote-057: Results

Cohort A: Radical Cystectomy

	Patients (n=38)	N Stage	Achieved initial complete response	Interval between last dose of Pembrolizumab and radical cystectomy in days	Pembrolizumab doses
Non-Muscle Invasive Bladder Cancer					
pT0	6	N0=5 Nx=1	4	135 (91-138	11.5 (7-14)
pTa	5	N0=5	0	103 (79-209)	5 (5-6)
pTis	18	N0=16, Nx=2	6	77 (61-176)	6.5 (6-7)
pT1	6	N0=6	0	133 (77-170)	6.5 (6-7)
Muscle-Invasive Bladder Cancer					
pT2	2	N0=1, N1=1	0	60	3.5 (3-4)
pT3	1	N1	0	457	6

Balar et al, Lancet Oncol. 2021;22(7)

Study Keynote-057: Results

Cohort B

- 12-month DFS rate in high-risk NMIBC was 43.5% (95% CI, 34.9%-51.9%)
  - Median DFS was 7.7 months (95% CI, 5.5-13.6).
- 12-month rate of any-disease DFS (defined as low-grade Ta, high-risk NMIBC, and progressive disease) was 41.7% (95% CI, 33.1%-50.0%)
  - Median was 6.0 months (95% CI, 4.3-12.0).
- 12-month PFS rate to worsening of grade, stage, or death was 88.2% (95% CI, 80.0%-93.2%)
  - Median of 44.5 months (95% CI, 34.6-not available).
- 12-month PFS rate to muscle invasion, metastasis, or death was 88.2% (95% CI, 79.4%-93.3%)
  - Median of 46.2 months (95% CI, 36.8-not available).
- 12-month OS rate was 96.2% (95% CI, 91.1%-98.4%), and the
  - Median was not reached.

Balar et al, Lancet Oncol. 2021;22(7)

Study Keynote-057: Safety

Cohort B

- 97 patients (73.5%) experienced a treatment-related adverse events
  - 19 (14.4%) experienced a grade 3 or 4 treatment-related adverse events
  - 17 (12.9%) experienced a serious treatment-related adverse events
  - 14 (10.6%) discontinued treatment due to treatment-related adverse events

There were no deaths from treatment-related adverse events

Balar et al, Lancet Oncol. 2021;22(7)

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Nadofaragene firadenovec-vncg

Mechanism of action: non-replicating adenoviral vector-based gene therapy designed to deliver a copy of a gene encoding a human interferon-alfa 2b (IFNa2b) to the bladder urothelium

- Intravesical instillation of nadofaragene firadenovec-vncg results in cell transduction and transient local expression of the IFNa2b protein that is anticipated to have anti-tumor effects

Boorjian et al, Lancet Oncol 2021; 22: 107–17

Study CS-003

Intravesical nadofaragene firadenovec-vncg gene therapy for BCG-unresponsive non-muscle invasive bladder cancer

Design

- Phase 3 multicenter, single-arm, open-label, repeat-dose clinical study

Intervention

- Nadofaragene ($3x10^{11}$ vp/mL [75 mL]) was administered intravesically once every 3 months for up 4 doses over 12 months
  - Patients without evidence of high-grade disease at month 12 were offered continued treatment at the investigator's discretion

Study Endpoints

- Primary objective: Complete response, defined as negative urine cytology and cystoscopy as assessed by the treating physician
- Secondary objectives:
  - Durability of complete response in CIS patients
  - High grade recurrence free survival
  - Durability of high-grade recurrence-free survival in both cohorts
  - Radical cystectomy-free survival in both cohorts

Boorjian et al, Lancet Oncol 2021; 22: 107–17

Study CS-003: Results

Outcome	Carcinoma in situ cohort (n=103)	High grade Ta or T1 cohort (n = 48)	All patients (n = 151)	P value
Complete response at month 3	55 (53.4%)	35 (72.9%)	90 (59.6%)	<0.0001
Duration of complete response† or high-grade recurrence free survival‡, months	9.69 (95% CI: 9.17 – NE)	12.35 (95% CI: 6.67 – NE)	7.31 (95% CI: 5.68 – 11.93)	
Patients free from high-grade recurrence:				
At month 6	42 (40.8%)	30 (62.5%)	72 (47.7%)	
At month 9	36 (35.0%)	28 (58.3%)	64 (42.4%)	
At month 12	25 (24.3%)	21 (43.8%)	46 (30.5%)	

†Patients in the carcinoma in situ cohort
‡Patients in the high-grade Ta or T1 cohort

- 74% of patients were cystectomy-free at the time of 12-month data cutoff
- Of patients who achieved CR, 36% of patients in a post-hoc analysis remained free of high-grade recurrence for up to 2 years

Boorjian et al, Lancet Oncol 2021; 22: 107–17

Study CS-003: Safety

Study drug-related adverse events	Grade 1-2	Grade 3	Grade 4-5
Patients with study drug-related adverse events	103 (66%)	6 (4%)	0
Type of event			
Discharge around the catheter during instillation	39 (25%)	0	0
Fatigue	31 (20%)	0	0
Bladder spasm	24 (15%)	1 (1%)	0
Micturition urgency	22 (14%)	2 (1%)	0
Chills	18 (12%)	0	0
Dysuria	17 (11%)	0	0
Pyrexia	16 (10%)	0	0
Syncope	0	1 (1%)	0
Hypertension	2 (1%)	1 (1%)	0
Urinary incontinence	4 (3%)	1 (1%)	0

- No grade 4 – 5 adverse events due to study drug observed
- 3 patients discontinued the study drug due to adverse events
  - One due to bladder spasms, one due to discharge around the catheter during instillation, and one due to the identification of a benign neoplasm of the bladder [urothelial hyperplasia] that was believed by the investigators to be related to the study drug

Boorjian et al, Lancet Oncol 2021; 22: 107–17

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Nogapendekin alfa inbakicept-pmln

Mechanism of action: immune cell-activating interleukin-15 superagonist, with high affinity to a dimeric human IL-15 alpha domain.

It is an immunostimulatory protein complex that acts as a growth and activation factor for NK cells and effector and memory T cells, stimulating cellular immune responses and exhibiting potent activity against human tumor cells, especially in combination with BCG.

Chamie et al,NEJM. 2023;2(1)

Study QUILT-3.032

A Multicenter Clinical Trial of Intravesical Bacillus Calmette-Guerin (BCG) in Combination with ALT-803 in Patients with BCG Unresponsive High Grade Non-Muscle Invasive Bladder Cancer

Design

- Phase 2/3, open label, single-arm, three-cohort, multicenter study of intravesical BCG plus N-803 or N-803 alone in patients with BCG unresponsive high grade NMIBC

Intervention

- Cohort A (n=84): BCG unresponsive CIS [with or without Ta/T1 papillary disease]
- Cohort B (n=77): BCG unresponsive high-grade Ta/T1 papillary disease
- Cohort C (n=10): Exploratory: BCG unresponsive CIS [with or without Ta/T1 papillary disease]
  - Cohorts A and B: 400mcg N-803 + 50mg BCG weekly for 6 consecutive weeks. Reinduction allowed if residual CIS and/or high-grade Ta
  - Cohort C received 400mcg N-803 alone, weekly for 6 consecutive weeks. Reinduction allowed if residual CIS and/or high-grade Ta

Primary Endpoints

- Cohorts A and C: Incidence of Complete response (CR) of CIS at any time
- Cohort B: Disease-free rate at 12 months since first instillation of BCG + N-803

Secondary Endpoints

- Cohort A and C: Duration of complete response; CR rate at 3, 6, 9, 12, 15, 18, 21, 24, 30, 36, 42, 48, 54, and 60 months
- Cohort B: Disease-free survival (DFS); disease-free rate at 3, 6, 9, 12, 15, 18, 21, 24, 30, 36, 42, 48, 54, and 60 months

Complete response (either):
Negative cystoscopy and negative urine cytology
Positive cystoscopy with biopsy-proven benign or low-grade Ta NMIBC and negative cytology
Negative cystoscopy with malignant urine cytology if cancer is found in the upper tract or prostatic urethra and random bladder biopsies are negative.

Disease Free is defined as the absence of the following:
High-grade Ta (excluding low-grade Ta), any grade T1, persistent CIS ≥ 6 months, new CIS, disease progression, cystectomy, change in therapy
indicative of more advanced disease, and death (any cause) since first instillation of the study drug.

Chamie et al,NEJM. 2023;2(1)

Study QUILT-3.032

A Multicenter Clinical Trial of Intravesical Bacillus Calmette-Guerin (BCG) in Combination with ALT-803 in Patients with BCG Unresponsive High Grade Non-Muscle Invasive Bladder Cancer

Endpoints	Cohort A	Cohort B	Cohort C
Additional Secondary Endpoints	1- CR rate at any time per CPR 2- CR rate (all recurrent BC, including low grade Ta disease) 3- Duration of CR (all recurrent BC, including low grade Ta disease)	1- DFS (all recurrent BC, including low grade Ta disease) 2- Disease free rate at previously determined frequency (all recurrent BC, including low grade Ta disease) 3- DFS (adjusted for re-induction) 4- Disease free rate at previously determined frequency (adjusted for re-induction)	
	1- Progression-free survival (PFS) 2- Overall Survival (OS): Time from first instillation of study drug to death resulting from any cause 3- Disease-specific survival (DSS): Time from first instillation of study drug to death resulting from bladder cancer 4- Time to disease worsening: Cystectomy or change in therapy indicative of more advanced disease, including systemic chemotherapy or radiation therapy 5- Time to cystectomy 6- Safety 7- Immunogenicity 8- Quality of Life (QOL)		1- Safety 2- Immunogenicity 3- Quality of Life (QOL)

Chamie et al,NEJM. 2023;2(1)

Study QUILT-3.032: Results

Efficacy in Cohort A: Complete response and duration of response

Response	Value
Complete response (number of patients)	58/82 45 patients at initial treatment 13 patients at reinduction
CR rate (95% CI) 3 months 6 months 12 months	71% (59.6 to 80.3) 55% (45 of 82 patients; 95% CI=43.5% to 65.9%) 56% (46 of 82 patients; 95% CI=44.7 to 67%) 45% (37 of 82 patients; 95% CI=34.1 to 56.5%)
Median duration of follow up	23.9 months (3.2-37.5 months)
Duration of Response	
Median (month) (95% CI)	26.6 (9.9 to upper bound not reached)
Patients with Duration of response ≥12mo (%) (n/N)	37 (30/82)
Patients with Duration of response ≥18mo (%) (n/N)	24 (20/82)

28 patients had ongoing CR at the time of data cutoff or withdrawal from the study

Chamie et al,NEJM. 2023;2(1)

Study QUILT-3.032: Results

Efficacy in Cohort A: Survival

Progression Free Survival Rate (%) (95% CI)	Responders	All
12 mo	91.1 (79.8-96.2)	88.4 (78.9-93.8)
18 mo	91.1 (79.8-96.2)	86.9 (77-92.8)
24 mo	88.1 (74.9-94.6)	84.7 (73.6-91.3)
Disease-specific survival (%) (95% CI)		
12 mo	100 (100-100)	100 (100-100)
24 mo	100 (100-100)	100 (100-100)
Overall Survival (%) (95% CI)		
12 mo	94.8 (84.8-98.3)	96.2 (88.8-98.8)
18 mo	94.8 (84.8-98.3)	96.2 (88.8-98.8)
24 mo	92.1 (79.7-97)	94.3 (85.1-97.7)

Chamie et al,NEJM. 2023;2(1)

Study QUILT-3.032: Results

Efficacy in Cohort A: Reinduction

- Patients without a CR with residual CIS or high-grade Ta at the 3 month
  - Total: 24 patients
    - CR: 54% (13/24; 95%CI=32.8% to 74.4%)

	CR	Duration of CR Kaplan-Meier estimated probability
6 months	46% (11/24; 95%CI=25.6 to 67.2%)	76.9% (95%CI=44.2 to 91.9%)
12 months	42% (10/24; 95%CI=22.1 to 63.4%)	43.3% (95%CI=12.7 to 71.1%)
18 months	21% (5/24; 95%CI=7.1 to 42.2%)	43.3% (95%CI=12.7 to 71.1%)
24 months and beyond		21.6% (95%CI=1.4 to 57.9%)

Chamie et al,NEJM. 2023;2(1)

Study QUILT-3.032: Results

Efficacy in Cohort A: Cystectomy

	Responders	Non-Responders
Cystectomy	7% (4/58)	33% (8/24)
Median time to cystectomy	11 months	7.8 months
Kaplan-Meier estimated probability		
Cystectomy free for at least 12 months (Kaplan-Meier estimated probability)	94.3%	68.5%
Cystectomy free for at least 24 months (Kaplan-Meier estimated probability)	89.2%	63.2%

Chamie et al,NEJM. 2023;2(1)

Study QUILT-3.032: Results

Efficacy in Cohort B: Disease Free Survival

Response	Value
Complete number of evaluable patients	72
Median duration follow-up	20.7 months
Range of follow-up of all patients	2.9-37.1 months
Median disease-free survival (95% CI)	19.3 (7.4 to upper bound not reached)
Disease-free survival rate (95% CI)	
12 months	55.4 (42-66.8)
18 months	51.1 (37.6-63.1)
24 months	48.3 (34.5-60.7)
Progression-free survival rate (95% CI)	
12 months	97.1 (88.8-99.3)
18 months	94.8 (84.3-98.3)
24 months	88.8 (74.1-95.4)

Chamie et al,NEJM. 2023;2(1)

Study QUILT-3.032: Results

Efficacy in Cohort B: Disease Free Survival

Response	Value
Disease-specific survival (95% CI)	
12 months	100 (100-100)
24 months	97.7 (84.6-99.7)
Overall Survival (95% CI)	
12 months	98.6 (90.2-99.8)
18 months	94.3 (82.9-98.1)
24 months	91.7 (79-96.9)
Cystectomy range	7% (5 patients)

Chamie et al,NEJM. 2023;2(1)

Study QUILT-3.032: Results

Efficacy in Cohort C: Response to N-803 monotherapy

- Total patients:10
  - CR at 3 months: 2/10 patients (20%)
  - Reinductions: 3/10 patients (30%)
  - CR at 6 months: 1/10 patients (10%)

Cohort C discontinued at 6 months into study conduct

Chamie et al,NEJM. 2023;2(1)

Study QUILT-3.032: Treatment Related Adverse Events

Cohort A and B

- Grade 1-2: 86%
- Grade 3: 20%
- Grade 4: 2%
- Grade 5: 1%

ADR requiring hospitalization

- 24/161 patients (15%)
  - 8 patients (5%)—bladder related
    - hematuria 2%
    - UTI 1%
    - Bladder perforation 1%
    - Cystitis hemorrhagic 1%

Most common ADRs ≥15%:

- Dysuria
- Hematuria
- Urinary frequency
- Micturition urgency
- Urinary tract infection
- Musculoskeletal pain
- Chills
- Pyrexia
- Increased serum creatinine
- Increased potassium

Grade 3 or 4 ADRs:

- Hematuria (2%)
- Urinary tract infection (2%)
- Musculoskeletal pain (1%)

Fatal adverse reaction

- Cardiac arrest
  - 1 (1.1%) patient

Chamie et al,NEJM. 2023;2(1)

Advancements in Therapy Options for BCG Refractory patients | Private and confidential. Not for distribution.

Summary

Systemic Pembrolizumab
Category 2A: high-risk NMIBC with Tis (with or without papillary tumors)
Category 2B: high-risk NMIBC high-grade papillary Ta/T1 only tumors without Tis who are ineligible for cystectomy

Intravesical Nadofaragene firadenovec-vncg
Category 2A: high-risk NMIBC with CIS (with or without papillary)
Category 2B: high-risk NMIBC with high-grade papillary Ta/T1 only tumors without CIS

Intravesical Nogapendekin alfa inbakicept
Category 2A recommendation for high-risk BCG unresponsive, high risk NMIBC with CIS with or without papillary tumors.

The clinical trials for pembrolizumab, nadofaragene firadenovec-vncg, and nogapendekin alfa inbakicept underscore their roles as active, non-surgical treatment options for patients with BCG-unresponsive NMIBC (non-muscle invasive bladder cancer).

This address a major unmet need, providing alternatives for patients who do not respond to BCG therapy and wish to avoid cystectomy.

The success of these agents also establishes a foundation for future trials to explore expanded indications, potential combination therapies, and improved outcomes in NMIBC treatment.

References

1. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Access 11/1/2024
2. Mary Vogel Nadofaragene
3. Chamie K, Chang S, Kramolowsky E, et al. IL-15 Superagonist NAI in BCG-Unresponse Non-Muscle-Invasive Bladder Cancer. NEJM Evid 2023; 2(1): EVIDoa2200167. doi: 10.1056/EVIDoa2200167. Epub 2022 Nov 10. PMID: 38320011.
4. Burger M, Catto JW, Dalbagni G, et al. Epidemiology and risk factors of urothelial bladder cancer. Eur Urol. 2013;63(2):234-41.
5. Al Hussein Al Awamlh B, Chang SS. Novel Therapies for High-Risk Non-Muscle Invasive Bladder Cancer. Curr Oncol Rep. 2023;25(2):83-91. doi:10.1007/s11912-022-01350-9
6. ANKTIVA (nogapendekin alfa inbakicept-pmln) [prescribing information]. AGC Biologics; 2024.
7. nogapendekin alfa inbakicept-pmln. Lexi-Drugs. Lexicomp Online. Lexicomp; 2024. Accessed August 22, 2024. https://online.lexi.com
8. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer V.1.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. NCCN.org.
9. Dinney CP, Greenberg RE, Steinberg GD. Intravesical valrubicin in patients with bladder carcinoma in situ and contraindication to or failure after bacillus Calmette-Guérin. Urol Oncol. 2013;31(8):1635-1642. doi:10.1016/j.urolonc.2012.04.010
10. Steinberg G, Bahnson R, Brosman S, Middleton R, Wajsman Z, Wehle M. Efficacy and safety of valrubicin for the treatment of Bacillus Calmette-Guerin refractory carcinoma in situ of the bladder. The Valrubicin Study Group [published correction appears in J Urol. 2008 Jan;179(1):386]. J Urol. 2000;163(3):761-767.
11. McKiernan JM, Masson P, Murphy AM, et al. Phase I trial of intravesical docetaxel in the management of superficial bladder cancer refractory to standard intravesical therapy. J Clin Oncol. 2006;24(19):3075-3080. doi:10.1200/JCO.2005.03.1161
12. Barlow LJ, McKiernan JM, Benson MC. Long-term survival outcomes with intravesical docetaxel for recurrent nonmuscle invasive bladder cancer after previous bacillus Calmette-Guérin therapy. J Urol. 2013;189(3):834-839. doi:10.1016/j.juro.2012.10.068
13. Balar AV, Kamat AM, Kulkarni GS, et al. Pembrolizumab monotherapy for the treatment of high-risk non-muscle-invasive bladder cancer unresponsive to BCG (KEYNOTE-057): an open-label, single-arm, multicentre, phase 2 study [published correction appears in Lancet Oncol. 2021 Aug;22(8):e347]. Lancet Oncol. 2021;22(7):919-930. doi:10.1016/S1470-2045(21)00147-9

Thank You.

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