Teaching. Discovering. Caring

Bladder cancer: 4th Most common cancer in men

Michael B. Williams, MD, MS
Urologic Oncology
Associate Professor
Department of Urology
Eastern Virginia Medical School
Norfolk

EVMS
Eastern Virginia Medical School

Urology of Virginia

Disclosures

- Janssen
- Merck
- Astellas
- Pfizer
- Fergene

Objectives

- Defining NMIBC
- Important steps with respect to TURBT
  - Why restaging?
- Therapies

Basic Statistics

TABLE 1 Estimated number of new cancer cases and deaths by sex, United States, 2025.

	Estimated new cases			Estimated deaths		
	Both sexes	Male	Female	Both sexes	Male	Female
Urinary system	170,470	120,320	50,150	33,140	22,840	10,300
Urinary bladder	84,870	65,080	19,790	17,420	12,640	4780

~ 20% of those diagnosed will die of disease

Globally- 600,000 new cases per year

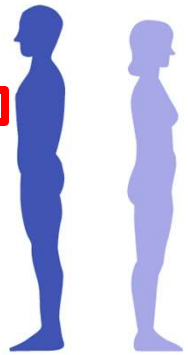
~1970 new cases in Virginia

CA Cancer J Clin. 2025;75:10–45.

New Cases and Deaths

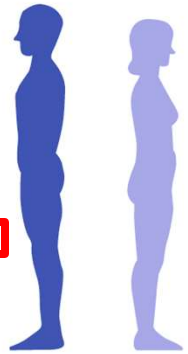
Estimated New Cases

Male			Female		
Prostate	313,780	30%	Breast	316,950	32%
Lung & bronchus	110,680	11%	Lung & bronchus	115,970	12%
Colon & rectum	82,460	8%	Colon & rectum	71,810	7%
Urinary bladder	65,080	6%	Uterine corpus	69,120	7%
Melanoma of the skin	60,550	6%	Melanoma of the skin	44,410	4%
Kidney & renal pelvis	52,410	5%	Non-Hodgkin lymphoma	35,210	4%
Non-Hodgkin lymphoma	45,140	4%	Pancreas	32,490	3%
Oral cavity & pharynx	42,500	4%	Thyroid	31,350	3%
Leukemia	38,720	4%	Kidney & renal pelvis	28,570	3%
Pancreas	34,950	3%	Leukemia	28,170	3%
All sites	**1,053,250**		**All sites**	**988,660**	



Estimated Deaths

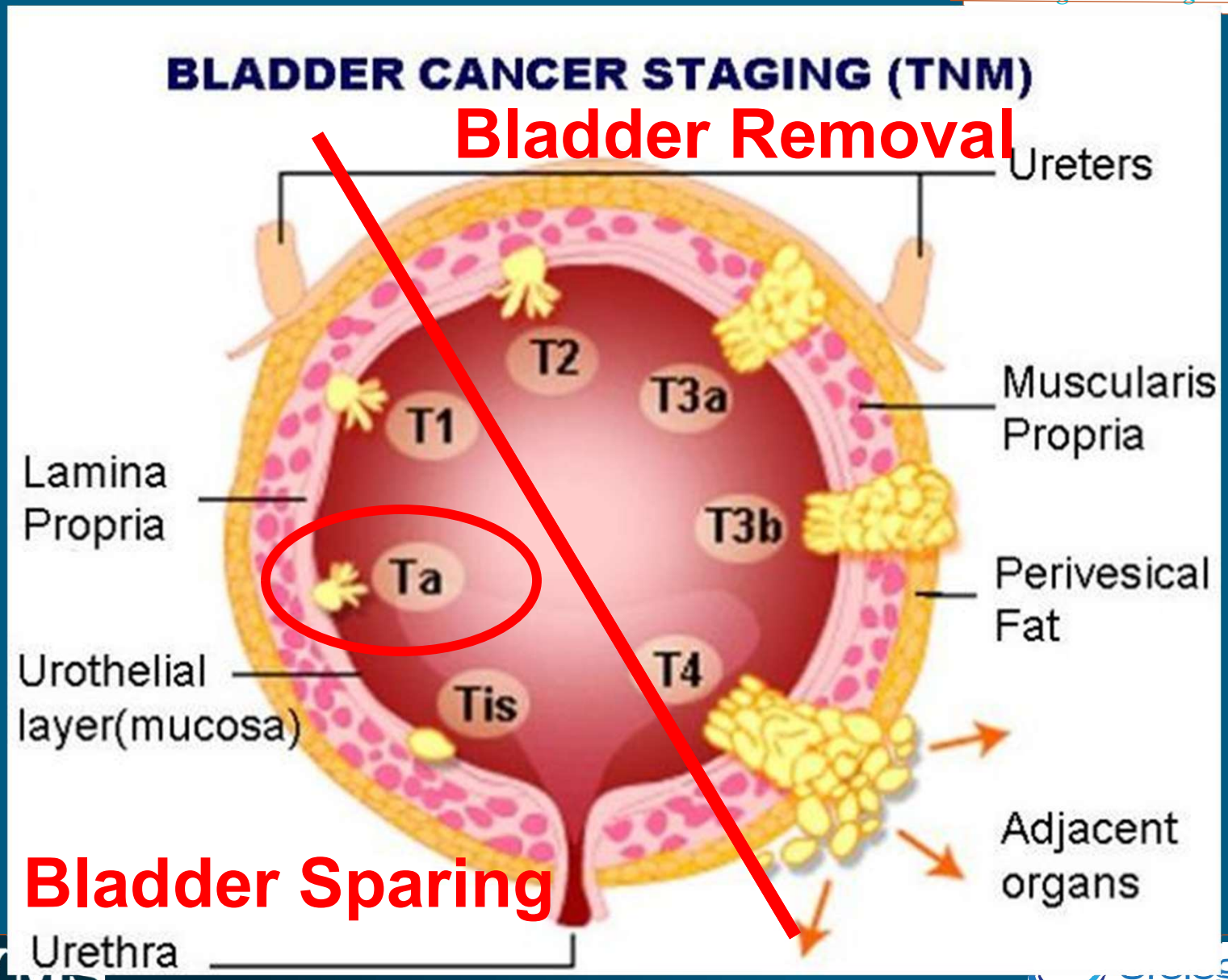
Male			Female		
Lung & bronchus	64,190	20%	Lung & bronchus	60,540	21%
Prostate	35,770	11%	Breast	42,170	14%
Colon & rectum	28,900	9%	Pancreas	24,930	8%
Pancreas	27,050	8%	Colon & rectum	24,000	8%
Liver & intrahepatic bile duct	19,250	6%	Uterine corpus	13,860	5%
Leukemia	13,500	4%	Ovary	12,730	4%
Esophagus	12,940	4%	Liver & intrahepatic bile duct	10,840	4%
Urinary bladder	12,640	4%	Leukemia	10,040	3%
Non-Hodgkin lymphoma	11,060	3%	Non-Hodgkin lymphoma	8,330	3%
Brain & other nervous system	10,170	3%	Brain & other nervous system	8,160	3%
All sites	**323,900**		**All sites**	**294,220**	



EVMS Eastern Virginia Medical School

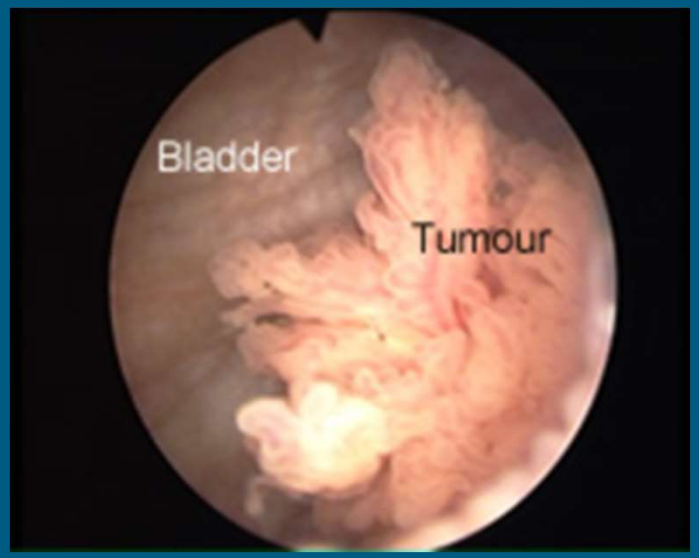
CA Cancer J Clin. 2025;75:10–45.

Urology of Virginia


BLADDER CANCER STAGING (TNM)
Bladder Removal
Ureters
T2
T3a
T1
Muscularis Propria
Lamina Propria
T3b
Ta
Perivesical Fat
Urothelial layer(mucosa)
T4
Tis
Adjacent organs
Bladder Sparing
Urethra

TURBT

- Important concepts
  - Complete resection
  - Path sent with "deep biopsy"



Teaching. Discovering. Caring

Therapies for NMIBC

Risk stratification
Intravesical Medications
BCG refractory medications

EVMS
Eastern Virginia Medical School

Urology of Virginia

Risk stratification

AUA 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 ▸ Ta and ▸ ≤3 cm and ▸ Solitary	• Low grade urothelial carcinoma ▸ T1 or ▸ >3 cm or ▸ Multifocal or ▸ Recurrence within 1 year • High grade urothelial carcinoma ▸ Ta and ▸ ≤3 cm and ▸ Solitary	• High grade urothelial carcinoma ▸ CIS or ▸ T1 or ▸ >3 cm or ▸ Multifocal • Very high risk features (any): ▸ BCG unresponsive[l] ▸ Variant histologies[m] ▸ Lymphovascular invasion ▸ Prostatic urethral invasion

Observe

MMC
Gemcitabine

BCG

BCG

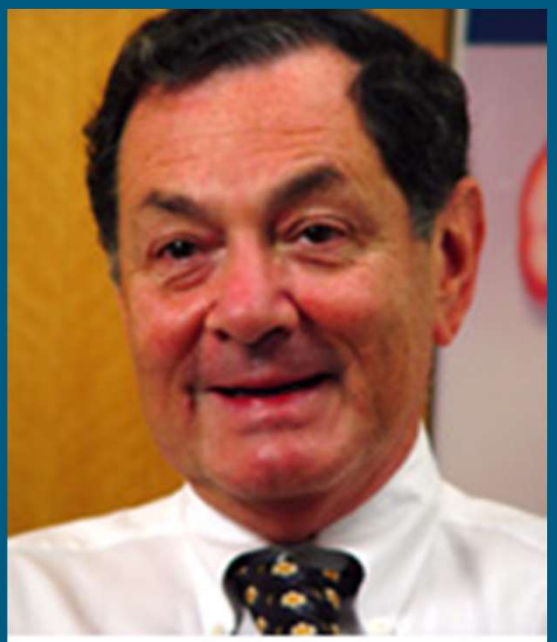
- Bacillus Calmette–Guerin
- Attenuated strain of Mycobacterium bovis

Albert Calmette
(1863-1933)

Camille Guerin
(1872-1961)

BCG History

- 1970s BCG introduced to UC Bladder
- Serendipity



Alvaro Morales, MD

- N=7

INTRACAVITARY BACILLUS CALMETTE-GUERIN IN THE TREATMENT OF SUPERFICIAL BLADDER TUMORS

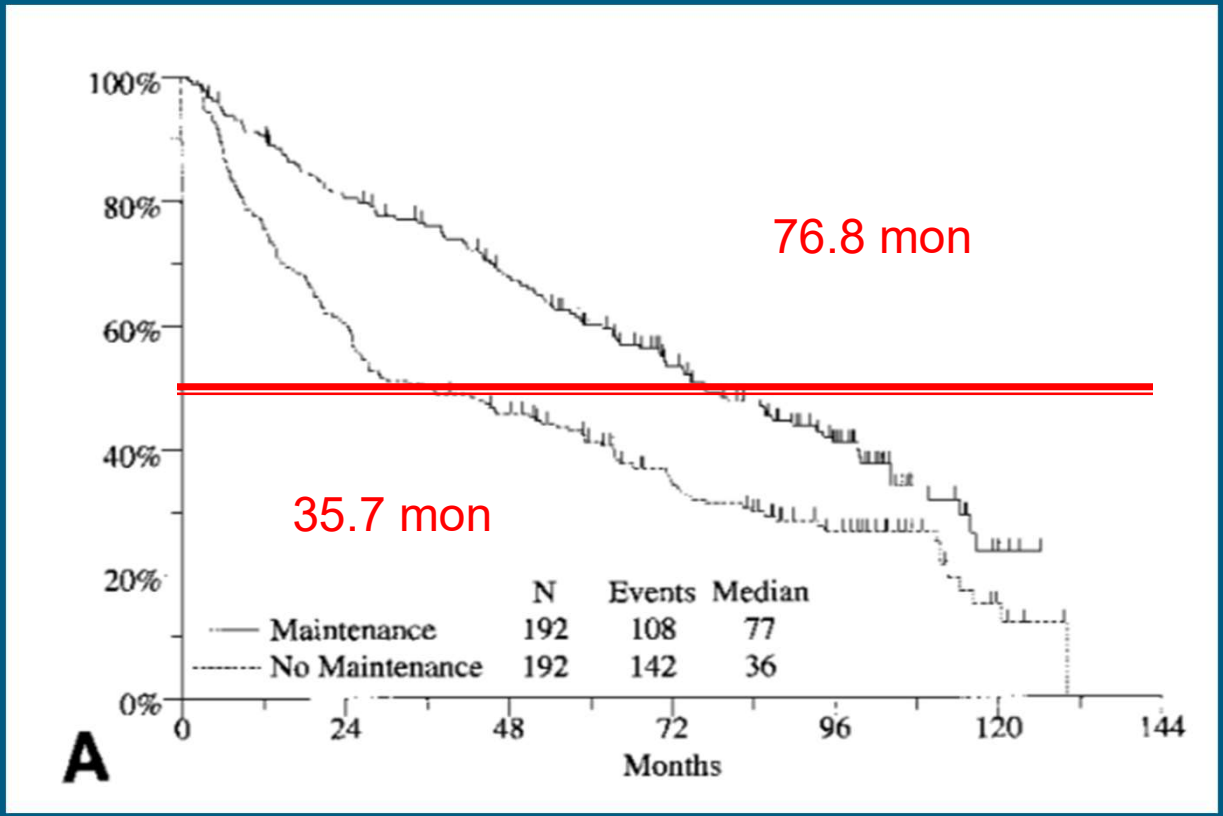
A. MORALES,* D. EIDINGER AND A. W. BRUCE

From the Departments of Urology, and Microbiology and Immunology, Queen's University, Kingston, Ontario, Canada

(Reprinted from J Urol, 116: 180–183, 1976)

MAINTENANCE BACILLUS CALMETTE-GUERIN IMMUNOTHERAPY FOR RECURRENT TA, T1 AND CARCINOMA IN SITU TRANSITIONAL CELL CARCINOMA OF THE BLADDER: A RANDOMIZED SOUTHWEST ONCOLOGY GROUP STUDY

DONALD L. LAMM,*,† BRENT A. BLUMENSTEIN, JOHN D. CRISSMAN, JAMES E. MONTIE, JAMES E. GOTTESMAN, BRUCE A. LOWE, MICHAEL F. SAROSDY,‡ ROBERT D. BOHL, H. BARTON GROSSMAN,§ THOMAS M. BECK, JOSEPH T. LEIMERT AND E. DAVID CRAWFORD‖



Recurrence Free Survival

OS

Main 83%

No-Main 78%

16% of Maint patients Completed all 27 Instillations over 3-yrs

JU Vol. 163, 1124–1129, April 2000

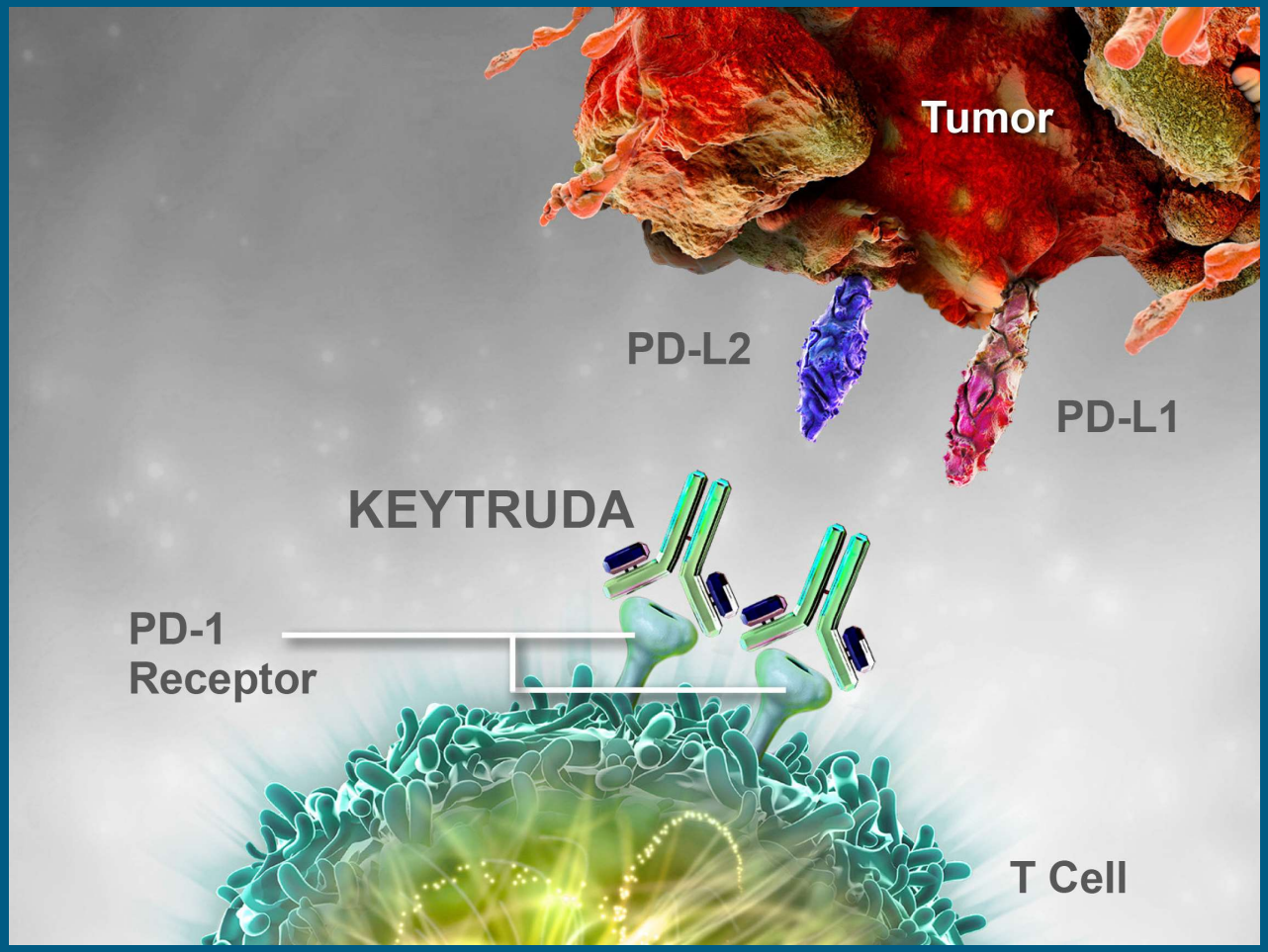
Key side effects for intravesical instillation

- LUTS
  - Activation of cytokines within the bladder
  - Chemical changes to urothelium
- Fever
  - Common with immunotherapy for low grade temp and treated with scheduled Tylenol 48 hrs around instillation
  - Rare (<0.2%) for 103-105°F- suspect systemic absorption and needs hospitalization

NMIBC BCG refractory

- When patients have recurrence of high grade disease following BCG therapy
- Standard of Care is Cystectomy
- Alternatives to cystectomy
  - Pembrolizumab
  - Nadoferogene firodenovec
  - N803 + BCG (nogapendakin alpha inbakicept)
  - TAR 200 (pending)

Pembrolizumab (Keytruda)



PD1 inhibitor

Q 3 wk IV infusion over one hour

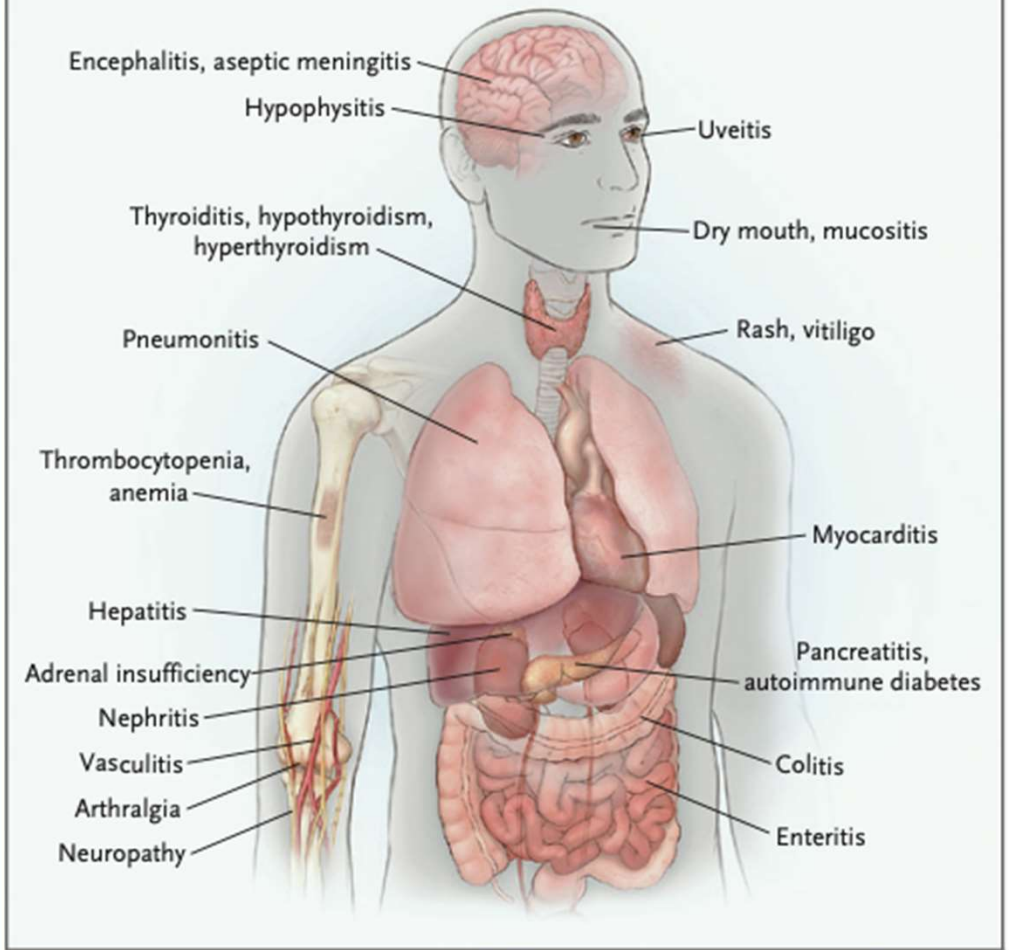


Figure 1. Organs Affected by Immune Checkpoint Blockade.

Immune checkpoint blockade can result in inflammation of any organ. Shown are the most common immune-related adverse events that clinicians encounter in patients treated with immune checkpoint blockade.

G3 AE ~13%

Rx: steroids

Nadoferogene Firadenovec

- Adenoviral vector that infects the urothelial and cancer cells within the bladder
  - One hour instillation
- 20% rate of LUTS and bladder spasms
  - Administration of antispasmodic important
    - Anticholinergic
- Administered q 3 months for one hour

Nogapendakin alfa inbakicept

- Utilizes the combination of BCG with N803
  - Instillation for 60 minutes
  - Weekly for 6 weeks
  - Maintenance schedules as well
- LUTS primarily noted
  - Utilization of anticholinergics

TAR 200

- Device that contains gemcitabine
  - Placed into the bladder via catheter for ~ 3 weeks
  - Administered every 3 weeks for 6 months than every 3 months

- LUTS
  - Anticholinergics utilized

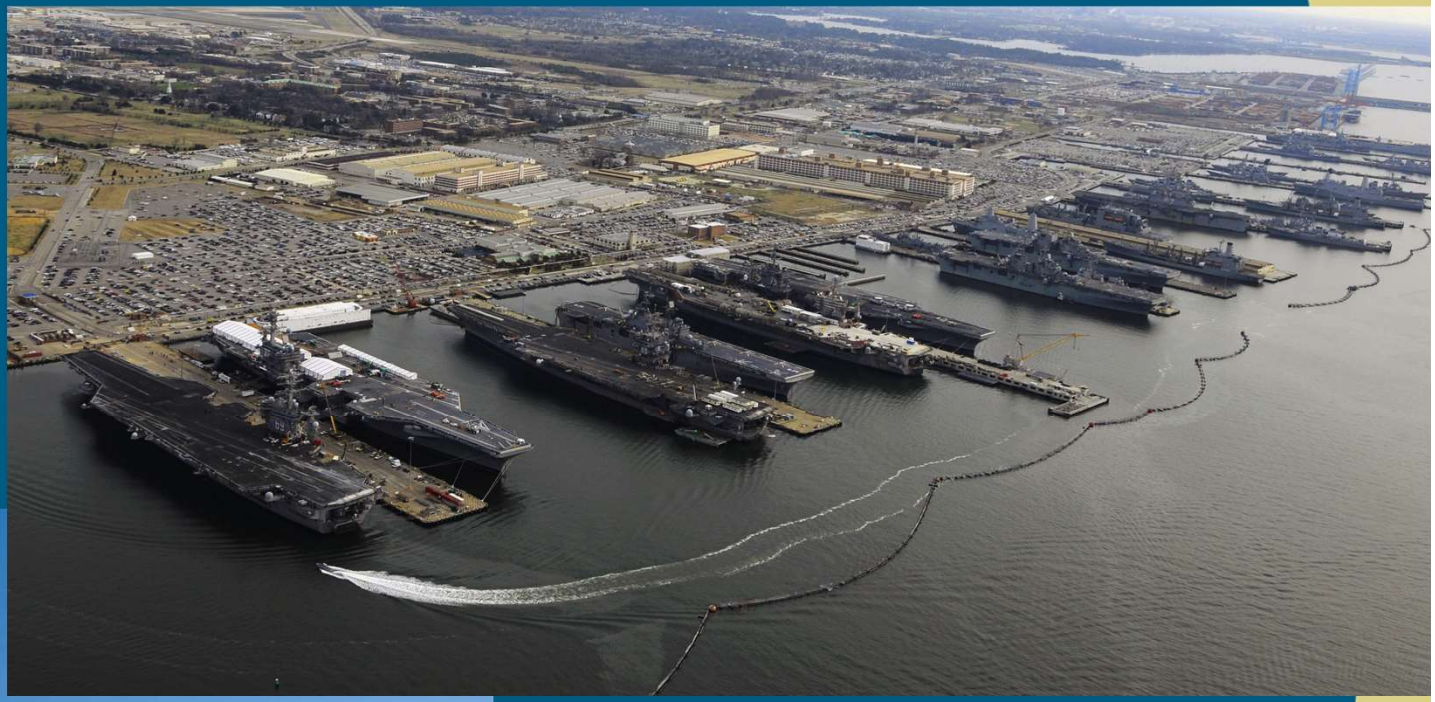
Summary

Key Points

- Risk stratification is key for success in the management of NMIBC
- BCG remains the standard of care for primary management of high risk NMIBC
- Patients that progress on BCG should undergo cystectomy for cure, however, newer agents are available that offer acceptable outcomes

Thank you

Teaching. Discovering. Caring.™



EVMS
Eastern Virginia Medical School

mwilliams@urologyofva.net
757-457-5177 x3936

Urology of Virginia