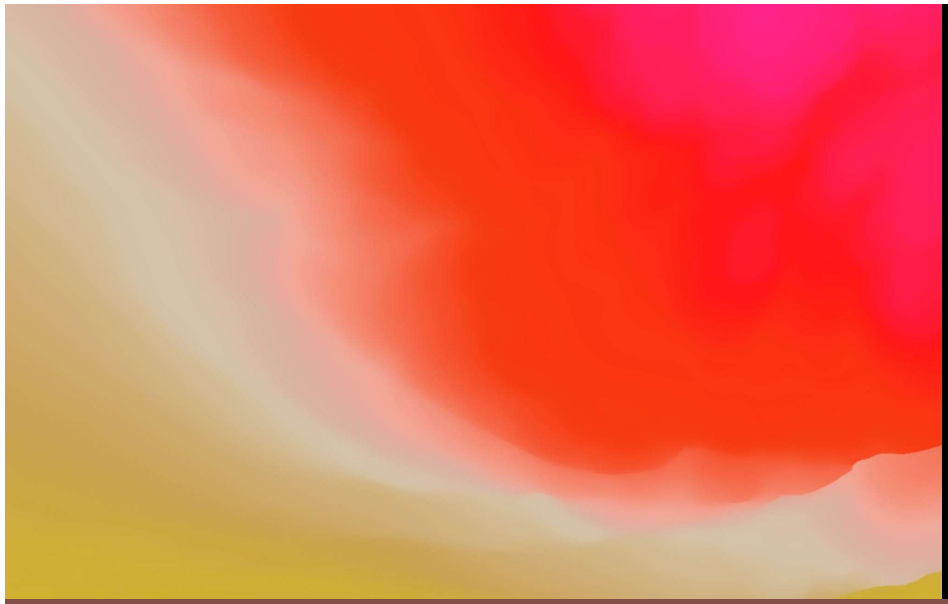
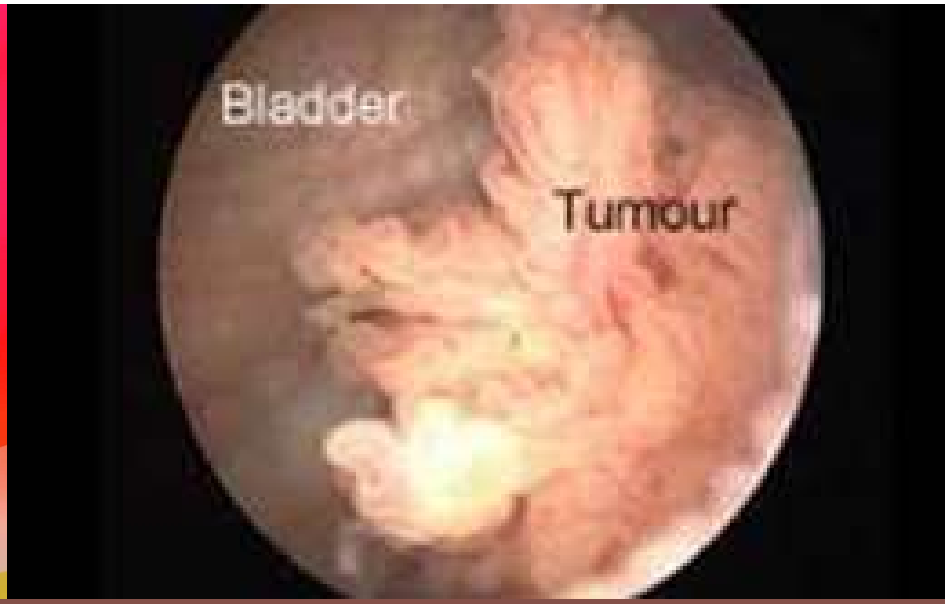




BLADDER CANCER

Josselyn G. Molina Avila, MD

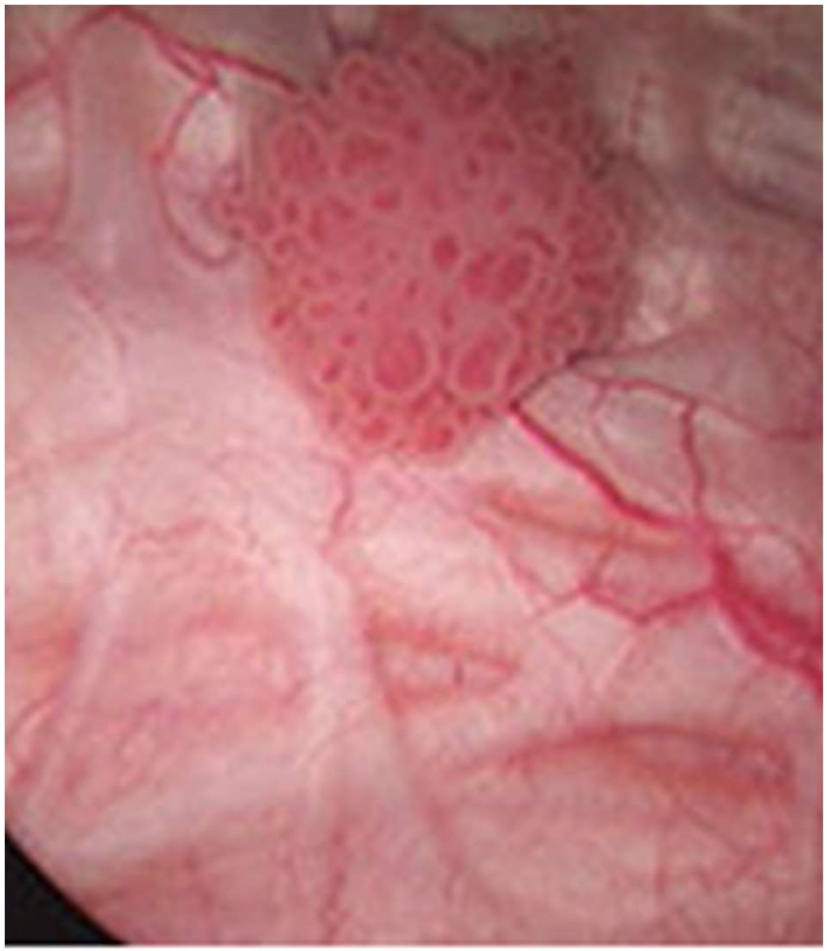
Hematology Oncology

DISCLOSURE

No conflict of interest

OBJECTIVES

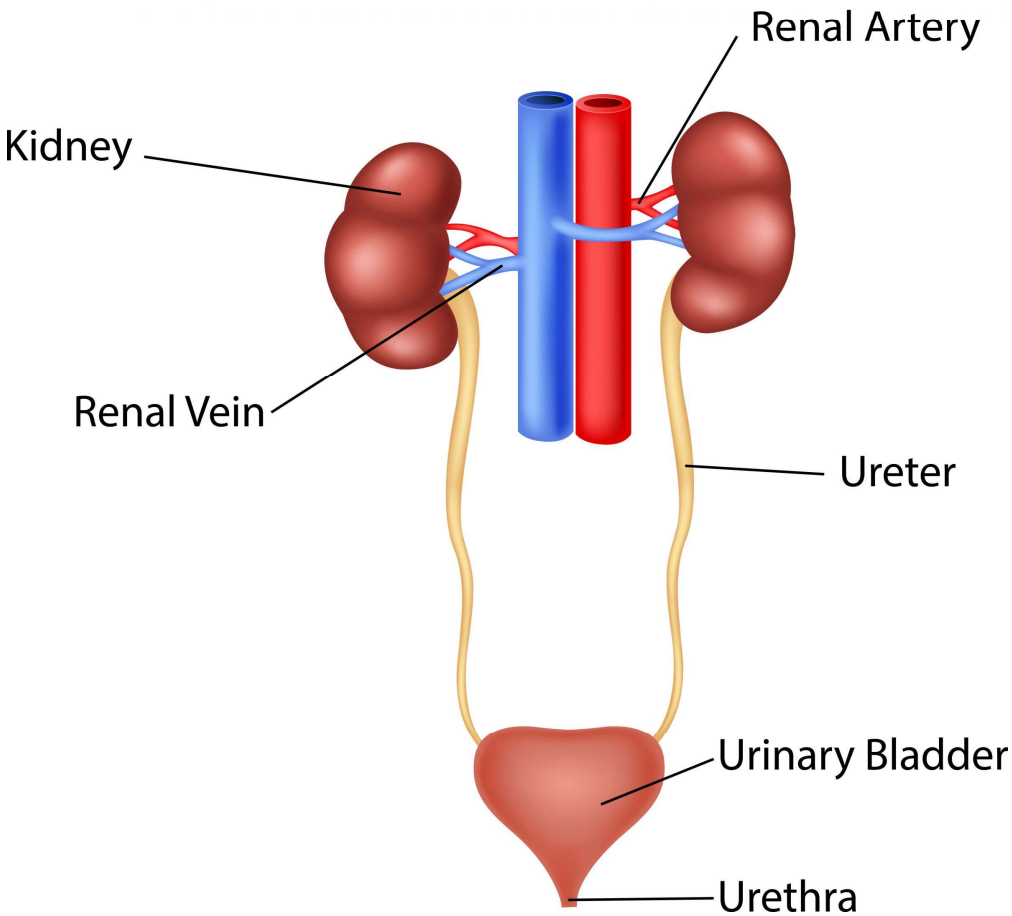
- Definition
- Epidemiology
- Etiology and Risk Factors
- Pathology
- Clinical presentation
- Diagnosis
- Staging of bladder cancer
- Prognostic factors
- Treatment
- Onco nurse role



DEFINITION

- Bladder cancer = Urothelial Cancer
- Urothelial Cancer is the invasion of neoplastic cells of urothelial origin to the basement membrane or lamina propria or deeper

Urinary System



- Urothelial cancers can arise in the bladder, renal pelvis, ureter, or urethra.

https://www.gstatic.com/culturalinstitute/searchar/assets/edu_concepts_urinary_system/desktop_dark.mp4

EPIDEMIOLOGY

- Average age at diagnosis 70's
- New cases of UC have been falling on average 1% per year for the last 10y
- Urothelial cancer is the most common malignancy involving the urinary system.
- 6th most common form of cancer
- 4th most common cancer in men
- More common in men (3:1)
  - Men 1 in 27 lifetime risk
  - Women 1 in 89 lifetime risk

Puerto Rico

Source: Globocan

Incidence, Mortality and Prevalence by cancer site

	New cases				Deaths				5-year prevalence (all ages)	
Cancer	**Number**	**Rank**	**(%)**	**Cum.risk**	**Number**	**Rank**	**(%)**	**Cum.risk**	**Number**	**Prop. (per 100 000)**
Prostate	2 742	1	21.0	12.94	521	3	9.4	0.92	10 306	760.30
Breast	2 027	2	15.5	7.48	490	4	8.8	1.58	8 239	547.32
Colon	1 239	3	9.5	2.06	707	1	12.7	0.97	3 539	123.70
Lung	704	4	5.4	1.15	582	2	10.4	0.88	829	28.98
Thyroid	476	5	3.6	1.18	20	25	0.36	0.03	1 822	63.69
Rectum	472	6	3.6	0.92	224	7	4.0	0.36	1 478	51.66
Non-Hodgkin lymphoma	468	7	3.6	0.90	198	9	3.6	0.31	1 479	51.70
Liver	426	8	3.3	0.75	402	6	7.2	0.65	405	14.16
Pancreas	418	9	3.2	0.66	406	5	7.3	0.62	303	10.59
Corpus uteri	396	10	3.0	1.62	98	17	1.8	0.32	1 460	96.99
Leukaemia	321	11	2.5	0.57	221	8	4.0	0.30	944	33.00
Bladder	320	12	2.4	0.45	132	11	2.4	0.12	1 017	35.55
Stomach	190	13	1.5	0.29	163	10	2.9	0.22	297	10.38
Kidney	190	14	1.5	0.39	99	16	1.8	0.15	570	19.92
Multiple myeloma	189	15	1.4	0.33	130	12	2.3	0.20	514	17.97
Ovary	174	16	1.3	0.58	115	14	2.1	0.36	489	32.48
Lip, oral cavity	158	17	1.2	0.29	57	19	1.0	0.09	485	16.95
Cervix uteri	156	18	1.2	0.71	83	18	1.5	0.29	472	31.36
Oesophagus	133	19	1.0	0.23	125	13	2.2	0.19	157	5.49
Brain, central nervous system	127	20	0.97	0.26	110	15	2.0	0.21	371	12.97
Melanoma of skin	109	21	0.83	0.20	22	23	0.39	0.03	365	12.76
Oropharynx	106	22	0.81	0.23	56	21	1.0	0.12	307	10.73
Larynx	94	23	0.72	0.19	57	20	1.0	0.10	312	10.91
Hodgkin lymphoma	77	24	0.59	0.19	23	22	0.41	0.04	291	10.17
Anus	64	25	0.49	0.12	21	24	0.38	0.04	204	7.13
Salivary glands	32	26	0.24	0.06	10	28	0.18	0.01	103	3.60
Vulva	32	27	0.24	0.11	8	32	0.14	0.01	107	7.11
Penis	31	28	0.24	0.13	8	31	0.14	0.04	102	7.52
Testis	28	29	0.21	0.16	5	33	0.09	0.02	118	8.71
Hypopharynx	27	30	0.21	0.05	9	29	0.16	0.02	50	1.75
Nasopharynx	25	31	0.19	0.05	15	26	0.27	0.02	80	2.80
Vagina	23	32	0.18	0.07	8	30	0.14	0.02	65	4.32
Gallbladder	20	33	0.15	0.03	12	27	0.22	0.02	21	0.73
Kaposi sarcoma	7	34	0.05	0.01	0	35	0	0	21	0.73
Mesothelioma	5	35	0.04	0.01	3	34	0.05	0.01	6	0.21
All cancer sites	13 080	-	-	22.57	5 570	-	-	7.88	40 641	1420.6

ETIOLOGY AND RISK FACTORS

Carcinogens

- Smoking (3X higher than non smokers)
- Occupational exposure: metal, leather, textile, electric, cement, rubber workers, painters, miners
- Arylamines
- Dyes/paint
- Benzene
- Petrochemicals
- Pesticide

Infections/Inflammation

- Chronic cystitis/UTI
- Schistosomas haematobium
- Urolithiasis
- Chronic catheterization

ETIOLOGY AND RISK FACTORS

Hereditary factors

- HNPCC: Hereditary non polipyposis colorectal cancer associated with MSH2 (increased upper urologic malignancies)

Common mutations in urothelial malignancy

Low grade noninvasive

HRAS mutation 30-40%

FGFR3 alteration 70%

Invasive

Rb loss

P53 loss

PATHOLOGY: HISTOLOGY TYPES

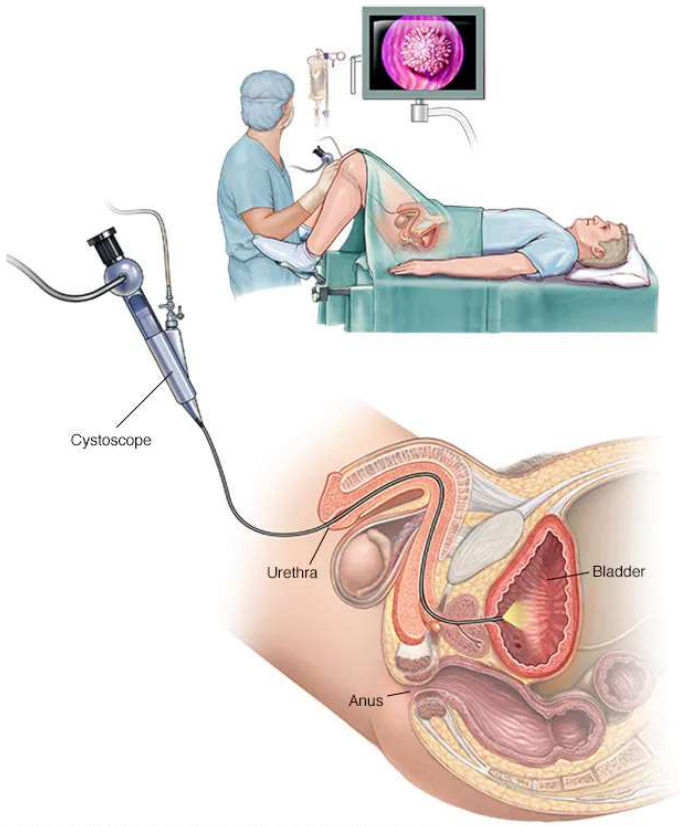
- Urothelial/Transitional (90-95%)
- Squamous (5%)
- Adenocarcinoma (1-2%)
- Small cell (<1%)

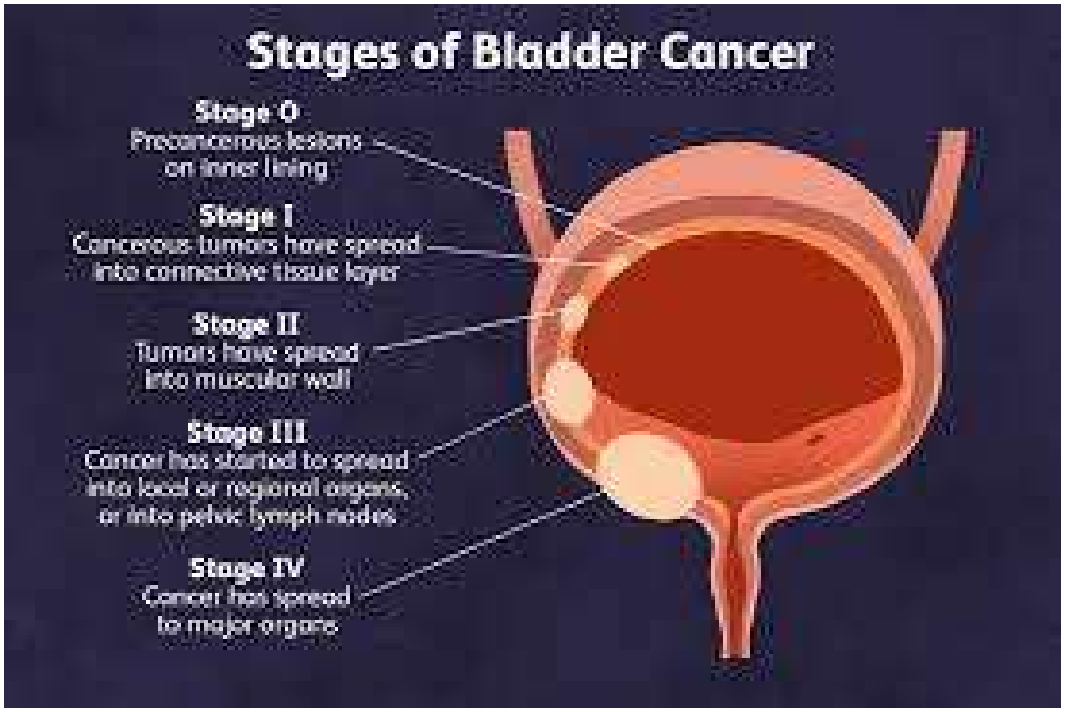
CLINICAL PRESENTATION

- Gross painless hematuria (75-85%)
- Hematuria (microscopic), dysuria, nocturia, urinary frequency, and urgency
- Incomplete bladder emptying
- Suprapubic, hypogastric, flank pain, or heaviness
- Pain (locally advanced disease)

DIAGNOSIS

- Physical exam
- U/A
- Urine cytology
- Cystoscopy with bladder biopsy or transurethral resection of bladder tumor (TURBT)- Gold Standard
- CT urogram, MRI, US





STAGING

- Bladder cancers are either non-muscle invasive or muscle invasive.
- Early-stage, or superficial, bladder cancer affects the bladder lining, whereas later stages, known as invasive bladder cancer, move beyond the lining to the muscle and can spread to nearby organs

STAGING IN MUSCLE INVASIVE BLADDER CANCER

- History and Physical exam (Bimanual exam under anesthesia)
- Abd/pelvic CT w contrast or MRI with gadolinium (before TURBT)
- CXR or Chest CT
- Bone Scan (if bone pain or high ALP)

STAGING

Tx: primary tumor cannot be assessed

Stage I	Stage II	Stage III	Stage IV
The cancer is superficial, confined to the layer of connective tissue and inner lining of the bladder.	The cancer has moved to the muscle layer of the bladder.	The cancer has spread (metastasized), beyond the muscle to the immediate tissue beyond the cell and toward the reproductive organs.	The cancer has metastasized completely from the bladder to the pelvis, abdomen, lymph nodes, or other areas such as the lungs.

5-YEAR RISK OF RECURRENCE AND RISK OF MUSCLE INVASION FOR NMIBC

Tumor (All <3cm)	Recurrence	Progression
Low grade Ta	31%	0.8%
High Grade Ta	46%	6%
High Grade T1	46%	17%
CIS	46%	Variable depending on T stage, up to 45% with T1, high grade tumor
Overall	70%	15%

Performance status

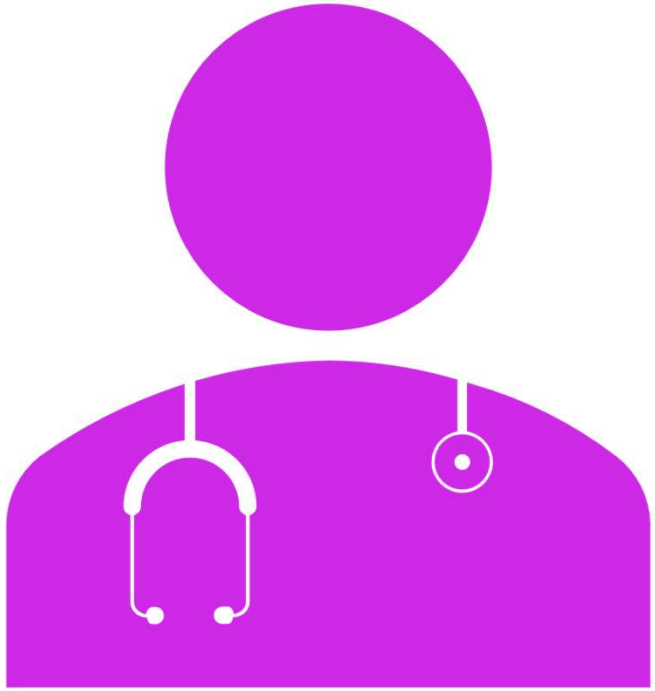
Karnofsky Scale		Zubrod Scale	
Normal, no evidence of disease Able to perform normal activity with only minor symptoms	100 90	Normal activity	0
Normal activity with effort, some symptoms Able to care for self but unable to do normal activities	80 70	Symptomatic and ambulatory Cares for self	1
Requires occasional assistance, cares for most needs Requires considerable assistance	60 50	Ambulatory >50% of time Occasional assistance	2
Disabled, requires special assistance Severely disabled	40 30	Ambulatory ≤50% of the time Nursing care needed	3
Very sick, requires active supportive treatment Moribund	20 10	Bedridden	4

PROGNOSTIC FACTOR

- In localized bladder cancer:
  - stage
  - grade
- In metastatic bladder cancer:
  - performance status <80%
  - visceral metastasis: lung, liver, bone

PROGNOSTIC FACTORS

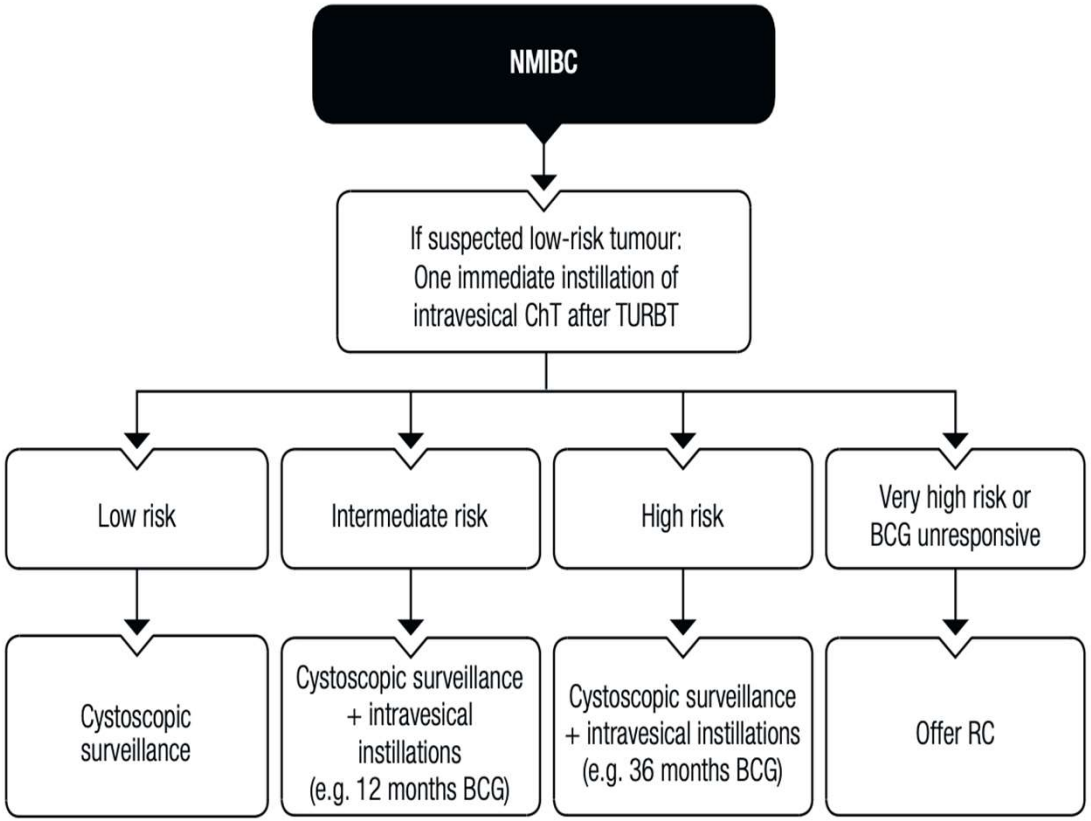
- Associated CIS
- Incomplete response to bacillus Calmette-Guerin (BCG) for high grade NMIBC
- Multifocal tumor for NMIBC
- Early/frequent recurrence for NMIBC
- Tumor size >3cm for NMIBC



TREATMENT

- The course of treatment depends on the type and stage of cancer, and your nursing care will be based on the medical treatment plan implemented.

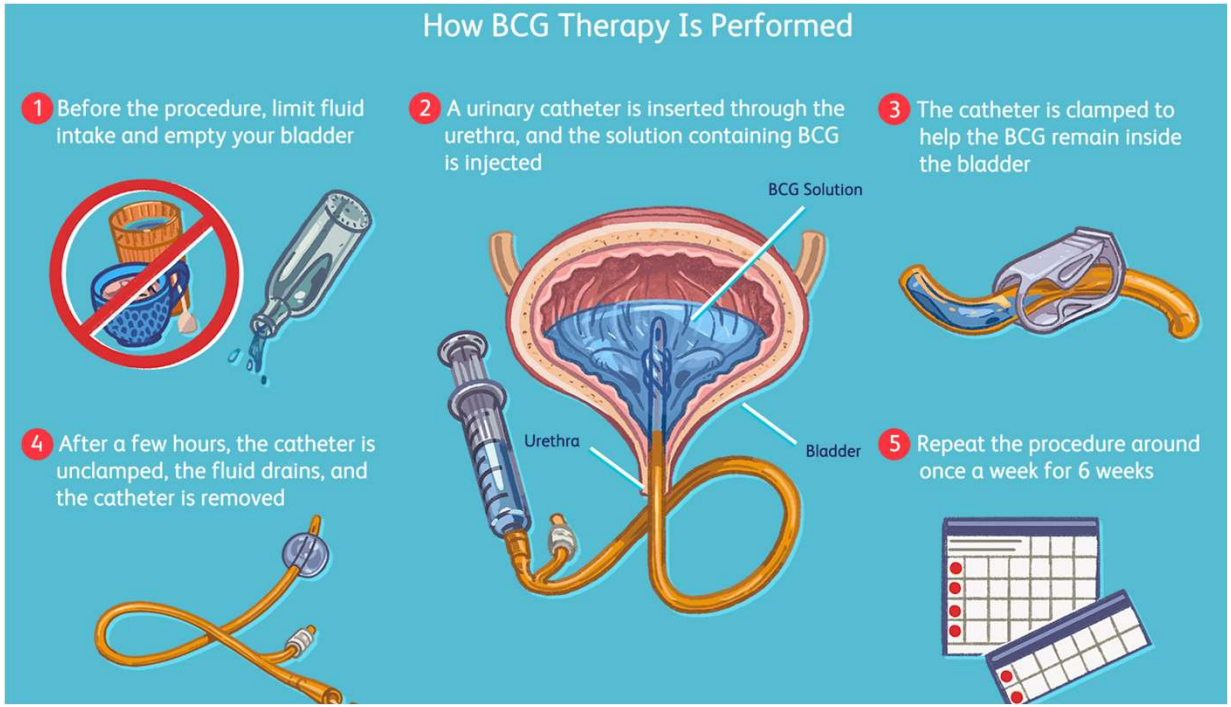
MANAGEMENT OF HISTOPATHOLOGICALLY CONFIRMED NMIBC



BCG, bacillus Calmette–Guerin; ChT, chemotherapy; NMIBC, non-muscle-invasive bladder cancer; RC, radical cystectomy; TURBT, transurethral resection of the bladder tumour

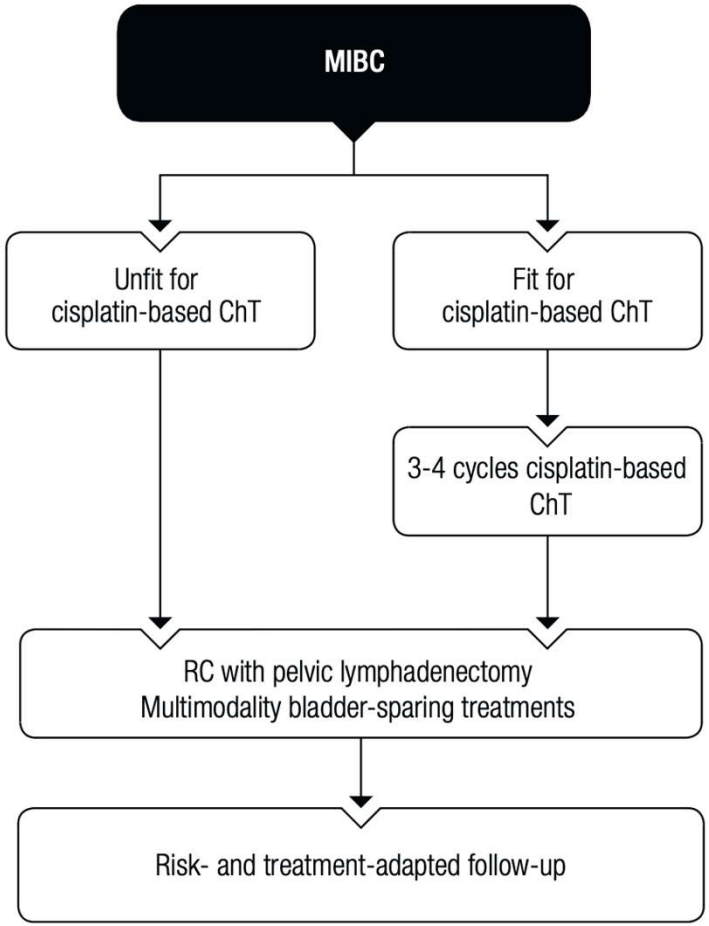
ESMO Guidelines, 2023

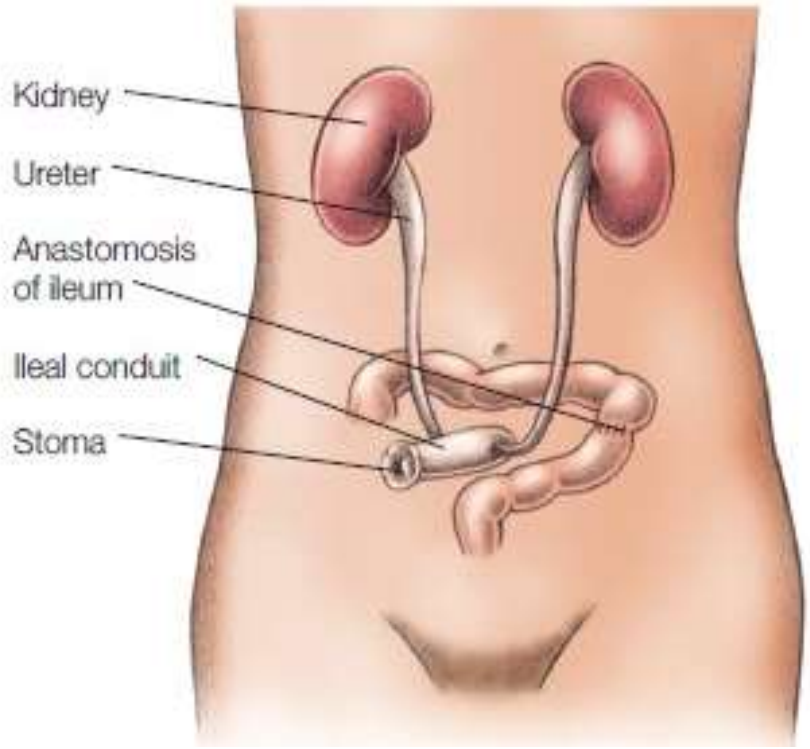
NON INVASIVE UROTHELIAL CANCER



Cancer confined to the first layer of the bladder wall, biologic therapy or immunotherapy is prescribed to boost the patient's immune system.

MANAGEMENT OF HISTOPATHOLOGICALLY CONFIRMED MIBC





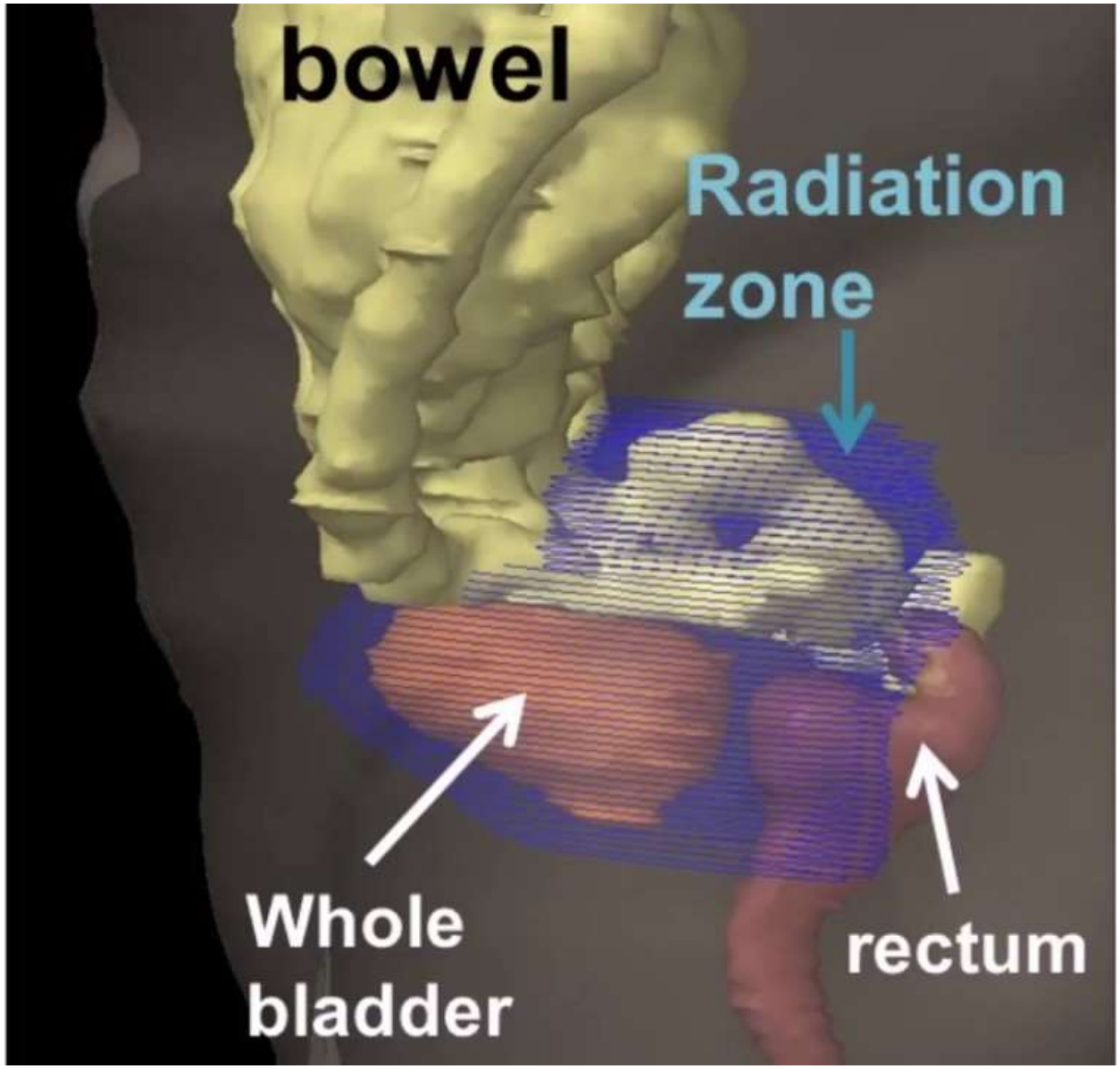
NEOADJUVANT AND ADJUVANT CHEMOTHERAPY

- Neoadjuvant:
  - Cisplatin based chemotherapy (3-4 cycles Cisplatin-Gemzar
  - MVAC Methotrexate, Vinblastine, Adryamicin, Cisplatin)

TREATMENT: ORGAN PRESERVATION

- Pt with MIBC but unfit for surgery
- Trimodal combination: TURBT + Rx + Chemo

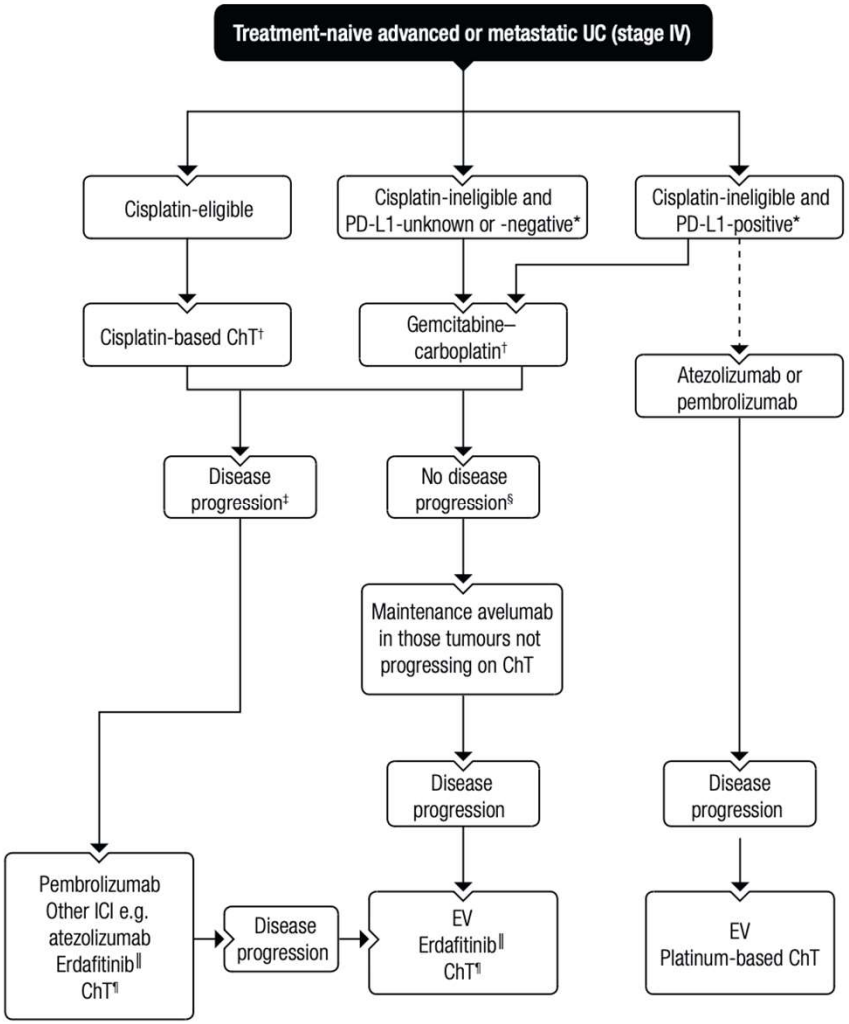
(No hydronephrosis, prostate invasion or diffused TIS)



Phase 1
Initial Large Radiation Zone in Blue

Includes the whole bladder and lymph

MANAGEMENT OF METASTATIC BLADDER CANCER



In the EV-302/KEYNOTE-A39 trial, a combination of the nectin 4-directed antibody–drug conjugate (ADC) enfortumab vedotin with pembrolizumab almost doubled median progression-free survival (PFS) (12.5 months versus 6.3 months, respectively; hazard ratio [HR] 0.45; 95% confidence interval [CI] 0.38–0.54; p<0.00001) and median overall survival (OS) (31.5 months versus 16.1 months, respectively; HR 0.47; 95% CI 0.38–0.58; p<0.00001) compared with chemotherapy (cisplatin or carboplatin plus gemcitabine) at a median follow-up of 17.2 months in 886 patients with previously untreated, locally advanced or metastatic urothelial carcinoma (LBA6).

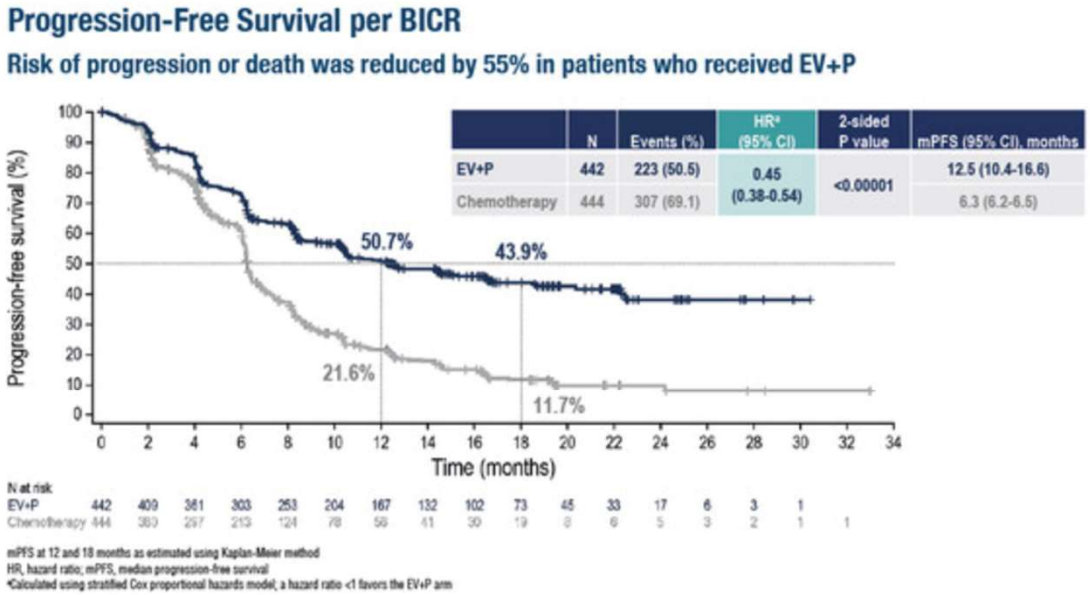


Figure. Improved progression-free survival with enfortumab vedotin and pembrolizumab versus chemotherapy in the EV-302/KEYNOTE-A39 trial (ESMO Congress 2023, LBA6)

TROPHY-U-01 Cohort 1

TROPHY-U-01: Study Design

TROPHY U-01

Cohort 1 (100 patients): patients with mUC who progressed after prior platinum-based and CPI-based therapies

Cohort 2 (40 patients): patients with mUC ineligible for platinum-based therapy and who progressed after prior CPI-based therapies[a]

Sacituzumab govitecan 10 mg/kg

Days 1 and 8, every 21 days

Continue treatment in the absence of unacceptable toxicity or disease progression

Primary objective:
- Objective response rate (ORR)

Secondary objectives:
- Safety/tolerability
- Duration of response (DOR)
- Progression-free survival (PFS)
- Overall survival (OS)

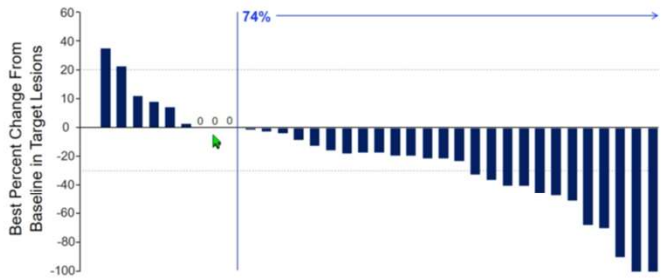
[a]CPI therapy (includes anti-PD-1/anti-PD-L1–based therapies).
CPI, immune checkpoint inhibitor; mUC, metastatic urothelial cancer; PD-1, programmed death-1; PD-L1, programmed death-ligand 1.
EudraCT Number: 2018-001167-23; ClinicalTrials.gov Number: NCT03547973; IMMU-132-06 study.

BARCELONA 2019 ESMO congress

Only two patients had progression of disease as their best response, and 74% (26/35) of patients achieved at least some tumor shrinkage.

TROPHY-U-01 Cohort 1

74% of Patients Demonstrated a Reduction in Tumor Size



BARCELONA 2019 ESMO congress

While follow-up is not yet mature, it appears that in general responses and disease stability were maintained during treatment.

NURSING ROLE

Prevention

Education

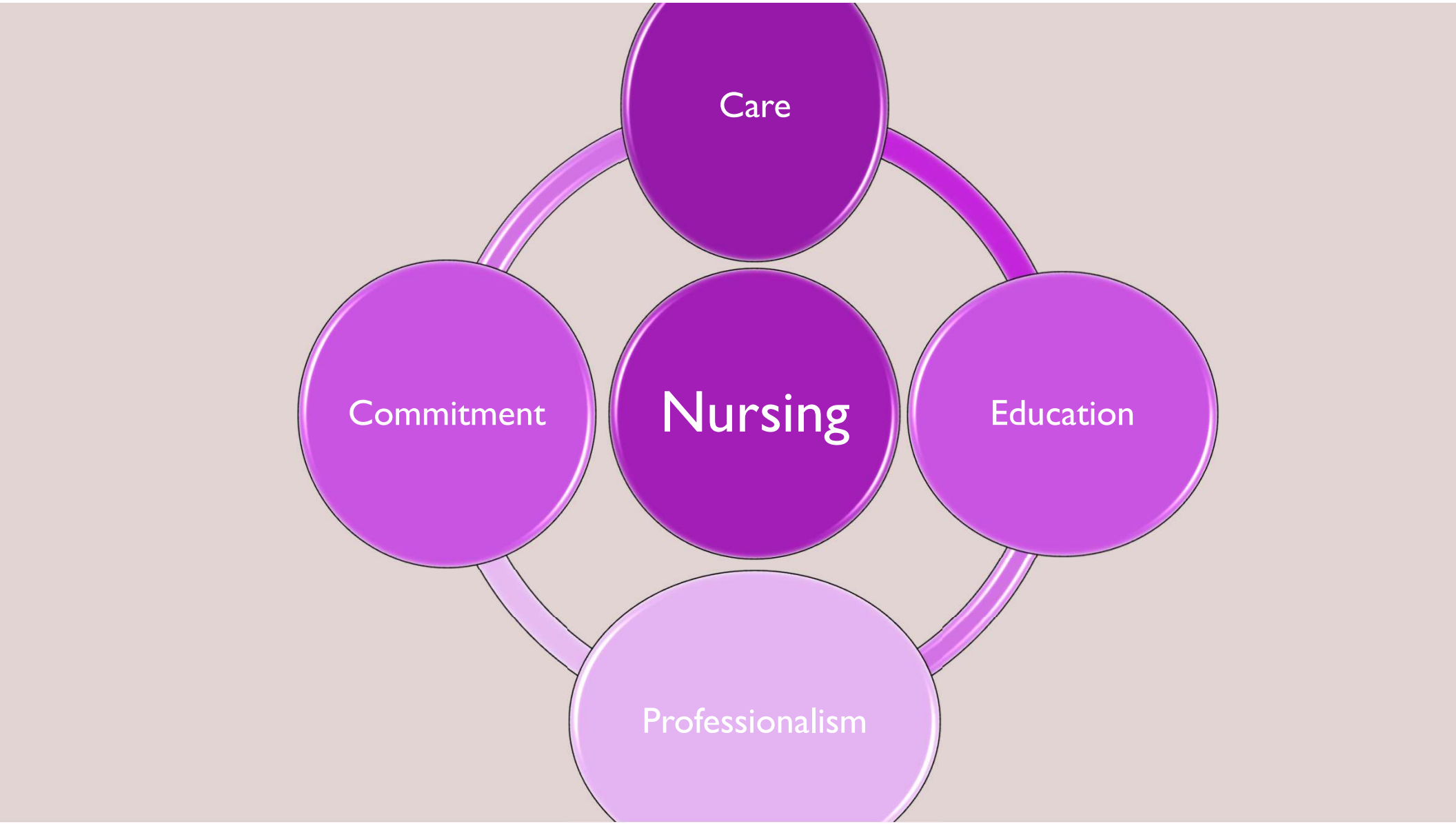
Coping strategies

Treatment

Adverse event management

REFERENCES

- ESMO 2019: TROPHY-U-01: Initial Results of a Phase 2 Open-Label Study of Sacituzumab Givotecan in Patients with Metastatic Urothelial Cancer after Failure of Platinum-Based Regimens or Immunotherapy
- Wyszynski A, et al. Body mass and smoking are modifiable risk factors for recurrent bladder cancer. Cancer. 2014;120(3):408–414.
- Shievon Smith, Jacqueline Duncan. The Critical Role of Nursing in Bladder Cancer Diagnostics and Treatment
- Puerto Rico Source: Globocan 2020 Summary statistic 2020 Males Females Both sexes Population
- Jessen. R. How Can BCG Immunotherapy Treat Bladder Cancer?
- Wallace DM, Raghavan D, Kelly KA, et al. Neo-adjuvant (pre-emptive) cisplatin therapy in invasive transitional cell carcinoma of the bladder. Br J Urol 1991; 67:608.
- Mitra AP, Skinner EC, Schuckman AK, et al. Effect of gender on outcomes following radical cystectomy for urothelial carcinoma of the bladder: a critical analysis of 1,994 patients. Urol Oncol 2014; 32:52.e1.
- MARSHALL VF. Current clinical problems regarding bladder tumors. Cancer 1956; 9:543.
- ESMO Guidelines 2023
- Tagawa ST, Faltas BM, Lam ET, Saylor PJ, Bardia A, Hajdenberg J, Morgans AK, Lim EA, Kalinsky K, Simpson PS, Galsky MD. Sacituzumab govitecan (IMMU-132) in patients with previously treated metastatic urothelial cancer (mUC): Results from a phase I/II study.


Care
Commitment
Nursing
Education
Professionalism

THANKS!