TỔNG QUAN VỀ CHẨN ĐOÁN VÀ ĐIỀU TRỊ UNG THƯ BÀNG QUANG

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NỘI DUNG

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3. ĐIỀU TRỊ UNG THƯ BÀNG QUANG XÂM LẤN CƠ
4. ĐIỀU TRỊ UNG THƯ BÀNG QUANG DI CĂN

TỔNG QUAN
UNG THƯ BÀNG QUANG

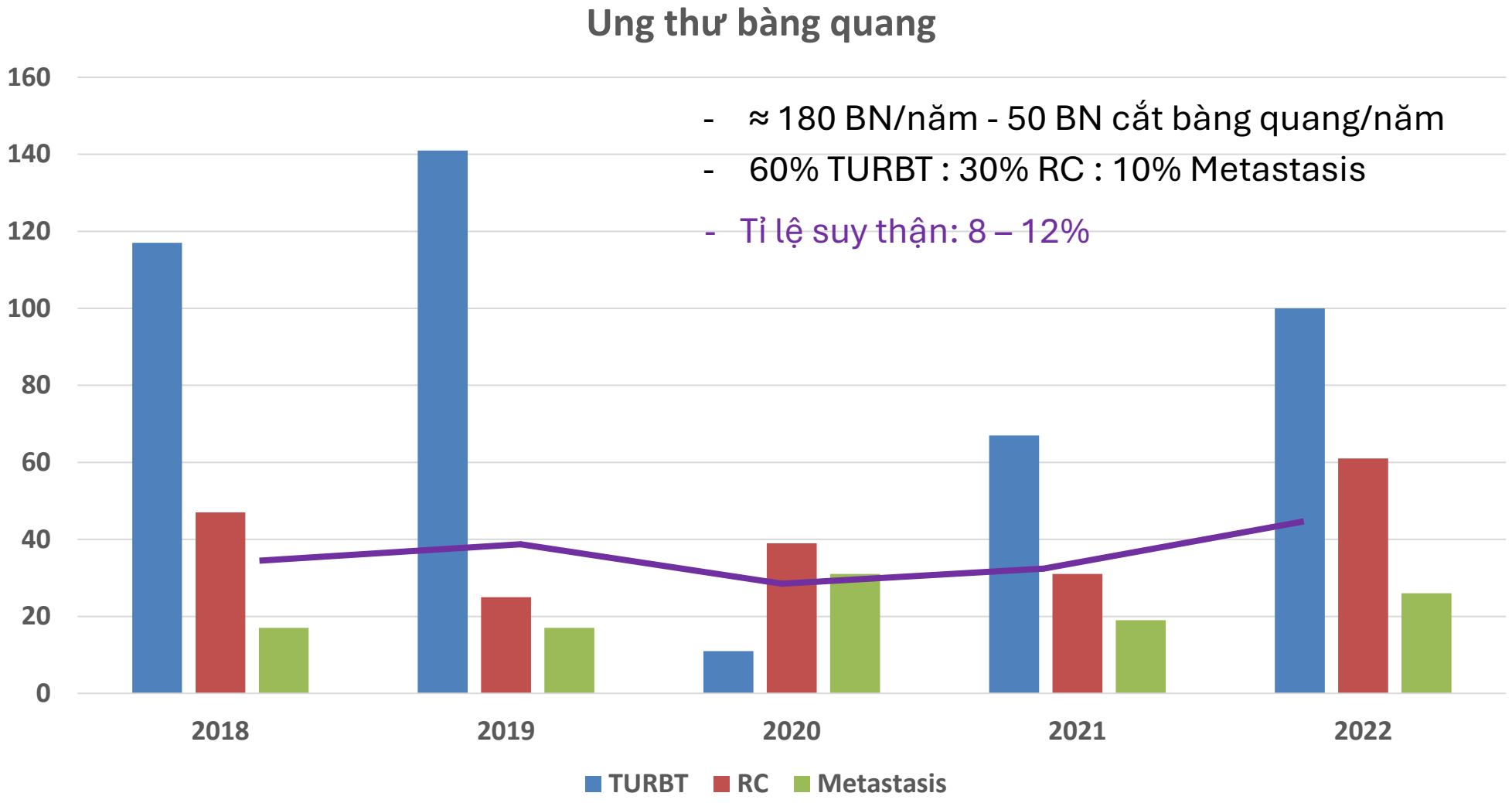
Tại Việt Nam, UTBQ đứng thứ 19 về tỷ lệ mắc mới, với 2000 ca mỗi năm

Incidence, Mortality and Prevalence by cancer site

		New cases			Deaths				5-year prevalence	
	Cancer	Number	Rank	(%)	Cum.risk	Number	Rank	(%)	Cum.risk	Number	Prop. (per 100 000)
	Breast	24 563	1	13.6	4.1	10 008	4	8.3	1.6	72 617	146.6
	Liver	24 502	2	13.6	2.4	23 333	1	19.4	2.3	33 191	33.5
	Lung	24 426	3	13.5	2.5	22 597	2	18.8	2.3	34 477	34.8
	Colorectum	16 835	4	9.3	1.7	8 454	5	7.0	0.80	46 140	46.6
	Stomach	16 277	5	9.0	1.6	13 264	3	11.0	1.3	25 458	25.7
	Thyroid	6 122	6	3.4	0.51	858	21	0.71	0.08	19 813	20.0
	Prostate	5 875	7	3.3	1.3	2 800	9	2.3	0.32	12 411	25.1
	Leukaemia	5 789	8	3.2	0.49	4 330	6	3.6	0.38	17 099	17.3
	Nasopharynx	5 613	9	3.1	0.52	3 453	8	2.9	0.34	16 007	16.2
	Corpus uteri	4 953	10	2.7	0.93	1 374	13	1.1	0.25	16 639	33.6
	Cervix uteri	4 612	11	2.6	0.80	2 571	10	2.1	0.46	13 157	26.6
	Oesophagus	3 686	12	2.0	0.37	3 470	7	2.9	0.35	5 752	5.8
	NHL	3 516	13	1.9	0.34	2 211	12	1.8	0.21	10 591	10.7
	Brain CNS	2 829	14	1.6	0.25	2 431	11	2.0	0.22	9 849	10.0
	Lip, oral cavity	2 449	15	1.4	0.24	1 279	14	1.1	0.12	6 742	6.8
	Hypopharynx	2 374	16	1.3	0.23	1 236	15	1.0	0.11	4 618	4.7
	Kidney	2 246	17	1.2	0.21	1 112	18	0.93	0.10	6 580	6.7
	Larynx	2 186	18	1.2	0.21	1 233	16	1.0	0.11	6 403	6.5
19	Bladder	1 972	19	1.1	0.19	1 004	19	0.84	0.09	5 785	5.9
	Ovary	1 534	20	0.85	0.27	1 003	20	0.84	0.19	4 293	8.7
	Pancreas	1 251	21	0.69	0.12	1 226	17	1.0	0.12	1 414	1.4
	Oropharynx	700	22	0.39	0.07	372	23	0.31	0.04	1 917	1.9

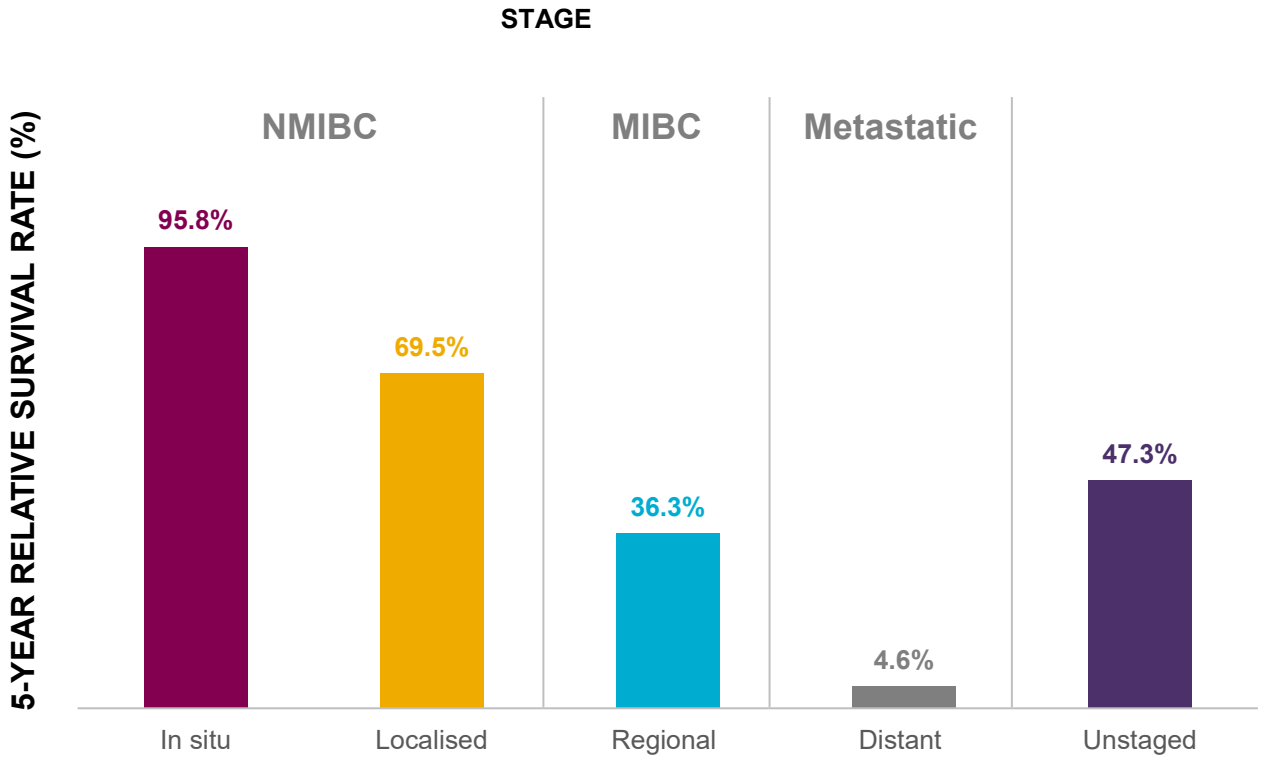
GLOBOCAN 2022

Thống kê tại Bệnh viện Chợ Rẫy



Tỷ lệ sống còn trong UTBQ giảm dần theo tiến triển bệnh

Tỷ lệ sống còn 5 năm giảm dần khi khối u bàng quang tiến triển và xâm lấn xa hơn: NMIBC có tiên lượng tốt nhất nhưng nguy cơ cao sẽ tái phát và tiến triển thành MIBC



Patients with NMIBC have favourable outcomes, with 10 year-survival of 70–85%[2]

- The rate was found to be much higher for low-grade disease

There is a high risk of recurrence after transurethral resection in NMIBC patients:[3]

- 15–61% after 1 year
- 31–78% after 5 years

Up to 17% of NMIBC tumours progress to MIBC tumours after 1 year, and up to 45% after 5 years[3]

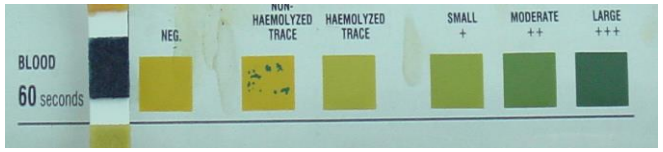
MIBC=muscle invasive bladder cancer; NMIBC=non-muscle-invasive bladder cancer.

1. Cancer of the Urinary Bladder (Invasive and In Situ). Available at: https://seer.cancer.gov/archive/csr/1975_2016/results_merged/sect_27_urinary_bladder.pdf. (Accessed November 2021); 2. Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline. Available at: http://www.auanet.org/guidelines/non-muscle-invasive-bladder-cancer-(aua/suo-joint-guideline-2016). (Accessed November 2021); 3. Van der Heijden AG, Witjes JA. Eur Urol Suppl. 2009;8:556–562.

CHẨN ĐOÁN UNG THƯ BÀNG QUANG

Phần lớn bệnh nhân UTBQ đi khám lần đầu với triệu chứng tiểu máu

Tiểu máu là triệu chứng khởi phát thường gặp nhất, xuất hiện ở khoảng 80% bệnh nhân ung thư bàng quang. Một số bệnh nhân có thể xuất hiện triệu chứng rối loạn tiểu tiện như tiểu gắt buốt, tiểu nhiều lần, tiểu đêm.



80% | 20%

Visible haematuria

Non-visible haematuria

UTI symptoms

Bladder storage symptoms: Frequency, urgency and dysuria

Other symptoms associated with the initial tumour may include:[1,2]

- Changes in bladder habits (increased frequency, urgency of urination)
- Pain or irritation during urination
- Nocturnal urination (increased frequency)

Symptoms of advanced/metastatic disease may also include:[1,2]

- Pain due to obstruction of upper urinary tract
- Inability to urinate
- Pain in the lower back on one side
- Appetite and weight loss
- Feeling tired / weak
- Oedema in the feet
- Bone pain

1. Bladder Cancer Early Detection, Diagnosis, and Staging. Available at: https://www.cancer.org/content/dam/CRC/PDF/Public/8559.00.pdf. (Accessed November 2021); 2. Smith A, et al. Chapter 83: Bladder Cancer. In: Niederhuber JE, et al (eds). Abeloff's Clinical Oncology. 5th ed. Philadelphia, PA: Elsevier; 2014

Hướng dẫn quốc tế khuyến nghị sử dụng nhiều phương pháp chẩn đoán xác định loại ung thư, giai đoạn và độ mô học

ESMO guidance[1]

- History and physical examination
- Cystoscopic evaluation
- Urine cytology
- Blood work
- Upper urinary tract imaging
- Metastatic workup in patients with high risk of metastases

NCCN guidance[2]

- History and physical examination
- Office cystoscopy
- Consider cytology
- Abdominal/pelvic CT or MRI before TURBT
- Imaging of upper tract collecting system
- Additional staging workup
  - Complete blood count
  - Chemistry profile including alkaline phosphatase
  - Chest imaging
  - Bone scan if symptoms of bone metastasis

AUA/SUO guidance[3]

- Cystoscopic examination
- Visual resection of the bladder tumor
- Urinary tract imaging
- Prostatic urethral biopsies and upper tract imaging in patients with a history of NMIBC with normal cystoscopy and positive cytology

AUA=American Urological Association; CT=computed tomography; ESMO=European Society of Medical Oncology; MRI=magnetic resonance imaging; NCCN=National Comprehensive Cancer Network; NMIBC=non-muscle-invasive bladder cancer; SUO=Society of Urologic Oncology; TURBT=transurethral resection of bladder tumour.

1. Ann Oncol. 2022;33(3):244-258; 2. NCCN bladder cancer guidelines 2025;
3. Holzbeierlein JM, Bixler BR, Buckley DI, Chang SS, Holmes R, James AC, Kirkby E, McKiernan JM, Schuckman AK. Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline: 2024 Amendment. J Urol. 2024 Apr;211(4):533-538. doi: 10.1097/JU.0000000000003846. Epub 2024 Jan 24. Erratum in: J Urol. 2024 Dec;212(6):936. doi: 10.1097/JU.0000000000004251. PMID: 38265030.

Patient Identification and Diagnosis

Sau khi khai thác triệu chứng và yếu tố nguy cơ, BN được thăm khám lâm sàng, xét nghiệm nước tiểu, nội soi bàng quang và chẩn đoán hình ảnh đường niệu trên để xác định chẩn đoán.

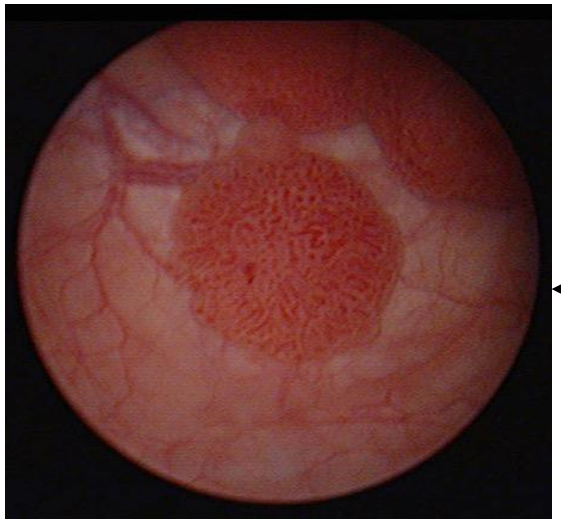
a. History: Symptoms and risk factors

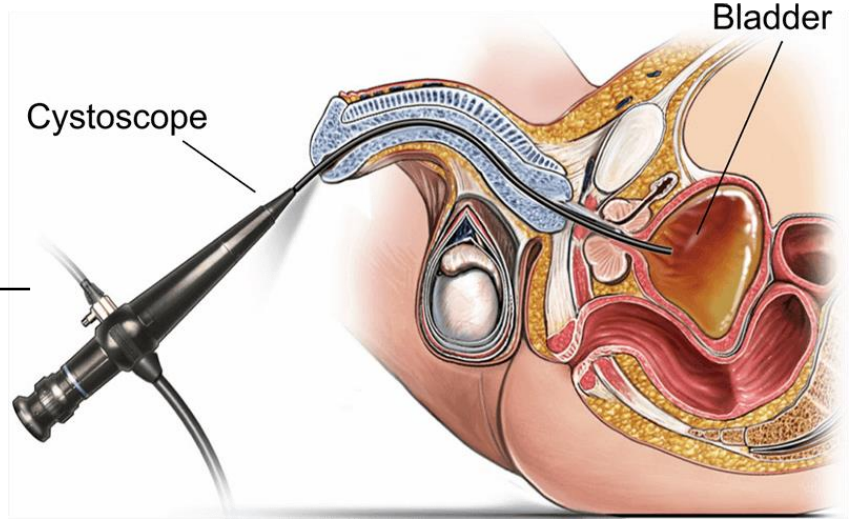
b. Examination

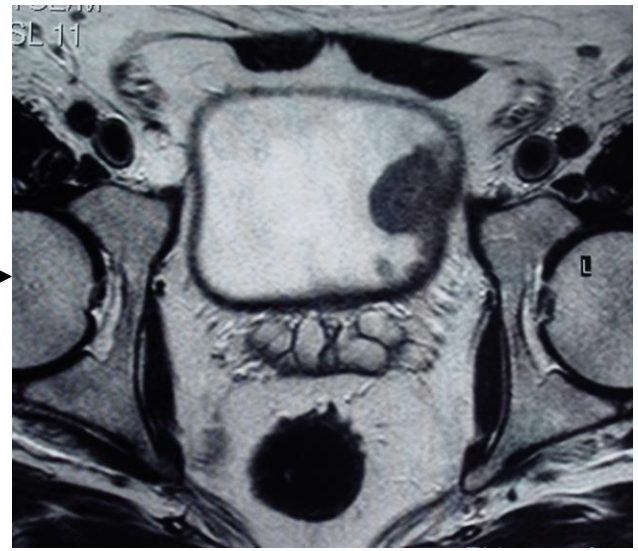
c. Urinary tests: Microscopy and cytology

d. Bladder: Flexible cystoscopy

e. Upper tracts: USS/CT/other

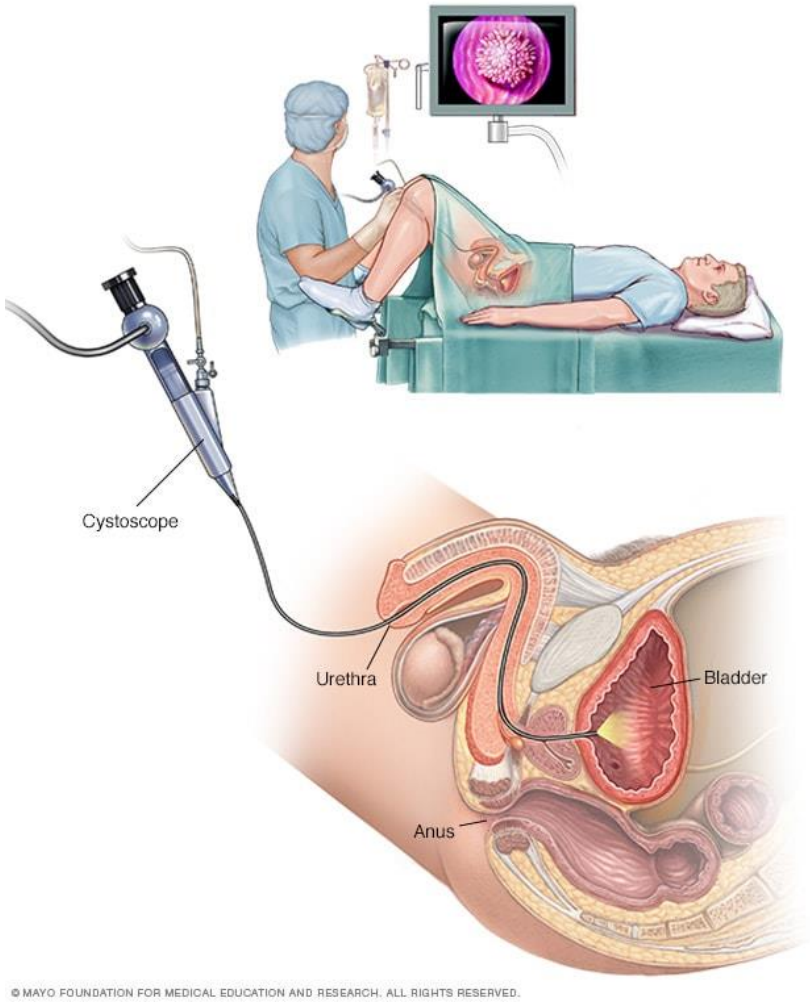


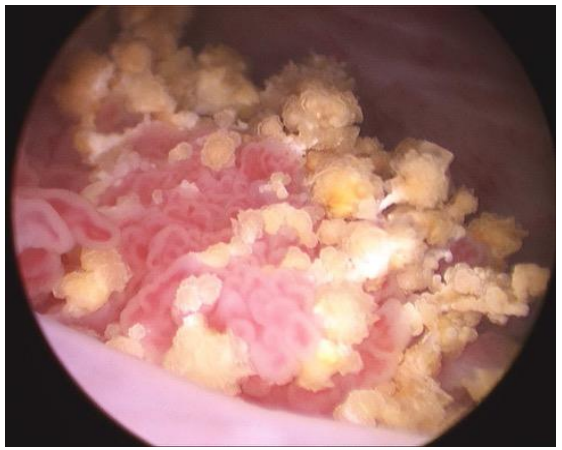




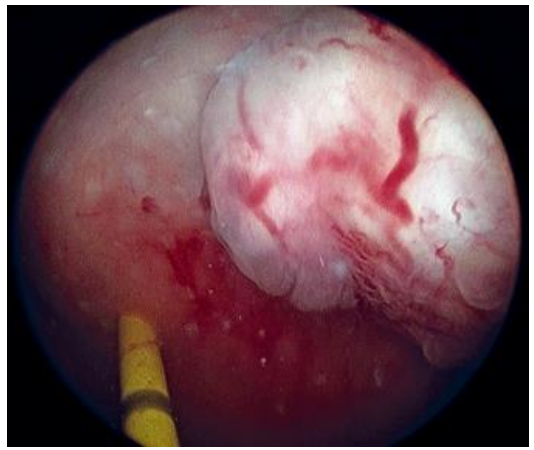
Nội soi bàng quang

Tiêu chuẩn vàng trong chẩn đoán UTBQ, giúp phân loại giai đoạn xâm lấn của khối u

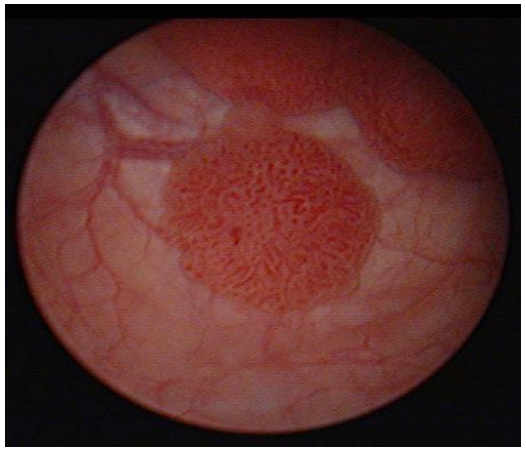




High grade, non-muscle, invasive



High grade, muscle invasive



Low grade, non-muscle, invasive

1. Bladder Cancer Early Detection, Diagnosis, and Staging. Available at: https://www.cancer.org/content/dam/CRC/PDF/Public/8559.00.pdf. (Accessed November 2021); 2. Smith A, et al. Chapter 83: Bladder Cancer. In: Niederhuber JE, et al (eds). Abeloff's Clinical Oncology. 5th ed. Philadelphia, PA: Elsevier; 2014

Phân loại giai đoạn UTBQ

Ung thư bàng quang được phân loại dựa trên mức độ xâm lấn vào các lớp thành bàng quang và vị trí khởi phát trong hệ tiết niệu.

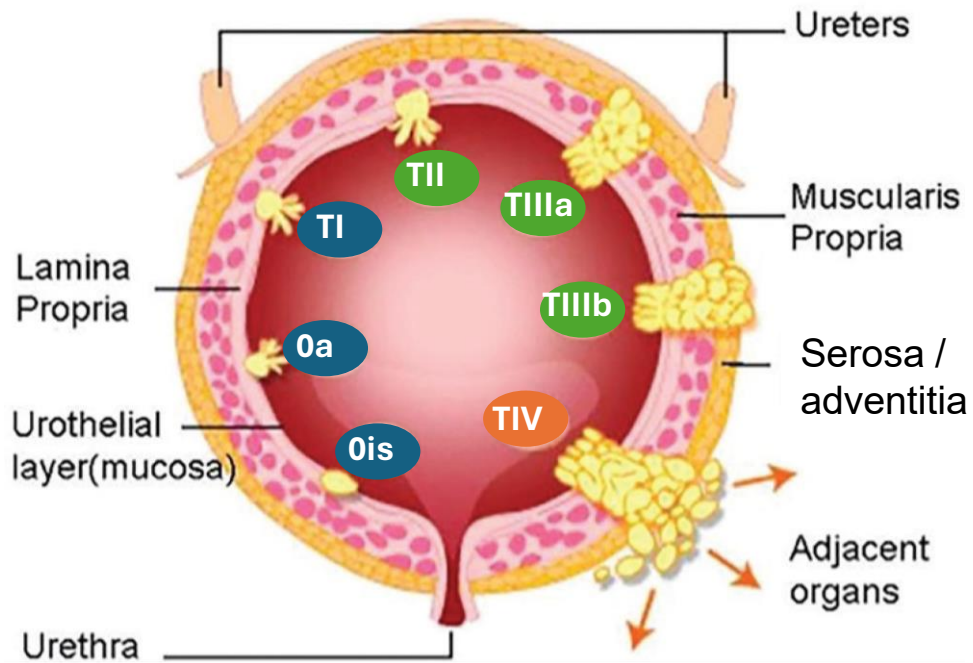
Phân giai đoạn và độ mô học của khối u sẽ giúp tiên lượng bệnh và lựa chọn điều trị - rất quan trọng trong UTBQ

NMIBC[1,2]

Position in bladder wall:

Urothelial layer (mucosa) –
a specialised epithelial layer consisting of a range of different cell types

Lamina propria –
a suburothelial layer which separates the urothelium and muscularis propria



Adapted from Durán N, J Braz Chem Soc 2018[5]

MIBC[1,2]

Position in bladder wall:

Muscularis propria –
also known as the detrusor muscle, consists of three layers

MBC[3,4]

Position in bladder wall:

Serosa / adventitia –
a thin layer of connective tissue that covers the bladder adjacent to the peritoneal layer of the abdominal wall

MBC=metastatic bladder cancer; MIBC, muscle-invasive bladder cancer; NMIBC=non-muscle-invasive bladder cancer

1. What is bladder cancer? Available at: https://www.cancer.org/cancer/bladder-cancer/about/what-is-bladder-cancer.html (Accessed June 2022); 2. Durán N, Fávaro WJ. J Braz Chem Soc 2018;29(5):973–981. 3. Stage IV bladder cancer. Available at: https://www.texasoncology.com/types-of-cancer/bladder-cancer/stage-iv-bladder-cancer. (Accessed June 2021); 4. Bolla SR, et al. StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK540963/. (Accessed June 2022)

Phân độ mô học

Urothelial

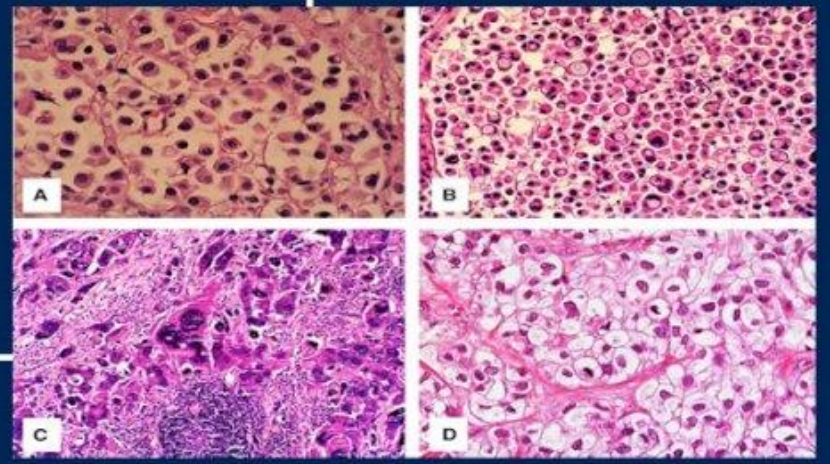
Squamous differentiation
Glandular differentiation

Micropapillary
Microcystic
Plasmacytoid/signet ring
Small cell/neuroendocrine
Sarcomatoid/carcinosarcoma
Lymphepithelioma-like

Giant Cell
Lipid-rich
Clear cell
Nested

Non-urothelial

Urachal carcinoma
Pure adneocarcinoma
(enteric, mucinous)
Pure squamous cell
Pure sarcomas
Lymphoma
Melanoma
Metastases



1. Barkin J, et al. *Can J Urol*. 2014;21 Suppl 2:55-63; 2. NCCN Bladder Cancer Guidelines. V3 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed May 2024.

Phân nhóm nguy cơ

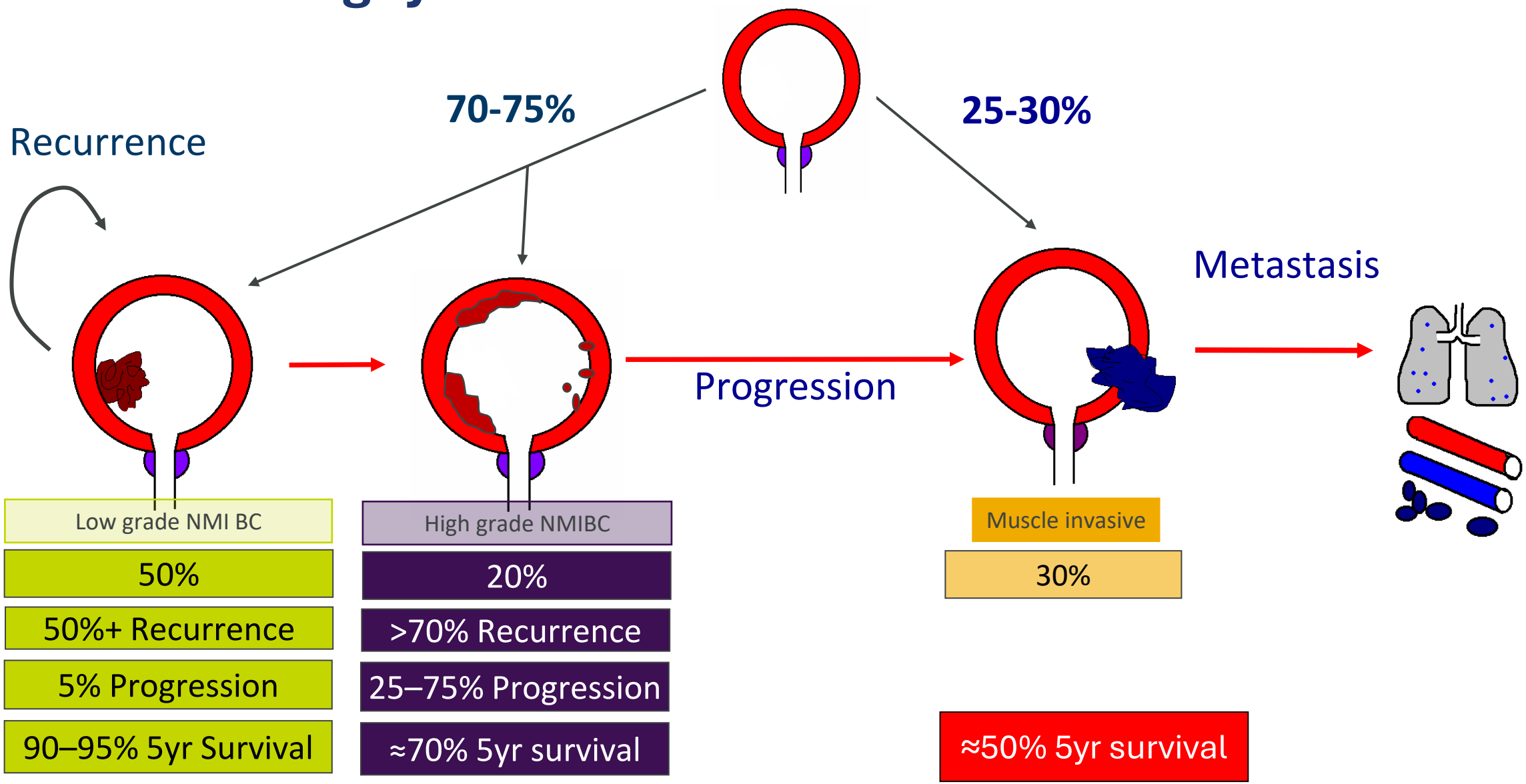
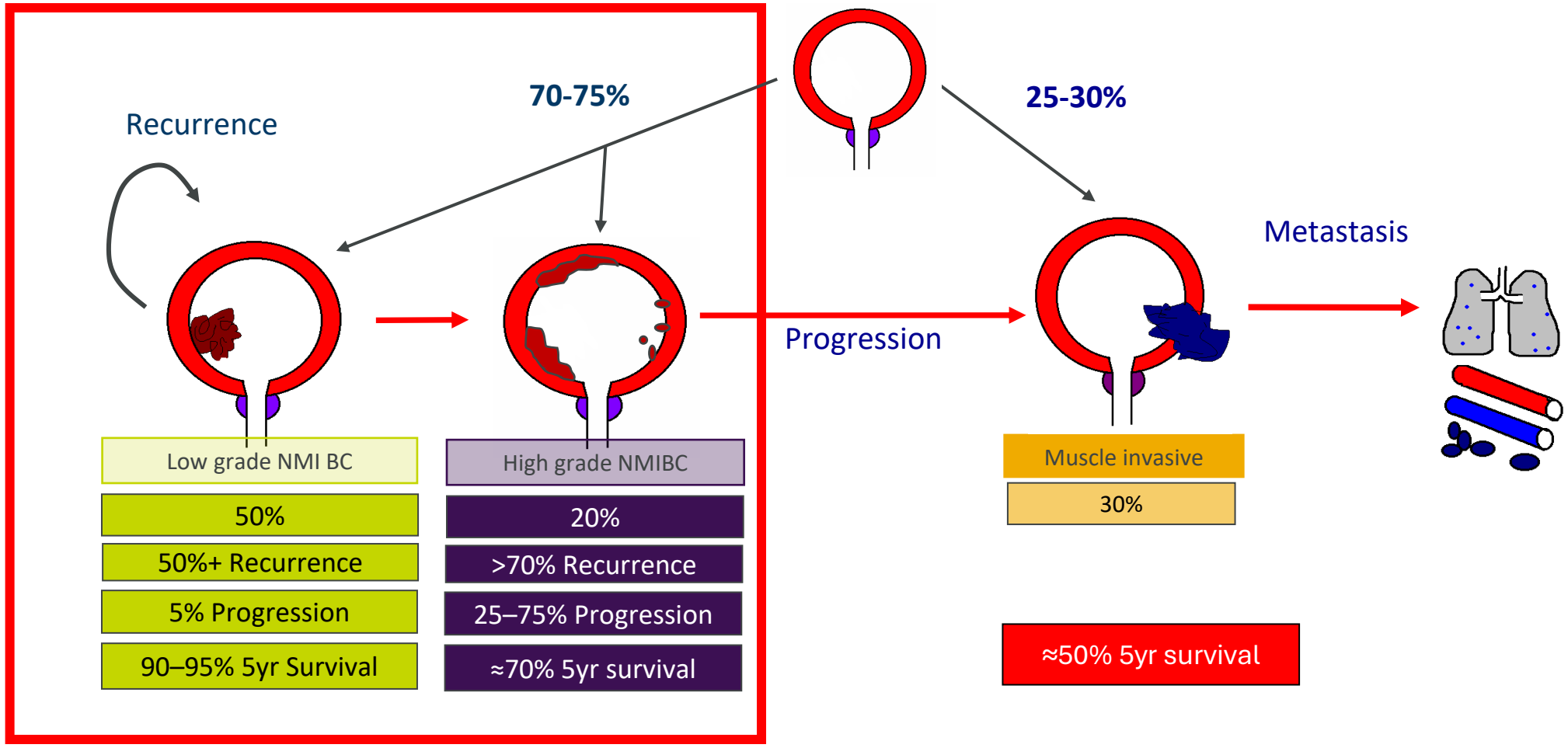


Image developed by speaker
BC=bladder cancer; NMI=non-muscle invasive; yr=year.

Điều trị UTBQ không xâm lấn cơ

NMIBC là thể bệnh thường gặp nhất tại thời điểm chẩn đoán UTBQ

NMIBC chiếm tới 70–80% các trường hợp UTBQ, trong đó: 60% là Ta, 30% là T1, 10% là Tis



Marko Babjuk. European Urology 76 (2019) 639 – 657

Phân nhóm nguy cơ NMIBC

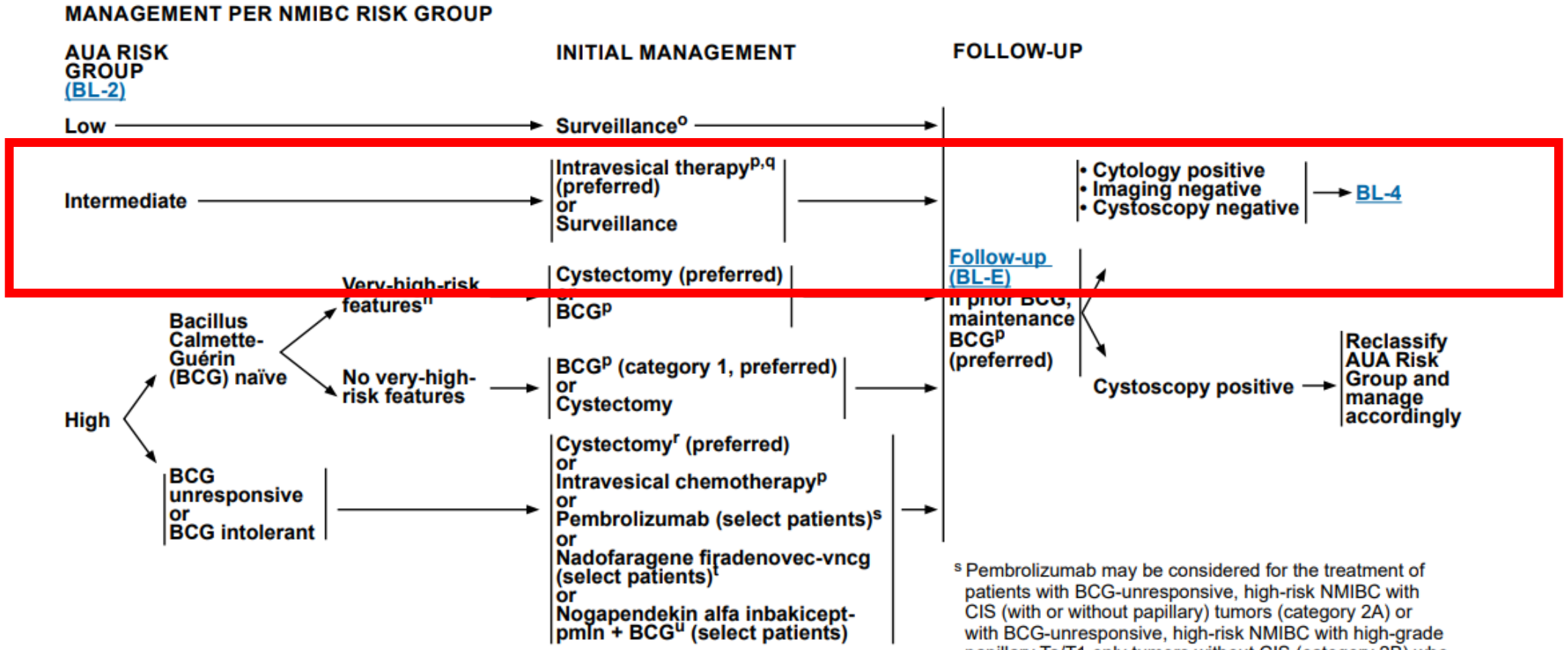
	AUA definition[1,*]	EAU 2022 definition[2]	IBCG definition[3]
Low risk	• Papillary urothelial neoplasm of low malignant potential • Low-grade urothelial carcinoma • Ta and ≤3 cm and solitary	• A primary, single, Ta or T1 low-grade / Grade 1 tumor <3 cm in diameter without CIS in a patient <70 years • A primary Ta low-grade / Grade 1 tumor without CIS with ≤1 additional clinical risk factor[†]	• Solitary, primary low-grade Ta <3 cm

Intermediate risk	• 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
		• Patients without CIS who are not included in either the low-, high-, or very high-risk groups	• Multiple and / or recurrent low-grade Ta
			  • Ta and ≤3 cm and solitary

High risk	• High-grade urothelial carcinoma
	  • CIS or T1 or >3 cm or multifocal
	  • HG Ta, >3cm, or multifocal
	• Any very high-risk features
	  • BCG unresponsive
	  • Variant histologies
	  • Lymphovascular invasion
	  • Prostatic urethral invasion
		• All T1 high grade / Grade 3 without CIS, EXCEPT those included in the very high-risk group
		• All CIS patients, EXCEPT those included in the very high-risk group
		• Ta low grade / Grade 2 or T1 Grade 1, no CIS with all 3 risk factors
		• Ta high grade / Grade 3 or T1 low grade, no CIS with at least 2 risk factors
		• T1 Grade 2 no CIS with at least 1 risk factor
		Very high risk
		• Ta high grade / Grade 3 and CIS with all 3 risk factors
		• T1 Grade 2 and CIS with at least 2 risk factors
		• T1 high grade / Grade 3 and CIS with at least 1 risk factor
		• T1 high grade / Grade 3 no CIS with all 3 risk factors
			• T1, any high-grade tumors and / or CIS

[*]NCCN Clinical Practice Guidelines for NMIBC also utilize the AUA risk stratification definitions; [†]age >70, multiple papillary tumors, tumor diameter ≥3 cm.
AUA, American Urological Association; BCG, Bacillus Calmette-Guérin; CIS, carcinoma in situ; EAU, European Association of Neurology; IBCG, International Bladder Cancer Group; NCCN, National Comprehensive Cancer Network; NMIBC, non-muscle-invasive bladder cancer.
1. Chang S, et al. *J Urol* 2016;196:1021–1029; 2. EAU. Non-muscle-invasive Bladder Cancer guidelines. https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer . Accessed October 6, 2022; 3. Kamat A, et al. *J Clin Oncol* 2016;34:1935–1944.

Điều trị UTBQ không xâm lấn cơ



[n] Lymphovascular invasion, prostatic urethral involvement of tumor, subtype histology (eg, micropapillary, plasmacytoid, sarcomatoid).
[o] Should consider single perioperative instillation of intravesical chemotherapy at time of TURBT.
[p] Principles of Instillation Therapy (BL-F).
[q] Options for intravesical therapy for intermediate-risk disease include BCG and chemotherapy; should consider BCG availability in decision-making.
[r] If not a cystectomy candidate, and recurrence is high-grade cTa or cT1, consider concurrent chemoradiotherapy (category 2B for cTa, category 2A for cT1) or a clinical trial. See Principles of Systemic Therapy (BL-G 5 of 7).

[s] Pembrolizumab may be considered for the treatment of patients with BCG-unresponsive, high-risk NMIBC with CIS (with or without papillary) tumors (category 2A) or with BCG-unresponsive, high-risk NMIBC with high-grade papillary Ta/T1 only tumors without CIS (category 2B) who are ineligible for or have elected not to undergo cystectomy.
[t] Nadofaragene firadenovec-vncg may be considered for the treatment of patients with BCG-unresponsive, high-risk, NMIBC with CIS (with or without papillary) (category 2A) or with BCG-unresponsive, high-risk, NMIBC with high-grade papillary Ta/T1 only tumors without CIS (category 2B).
[u] Nogapendekin alfa inbakicept-pmln in combination with BCG may be considered for the treatment of patients with BCG-unresponsive, high-risk NMIBC with CIS (with or without papillary) tumors.

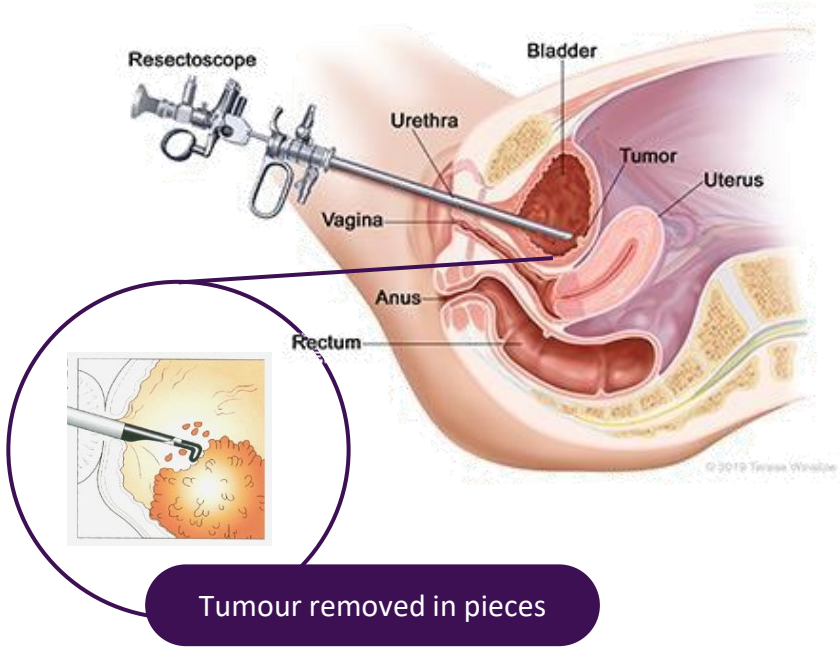
NCCN V1.2025

Điều trị ban đầu NMIBC: Phẫu thuật cắt khối u bàng quang qua niệu đạo (TURBT)

TURBT vừa được sử dụng để chẩn đoán và đánh giá giai đoạn bệnh, đồng thời cũng là phương pháp điều trị ban đầu để loại bỏ các khối u bàng quang nhìn thấy được.

- **AUA, EAU, ESMO** and **NCCN** guidelines recommend TURBT as the first treatment for bladder cancers[1–6]
- TURBT can completely eradicate most NMIBC tumours that are papillary in nature[1]
    - These are easily removed by cutting across their narrow stalk or base using endoscopy[1]
- A resectoscope, a thin, tube-like instrument is used for the procedure and has a small loop of wire at the end to remove visible tissue or tumours[1,7]
- TURBT can be performed repeatedly with minimal risk to the patient[8]
    - There is <10% risk of infection or injury to the bladder, and both are easily correctable[8]

Transurethral Resection of Bladder Tumour (TURBT)



AUA=American Urological Association; EAU= European Association of Urology; ESMO=European Society of Medical Oncology; NCCN=National Comprehensive Cancer Network; NMIBC=non-muscle invasive bladder cancer; TURBT=transurethral resection of bladder tumour.

1. Medscape.Transurethral Resection of Bladder Tumours. Available at: https://emedicine.medscape.com/article/1951622-overview#a1. Accessed March 2024; 2. Chang SS, et al. *J Urol.* 2016;196(4):1021–1029; 3. Alfred Witjes J, et al. *Eur Urol.* 2017;71(3):462–475; 4. Babjuk M, et al. *Eur Urol* 2017;7(3):447–461; 5. NCCN Clinical Practice Guidelines in Oncology. Bladder Cancer. V3. 2023; 6. Powles T, et al. *Ann Oncol.* 2022;33(3): 244–258; 7. National Cancer Institute. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/resectoscope. Accessed March 2024; 8. Bladder Cancer Advocacy Network. Transurethral Resection of a Bladder Tumour (TURBT) Procedure. Available at: https://bcan.org/bladder-cancer-turbt/. Accessed March 2024.

Sau TURBT ban đầu, hóa trị bàng quang (IVT) là điều trị tiêu chuẩn tiếp theo

IVT – truyền hóa trị dạng lỏng trực tiếp vào bàng quang qua ống thông mềm đặt qua niệu đạo – giúp làm giảm đáng kể nguy cơ tái phát của khối u bang quang

INTRAVESICAL CHEMOTHERAPY[1–4]

- Should be given within 24 hours of TURBT*. A single dose of **intravesical mitomycin-C** given within this timeframe can reduce the frequency of tumour recurrence[1,2]
- Gemcitabine can also be used and is now the preferred regimen recommended by NCCN[3]
- Intravesical chemotherapy post-TURBT should NOT be given if there is any suspicion of bladder perforation following the TURBT procedure[3,4]

Key information about IVT:[2–5]

- It allows the treatment to target any remaining tumour cells lining the inside of the bladder[2,3]
- It does not cause any major systemic effects in the body[2]
- It should be kept in the bladder for up to 2 hours before being passed through urination[5]
- It may deliver either chemotherapy (mitomycin C / gemcitabine) or BCG depending on the patient's risk of disease progression[2–4]
- Some patients with NMIBC also receive adjuvant intravesical chemotherapy, which may follow a second TURBT procedure[3–5]

Theo EAU và NCCN: Bệnh nhân có nguy cơ trung bình nên được điều trị bổ trợ IVT, bên cạnh đó **BCG cũng là một lựa chọn nên được cân nhắc**

BCG IVT là liệu pháp miễn dịch không đặc hiệu, sử dụng như điều trị bổ trợ cho NMIBC nguy cơ trung bình và cao

Tỷ lệ đáp ứng theo Dữ liệu đời thực

- Data from 160 RWE studies on patients with BCG-naïve high-risk NMIBC, receiving intravesical BCG treatment showed varied response rates based on guideline adherence and side effect tolerance[1]
- 5-year RFS (17–89%), PFS (58–89%) and OS (28–90%) were low without proper BCG schedules or administration[1]
- Although there is no formal statement on the optimal duration of BCG maintenance treatment, guidelines suggest 1–3 years[1]

BCG IVT điều trị hiệu quả trên NMIBC giai đoạn sớm

- ~70% of patients with early stage NMIBC achieve a complete response with intravesical BCG treatment, depending on the risk group and adherence to guidelines[1]
- However, T1 tumours are associated with significant rates of recurrence and progression[1]

EAU & NCCN: BCG là điều trị tiêu chuẩn cho NMIBC nguy cơ cao sau TURBT

- In an RCT, BCG outperformed epirubicin and interferon-alpha2b, mitomycin C, or epirubicin alone in preventing tumour recurrence in intermediate and high-risk NMIBC patients[2]
- However, despite BCG treatment's efficacy, approximately 30–40% of patients experience failure, leading to increased risks of recurrence and progression[2]

BCG=Bacillus Calmette-Guérin; EAU=European Association of Urology; NICE=National Institute for Health and Care Excellence; NMIBC=non-muscle invasive bladder cancer; OS=overall survival; PFS=progression-free survival; RFS=recurrence-free survival; SoC=standard of care; T=tumour; TURBT=transurethral resection of bladder tumour.

1. Bedke J, et al. *Urol Oncol.* 2023;41(12):461–475; 2. Kodera A, et al. *Cureus.* 2023;15(6):e40962.

~50–70% bệnh nhân NMIBC sẽ thất bại điều trị với BCG IVT: tái phát trong vòng 2 năm, và ~20–30% tiến triển thành MIBC[1,2]

NMIBC recurrence after BCG can be categorised into BCG refractory, relapsing or unresponsive. Patients with BCG relapse may have better outcomes than BCG refractory patients[3]

BCG refractory tumour[3]

1. T1 G3/HG tumour present at 3 months. Further administration of conservative BCG therapy associated with increased risk of progression

2. Ta G3/HG tumour present after 3 months and/or at 6 months, after either re-induction or first course of maintenance

3. CIS (without concomitant papillary tumour) at 3 months and persists at 6 months after either re-induction or first course of maintenance

4. If HG tumour appears during BCG maintenance therapy*

BCG relapsing tumour[3]

Recurrence of G3/HG tumour after completion of BCG maintenance, despite an initial response

BCG unresponsive tumour[3]

BCG refractory or T1/Ta HG BCG recurrence within 6 months of completion of adequate BCG exposure† or development of CIS within 12 months of completion of adequate BCG exposure

NMIBC không đáp ứng với BCG gần như không nhận được lợi ích từ việc tiếp tục điều trị BCG.
Phẫu thuật cắt bàng quang toàn bộ (radical cystectomy) là lựa chọn chuẩn và ưu tiên.

BCG=Bacillus Calmette-Guérin; CIS=carcinoma *in-situ*; G3=Grade 3; HG=high grade; MIBC=muscle invasive bladder cancer; NMIBC=non-muscle invasive bladder cancer.

1. Balar AV, et al. *Lancet Oncol.* 2021;22:919–930; 2. Aldousari S et all *Can Urol Assoc* J. 2010;4(1):56–64; 3. European Association of Urology. EAU Guidelines on Non-muscle-invasive Bladder Cancer (TaT1 and CIS). Available at: https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-Guidelines-on-Non-muscle-Invasive-Bladder-Cancer-2023_2023-03-10-101110_jued.pdf. Accessed March 2024; 4. Balar A et al. Presented at ASCO GU Annual Congress 2019. 14–16 February; San Francisco, CA. Poster #350; 5. Food and Drug Administration. FDA approves pembrolizumab for BCG-unresponsive, high-risk non-muscle invasive bladder cancer. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-bcg-unresponsive-high-risk-non-muscle-invasive-bladder-cancer. Accessed March 2024; 6. Food and Drug Administration.

KEYNOTE-057 investigated pembrolizumab in patients with high-risk BCG-unresponsive NMIBC unsuitable for radical cystectomy

Phase II open-label, single-arm, multi-centre study

Patient population:[2]

- High-risk NMIBC unresponsive to BCG
- Decline/not eligible for radical cystectomy
- ECOG PS 0–2
- Tissue for biomarker testing
- Adequate organ function

R 1:1
N=101

Pembrolizumab[2]
200 mg IV Q3W ≤35 up to 2y or until recurrence

Pembrolizumab / vibostolimab / favezelimab[2]
200 mg each IV Q3W ≤35 up to 2ys

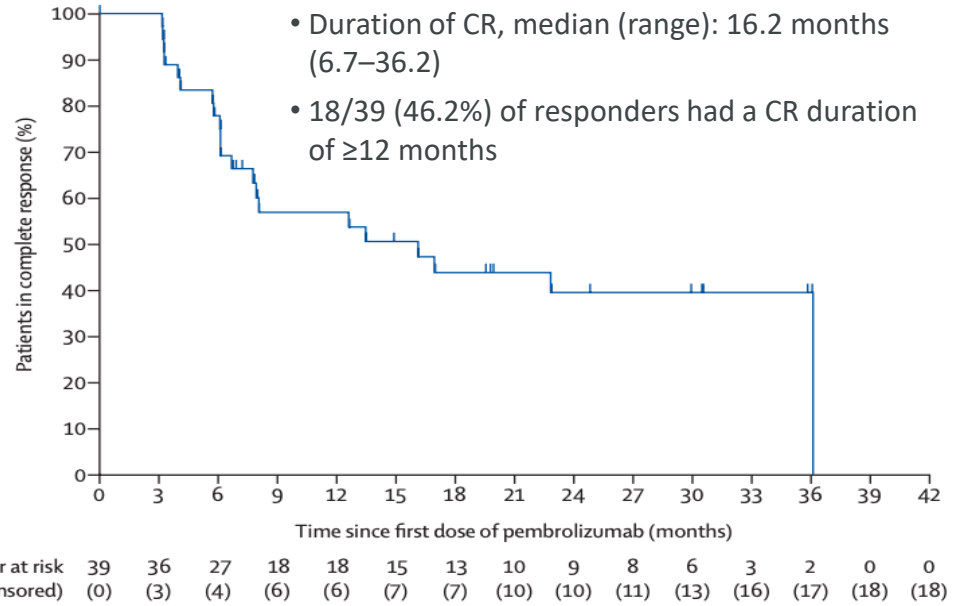
Primary endpoint[1,2]

- CRR
- DFS

Key secondary endpoints[1,2]

- DoR

Patients remaining in CR[§2]



Outcomes from Cohort A (patients with CIS ± papillary tumours):[2]

- **Complete response, duration of response and safety summary after ≥2 years follow-up (n=96)***
- Patients with complete response:‡ 41%
- No patients progressed to MIBC or metastatic disease on Tx
- Grade 3–4 TRAEs occurred in 13% of patients; Most common TRAEs were hyponatremia (3%) and arthralgia (2%)

Tỷ lệ đáp ứng hoàn toàn của Cohort A là 41% tại thời điểm 3 tháng

➔Pembrolizumab được phê duyệt cho NMIBC nguy cơ cao, không đáp ứng BCG, có CIS ± papillary tumours, và không đủ điều kiện/từ chối phẫu thuật

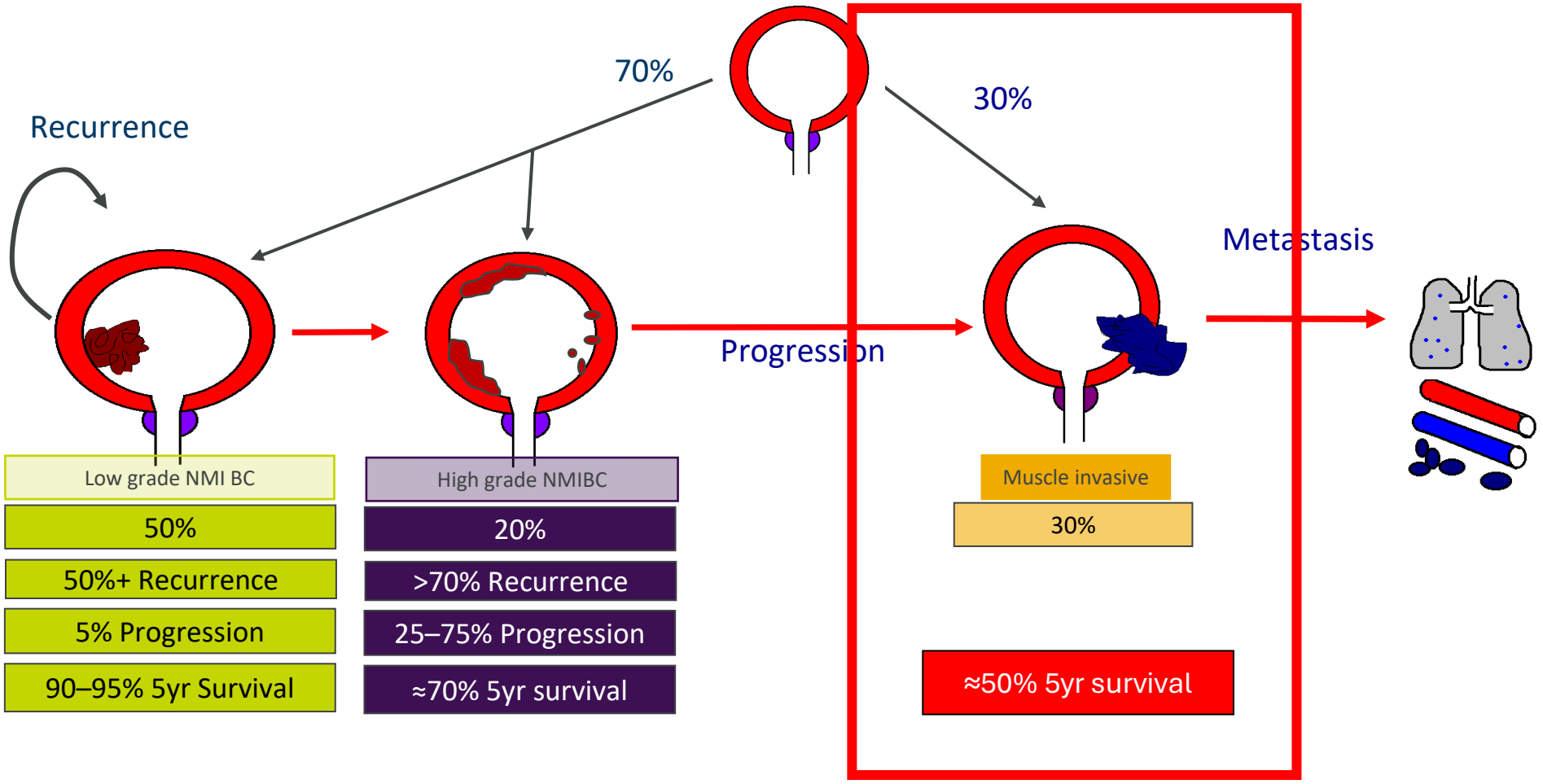
1. Balar A et al. Presented at ASCO GU Annual Congress 2019. 14–16 February; San Francisco, CA. Poster #350; 2. ClinicalTrials.gov. Study of Pembrolizumab (MK-3475) and Pembrolizumab With Other Investigational Agents in Participants With High Risk Non-muscle Invasive Bladder Cancer (MK-3475-057/KEYNOTE-057). Available at: https://clinicaltrials.gov/study/NCT02625961. Accessed March 2024.

Điều trị UTBQ xâm lấn cơ

Phẫu thuật, xạ trị, hóa trị và liệu pháp miễn dịch

MIBC chiếm khoảng ~25% các ca UTBQ mới chẩn đoán và thường có tiên lượng xấu

About 1 in 4 patients are diagnosed with MIBC; 10% to 20% of NMIBC patients will progress to muscle-invasive disease



Marko Babjuk. European Urology 76 (2019) 639 – 657

Phẫu thuật cắt bàng quang toàn bộ (RC) là điều trị tiêu chuẩn cho UTBQ xâm lấn cơ

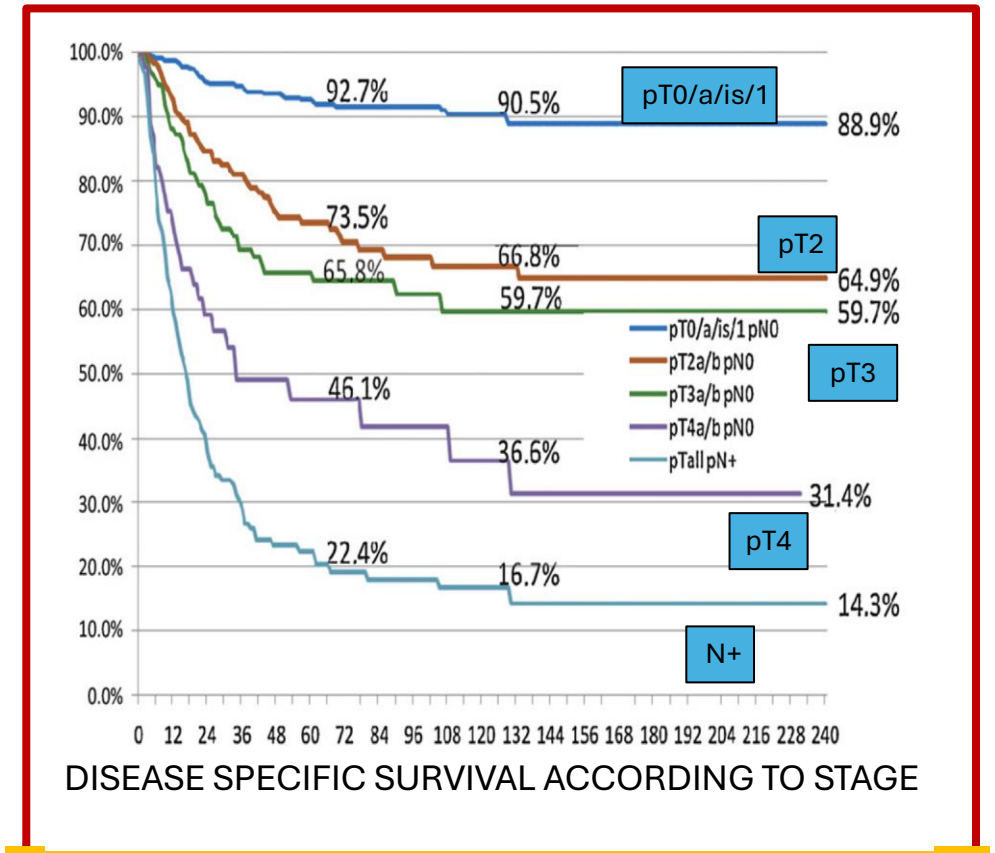
Bệnh nhân có đủ điều kiện sử dụng cisplatin: RC được thực hiện sau hóa trị tân bổ trợ.
Bệnh nhân không đủ điều kiện sử dụng cisplatin: RC là lựa chọn điều trị chính.

Treatment	Patient selection	Clinical outcomes
Radical cystectomy	Fit MIBC patients	**50%** cure with surgery alone, highly dependent on pathologic stage
Bladder-sparing partial cystectomy	Solitary tumours in dome of bladder are ideal	Variable, highly dependent on patient selection
Bladder-sparing chemoradiation	No CIS, no hydronephrosis, maximal TURBT required	**65%** cure, **55%** bladder intact, highly dependent on patient selection
Neoadjuvant cisplatin-based chemotherapy	Cisplatin-eligible MIBC patients	**5–10%** improvement in overall survival compared to RC alone
Adjuvant cisplatin-based chemotherapy	Cisplatin-eligible high-risk post-RC MIBC patients (pT3-4, N+)	Similar improvement as neoadjuvant treatment, data less robust, many patients not suitable for adjuvant treatment

CIS=carcinoma in situ; MIBC=muscle-invasive bladder cancer; RC=radical cystectomy; SoC=standard of care; TURBT=transurethral resection of bladder tumour

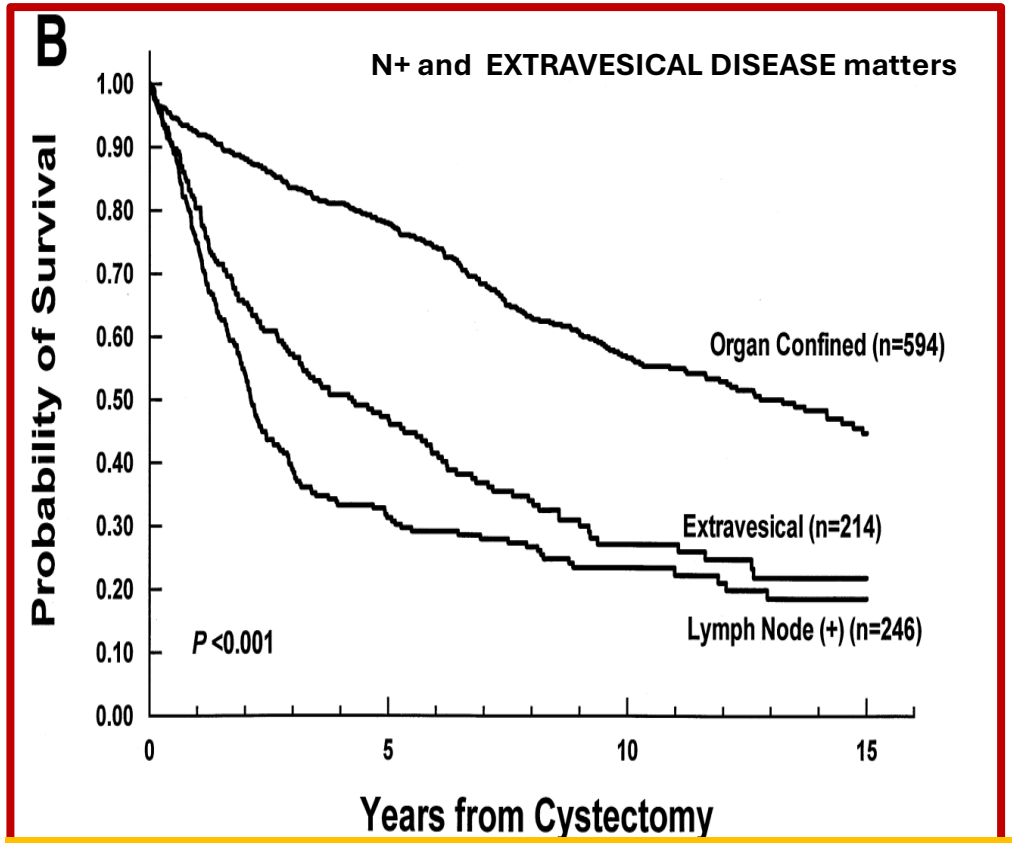
1. Hahn NM. Harrison's Principles of Internal Medicine, 20e. Chapter 82. Cancer of the Bladder and Urinary Tract.

Kết quả phẫu thuật cắt bàng quang toàn bộ phụ thuộc vào giai đoạn bệnh



DISEASE SPECIFIC SURVIVAL ACCORDING TO STAGE

German series of 1.100 cystectomies. University of Ulm. 1986-2009

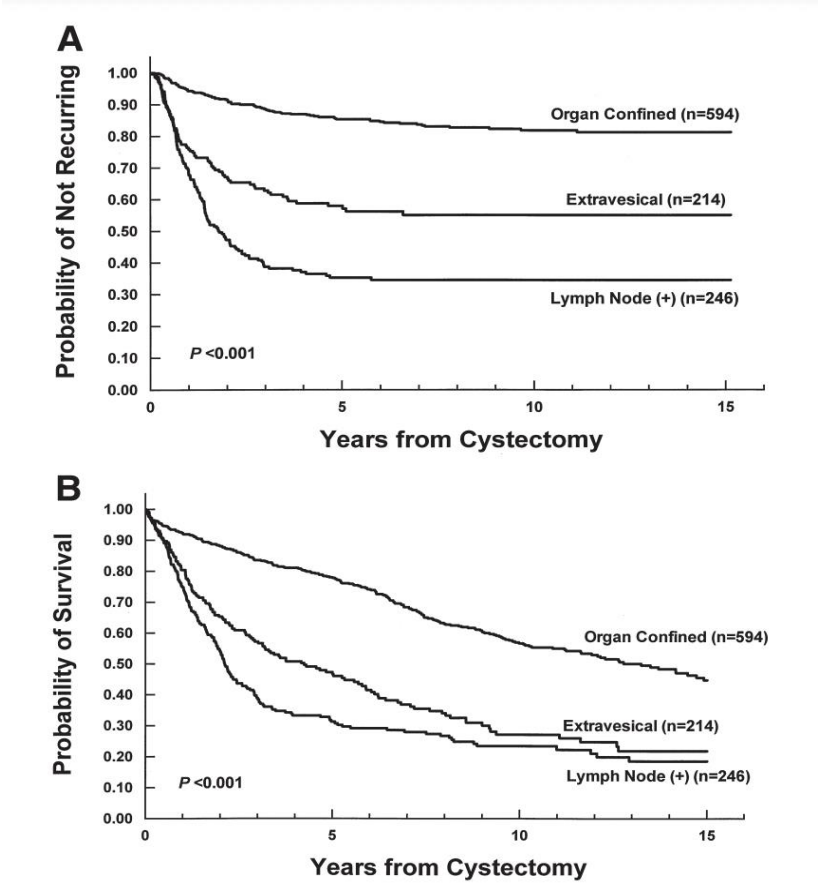


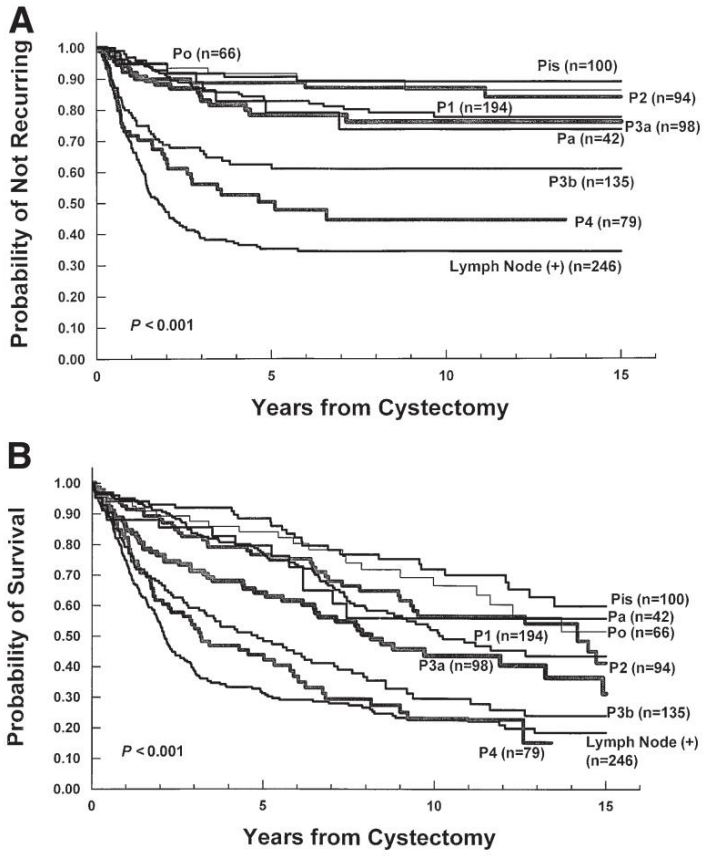
American series of 1.054 patients. 1971-1997

Các bệnh nhân MIBC mặc dù đã được điều tị với phẫu thuật cắt toàn bộ bang quang, nguy cơ taisphats vẫn đáng kể và gia tang khi có tình trạng u xâm lấn ngoài bang quang hoặc có xuất hiện di căn hạch (micro metastatic disease)

MIBC: Muscle-Invasive Bladder Cancer

Kết quả phẫu thuật cắt bàng quang toàn bộ phụ thuộc vào giai đoạn bệnh





The 5- and 10-year recurrence-free survival for patients with **organ-confined, lymph node-negative** tumors was **92%** and 86% for **pT0 disease**, **91%** and **89% for pTis, 79%** and 74% **for pTa,** and **83%** and 78% **for pT1** tumors, respectively.

Patients with muscle invasive **(pT2 and pT3a), lymph node-negative** tumors had **89%** and 87% and **78%** and 76% 5- and 10-year recurrence-free survival, respectively.

Stein JP et al. Radical Cystectomy in the Treatment of Invasive Bladder Cancer: Long-Term Results in 1,054 Patients. J Clin Oncol. 2023 Aug 1;41(22):3772-3781.

Một số trường hợp MIBC (như cần bảo tồn BQ): Xạ trị hoặc hóa xạ trị là lựa chọn

Radiotherapy alone may have comparable outcomes to chemoradiotherapy in older patients or those with a worse prognosis[4,5]

Radiotherapy or chemoradiotherapy may be used in selected MIBC patients as follows:[1,2]

- For patients suitable for organ (bladder) preservation therapy
- Patients ineligible for cystectomy
- Patients who do not want to undergo cystectomy (patient preference)
- As palliation therapy in patients with advanced metastatic disease

MIBC=muscle-invasive bladder cancer

1. Bellmunt J, et al. *Ann Oncol*. 2014;25(Suppl 3):iii40–iii48; 2. NCCN bladder cancer guidelines. V5 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed Nov 2024; 3. EAU Guidelines on Muscle-invasive Bladder Cancer https://d56bochluxqnz.cloudfront.net/documents/fullguideline/EAU-Guidelines-on-Muscle-Invasive-and-Metastatic-Bladder-Cancer-2024.pdf. Accessed October 2024; 4. Yamamoto Y, et al. Adv Radiat Oncol. 2022;7(6):101157. doi:10.1016/j.adro.2022.101157. 5. Gergelis KR, et al. Pract Radiat Oncol. 2020 Sep-Oct;10(5):e378-e387.

Lựa chọn hóa trị trong MIBC: Tân bổ trợ và bổ trợ

Các khuyến cáo quốc tế: Lựa chọn liệu pháp hóa trị tân bổ trợ (NAC) cho bệnh nhân MIBC để cải thiện kết quả phẫu thuật cắt bỏ bang quang toàn bộ

Neoadjuvant

Given **pre-surgery** to destroy **micro-metastases** outside the surgical field[1]

NACT administered prior to radical cystectomy **reduces risk of recurrence from micrometastases**,[2] and may be **more tolerable** than adjuvant chemotherapy[3]

Cisplatin-based NACT is the **recommended regimen for MIBC**, providing a **5–8% survival benefit vs. no NACT**[3]

RADICAL CYSTECTOMY

Adjuvant

Given **post-surgery** in **cystectomy patients** with **extensive disease**[4]

MIBC patients who have **not received NACT** and **have non-organ confined disease** at radical cystectomy may be treated with **adjuvant cisplatin-based chemotherapy**[2–5]

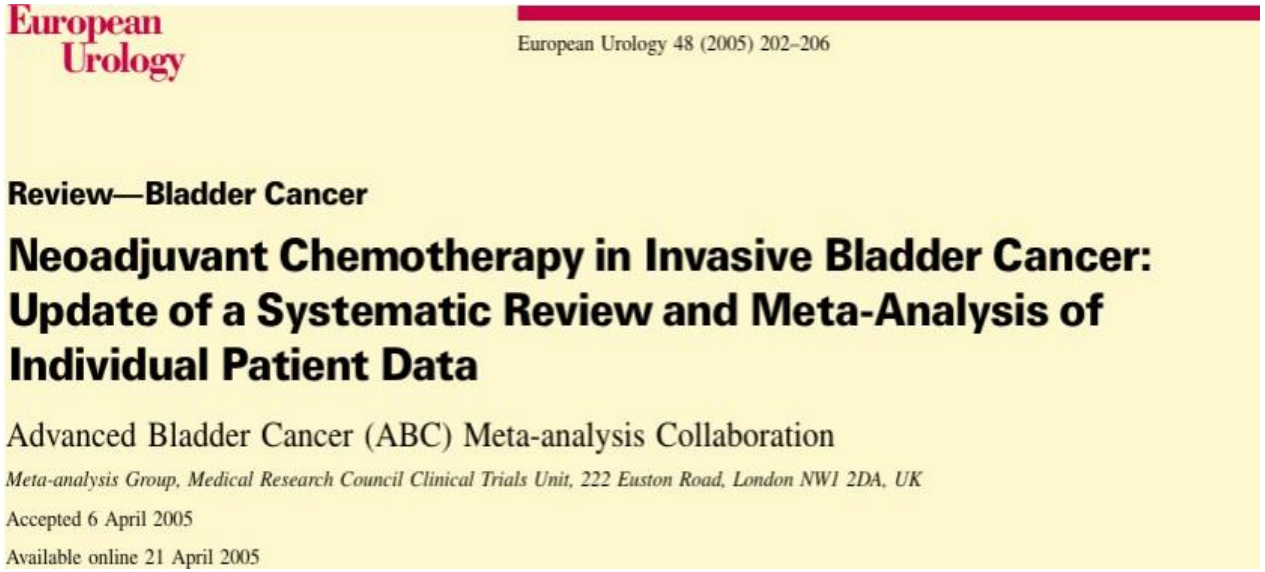
For **cisplatin-ineligible patients,** some guidelines state that there is **insufficient evidence** for **non-cisplatin therapy**,[3,4] but others recommend **gemcitabine (± paclitaxel)**[5]

MIBC=muscleinvasive bladder cancer; NACT=neoadjuvant chemotherapy.

1. Johnson DC, et al. *BJU Int.* 2014;114(2):221–228; 2. Apolo AB, et al. *Urol Oncol.* 2012;30(6): 772–780; 3. EAU Guidelines on Muscle-invasive Bladder Cancer. https://d56bochluxqnz.cloudfront.net/documents/fullguideline/EAU-Guidelines-on-Muscle-Invasive-and- Metastatic-Bladder-Cancer-2024.pdf. Accessed October 2024; 4. AUA Guidelines on Muscle-invasive Bladder Cancer. Available at: https://www.auanet.org/guidelines/bladder-cancer-non-metastatic-muscle-invasive-guideline Accessed Oct 2024; 5. NCCN bladder cancer guidelines. V5 2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed Oct 2024.

Hóa trị tân bổ trợ với cisplatin là điều trị tiêu chuẩn

Systematic Reviews & Meta-analysis (với 11 TNLS, 3005 bệnh nhân): Hóa trị tân bổ trợ với cisplatin giúp tăng **5% OS, 9% DFS**



European Urology

European Urology 48 (2005) 202–206

Review—Bladder Cancer

Neoadjuvant Chemotherapy in Invasive Bladder Cancer: Update of a Systematic Review and Meta-Analysis of Individual Patient Data

Advanced Bladder Cancer (ABC) Meta-analysis Collaboration

Meta-analysis Group, Medical Research Council Clinical Trials Unit, 222 Euston Road, London NW1 2DA, UK

Accepted 6 April 2005

Available online 21 April 2005

There are two preferred cisplatin-based NACT regimens recommended for treatment of MIBC:[1,2]

Gemcitabine + cisplatin (GC)

Dose-dense methotrexate, vinblastine, doxorubicin + cisplatin (ddMVAC)

Phân tích hồi cứu cho thấy hóa trị tân bổ trợ phác đồ GC và MVAC có hiệu quả tương đương, nhưng GC dung nạp tốt hơn.
Tuy nhiên, tỷ lệ tái phát tích lũy thấp hơn ở nhóm MVAC so với GC ở bệnh nhân có di căn hạch dương tính (LN+).
Dữ liệu cho thấy ddMVAC giúp giảm 25% nguy cơ tiến triển và giảm 20% nguy cơ tử vong so với MVAC.

CMV=cisplatin, methotrexate + vinblastine; ddMVAC=dose-dense methotrexate, vinblastine, doxorubicin and cisplatin; GC=gemcitabine + cisplatin; MIBC=muscle-invasive bladder cancer; MVAC=methotrexate, vinblastine, doxorubicin + cisplatin; NACT=neoadjuvant chemotherapy

1. NCCN bladder cancer guidelines. V5 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed Nov 2024; 2. EAU Guidelines on Muscle-invasive Bladder Cancer. https://d56bochluxqnz.cloudfront.net/documents/fullguideline/ EAU-Guidelines-on-Muscle-Invasive-and- Metastatic-Bladder-Cancer-2024.pdf. Accessed Oct 2024. 3. Fairey AS, et al. *Urol Oncol.* 2013;31(8):1737–1743; 4. Von der Maase H, et al. *J Clin Oncol.* 2000;18(17):3068–3077. 5. Sternberg C, et al. *J Clin Oncol.* 2001;19(10):2638–2646

~50% bệnh nhân không đủ điệu kiện sử dụng cisplatin, không có lựa chọn thay thế trong điều trị tân bổ trợ, tuy nhiên, định nghĩa của việc không đủ điều kiện hiện chưa được chuẩn hóa

Around **half of patients with MIBC** are considered **cisplatin ineligible** or **refuse cisplatin-based therapy**[1–4]

Even if patients are eligible, utilization of neoadjuvant chemotherapy is typically low due to relatively modest survival outcomes and HCP preference to go straight to surgery[5,6]

Risk factors for cisplatin ineligibility include:

- ECOG performance status >1
- Grade ≥2 peripheral neuropathy
- Renal impairment (GFR ≤60 mL/min)
- Grade ≥2 audiometric loss
- NYHA class-III heart failure

20–40%

Patients with MIBC who receive neoadjuvant chemotherapy[5,6]

Neoadjuvant cisplatin-based chemotherapy has a **low utilization rate** and an **unmet need** exists in the neoadjuvant setting

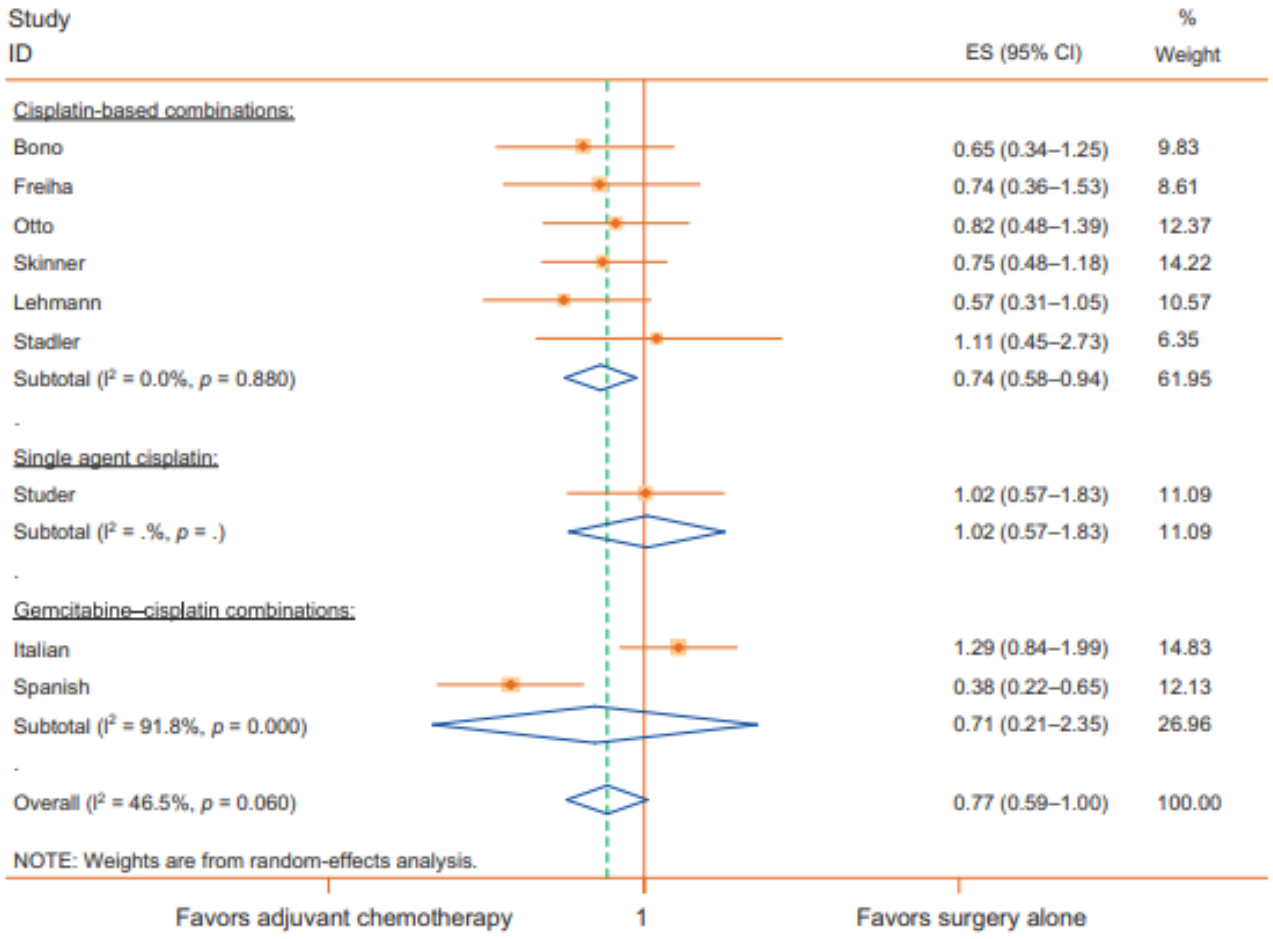
ECOG=Eastern Cooperative Oncology Group; GFR=glomerular filtration rate; MIBC=muscle-invasive bladder cancer; NAC=neoadjuvant chemotherapy; NYHA=New York Heart Association; SoC=standard of care.

1. NCCN Bladder Cancer Guidelines. V3 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed May 2024; 2. EAU Guidelines on Muscle-invasive and Metastatic Bladder Cancer. Available at: https://uroweb.org/guidelines/muscle-invasive-and-metastatic-bladder-cancer. Accessed May 2024; 3. Patil G, Basu A. Ther Adv Urol. 2022;14:17562872221134389; 4. Galsky MD, et al. Lancet Oncol 2011;12:211–214; 5. Roviello G, *et al*. *Front Oncol*. 2022;12:912699; 6. Liu W, et al. *Minerva Urol Nephrol.* 2021;73:144–153.

Một số bệnh nhân không thể nhận NACT có thể phù hợp với hóa trị bổ trợ để tránh làm trì hoãn RC

Though some evidence supports the benefits of adjuvant chemotherapy after RC in MIBC, it is still under debate and as such is used infrequently

Overall survival by therapy type and pooled data



- A meta-analysis of 9 randomised trials suggests adjuvant chemotherapy improves OS and DFS, however the trials included had limitations such as heterogeneity and lack of access to individual patient data
- In an updated analysis of an earlier meta-analysis, a total of 945 patients from 9 RCTs (5 previously analysed, 1 updated, and 3 new) were included
- The pooled HR for OS across all 9 trials was 0.77 (95% CI: 0.59–0.99; P=0.049)
- For DFS, the pooled HR across 7 trials that reported this outcome was 0.66 (95% CI: 0.45–0.91; P=0.014)
- DFS benefit was more pronounced among patients with positive nodal involvement (P=0.010)

CI=confidence interval; DFS=disease-free survival; ES=effect size; HR=hazard ratio; MIBC=muscle-invasive bladder cancer; OS=overall survival; RCT=randomised-controlled trial.

1. Leow JJ, et al. *Eur Urol.* 2014;66(1):42–54..

Liệu pháp miễn dịch điều trị MIBC

Bổ trợ và Tân bổ trợ

Có nhiều nghiên cứu điều trị bổ trợ với liệu pháp kháng PD-L1 trong MIBC, mặc dù kết quả giữa các thử nghiệm còn không thống nhất

	CheckMate 274[1]	IMvigor010[2]	AMBASSADOR[3]
	Nivolumab	Atezolizumab	Pembrolizumab
Neoadjuvant chemo use	43%	48%	64%
Presence in lymph nodes	47%	52%	50%
Upper tract disease	21%	7%	22%
Median DFS, months	20.8 vs. 10.8	19.4 vs. 16.6	29.0 vs. 14.0
DFS endpoint met	Yes	No	Yes

Nivolumab cho thấy hiệu quả tích cực và được phê duyệt trong điều trị bổ trợ MIBC

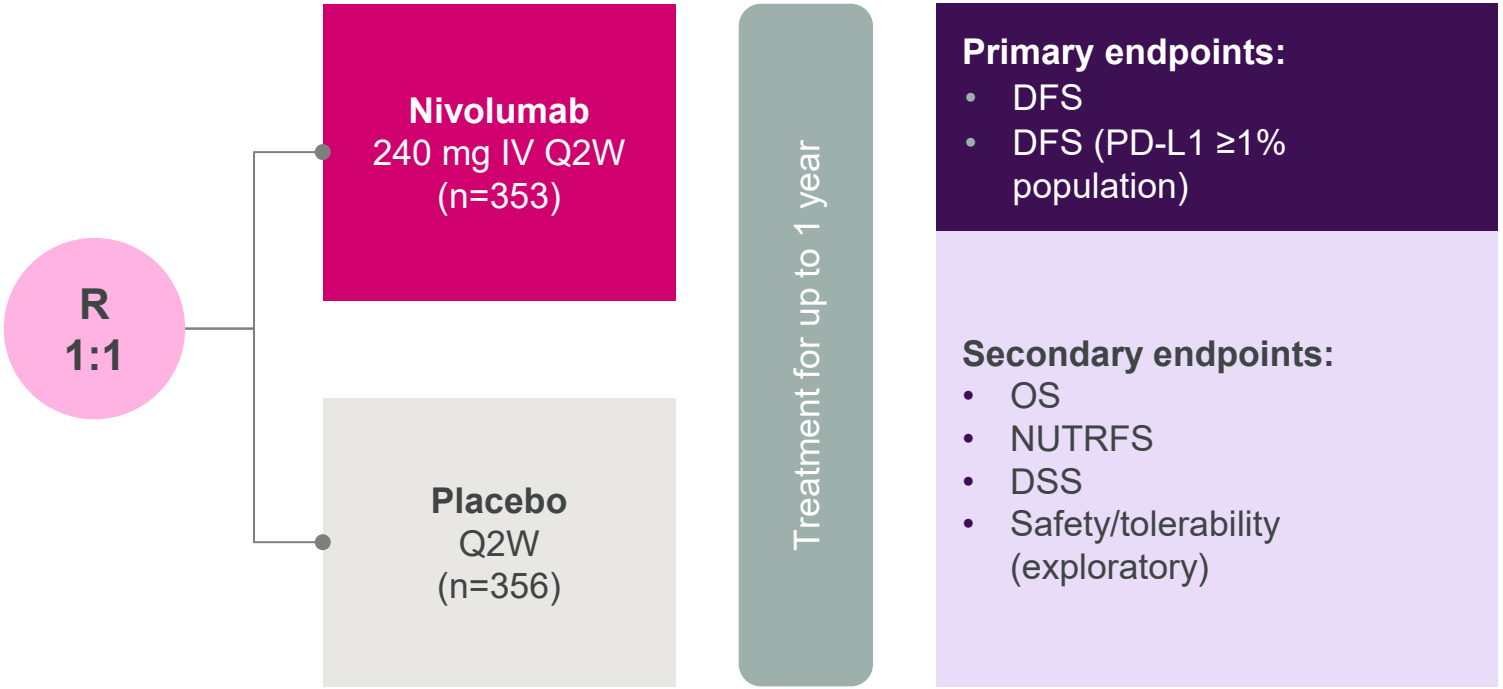
DFS=disease-free survival; MIBC=muscle-invasive bladder cancer; PD-L1=programmed death-ligand 1.

1. Bajorin DF, et al. Presented at ASCO Annual Meeting; 17–19 February 2020, Virtual Congress;
2. Bellmunt J, et al. Lancet Oncol. 2021;22(4):524–537; 3. Apolo AB, et al. J Clin Oncol. 2024;42 (suppl 4; abstr LBA531).

Dữ liệu đến từ các nghiên cứu có thiết kế khác nhau, chỉ mang tính chất tham khảo

TNLS pha III CheckMate 274 đánh giá hiệu quả của nivolumab so với giả dược trong điều trị bổ trợ MIBC, có nguy cơ tái phát cao

- Adults age ≥18 years
- Radical surgery within 120 days ± neoadjuvant cisplatin or ineligible for/declined cisplatin-based chemotherapy
- Evidence of urothelial cancer at high risk of recurrence per pathologic staging
- Disease free by imaging



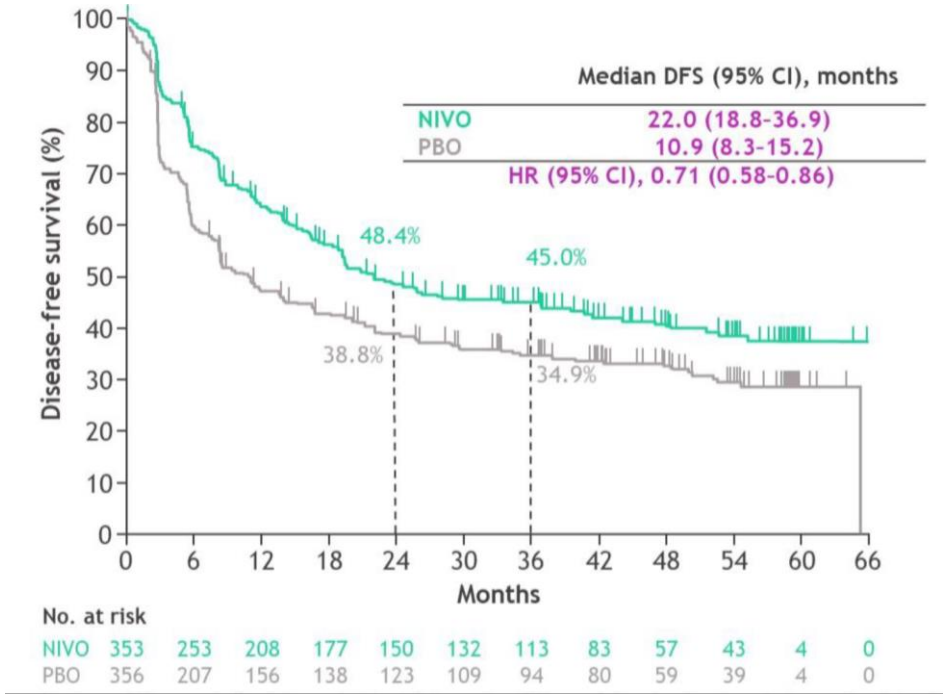
Primary endpoints:
- DFS
- DFS (PD-L1 ≥1% population)

Secondary endpoints:
- OS
- NUTRFS
- DSS
- Safety/tolerability (exploratory)

DFS=disease-free survival; DSS=disease-specific survival; IV=intravenous; MIBC=muscle-invasive bladder cancer; NACT=neoadjuvant chemotherapy; NUTRFS=non-urothelial tract recurrence-free survival; OS=overall survival; PD-L1=programmed death-ligand 1; Q2W=every 2 weeks; R=randomisation.

1. Bajorin DF, et al. Presented at ASCO Annual Meeting; 17–19 February 2020, Virtual Congress; 2. ClinicalTrials.gov. CheckMate 274. Available at: https://clinicaltrials.gov/study/NCT02632409. Accessed May 2024.

Điều trị bổ trợ với nivolumab giúp kéo dài DFS so với placebo[1]



Nivolumab showed an acceptable safety profile, in line with previous trials

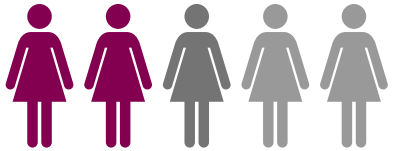
	Nivolumab (n=351)	Placebo (n=348)
Any Grade TRAE, %	79	56
Grade 3–4 TRAE, %	18	7

Nivolumab được phê duyệt trong điều trị bổ trợ MIBC dựa trên kết quả nghiên cứu[2,3]

Nivolumab hiện chưa được phê duyệt tại Việt Nam. Vui long tham khảo tờ thông tin kê toa trước khi sử dụng

AE=adverse event; CI=confidence interval; DFS=disease-free survival; EAU=European Association of Urology; EMA=European Medicines Agency; FDA=U.S. Food and Drug Administration; HR=hazard ratio; CI=confidence interval; HR=hazard ratio; MIBC=muscle-invasive bladder cancer; NIVO=nivolumab; PBO=placebo; PD-L1=programmed death-ligand 1; NCCN=National Comprehensive Cancer Network; TRAE=treatment-related adverse event.
References in slide notes.

Tuy nhiên, hiện vẫn còn nhiều nhu cầu chưa được đáp ứng trong điều trị MIBC



50%

Bệnh nhân tái phát hoặc tiến triển sau 5 năm phẫu thuật cắt bỏ bang quang tận gốc[1,2]

5–8%

Lợi ích sống còn khiêm tốn từ NACT + RC, và ít hơn một nửa số bệnh nhân đủ điều kiện sử dụng cisplatin được điều trị bằng NACT[2,3]

ICI

Chỉ định ICI bổ trợ bị hạn chế vì lợi ích chỉ được chứng minh trên nhóm dân số có nguy cơ cao + PD-L1 dương tính[4–8]

Hạn chế về OS

Còn thiếu kết quả sống còn toàn bộ có ý nghĩa thống kê trong những nghiên cứu ICI bổ trợ trên nhóm bệnh MIBC

cis=cisplatin; ICI=immune-checkpoint inhibitor; MIBC=muscle-invasive bladder cancer; NATC=neoadjuvant chemotherapy; OS=overall survival; PD-L1=programmed death-ligand 1; RC=radical cystectomy.

1. Patel VG, et al. *CA Cancer J Clin*. 2020;70:404–423; 2. Roviello G, et al. *Front Oncol*. 2022;12:912699; 3. Liu W, et al. *Minerva Urol Nephrol*. 2021;73:144–153; 4. Bellmunt J, et al. *Lancet Oncol*. 2021;22:525–537; 5. Bajorin DF, et al. *New Eng J Med*. 2021;384:2102–2114; 6. Apolo AB, et al. Abstract LBA531. *J Clin Oncol*. 2024;42(4_suppl):LBA531. doi:10.1200/JCO.2024.42.4_suppl.LBA531; 7. Opdivo EMA label. June 2024; 8. Opdivo FDA label. 2022.

Các TNLS về điều trị bổ trợ với liệu pháp miễn dịch, mở ra lựa chọn điều trị mới cho bệnh nhân nguy cơ cao và không còn liệu pháp hỗ trợ

Cis-eligible MIBC (neoadjuvant/perioperative)	Cis-ineligible MIBC (neoadjuvant/perioperative)
NIAGARA[1] Phase III, durvalumab* + CTx → RC → durvalumab*	**VOLGA**[5] Phase III, durvalumab* + enfortumab vedotin ± tremelimumab‡ → RC → durvalumab* ± tremelimumab‡
KEYNOTE-866[2] Phase III, pembrolizumab† + CTx → RC → pembrolizumab†	**KEYNOTE-905/EV-303**[6] Phase III, pembrolizumab† ± EV → RC → pembrolizumab† ± EV
ENERGIZE[3] Phase III, nivolumab† ± IDO + CTx → RC → nivolumab† ± IDO	**PIVOT IO 009**[7] Phase III, nivolumab† ± NKTR-214 → RC → nivolumab† ± NKTR-214
KEYNOTE-B15[4] Phase III, pembrolizumab† + EV → RC → pembrolizumab† + EV	

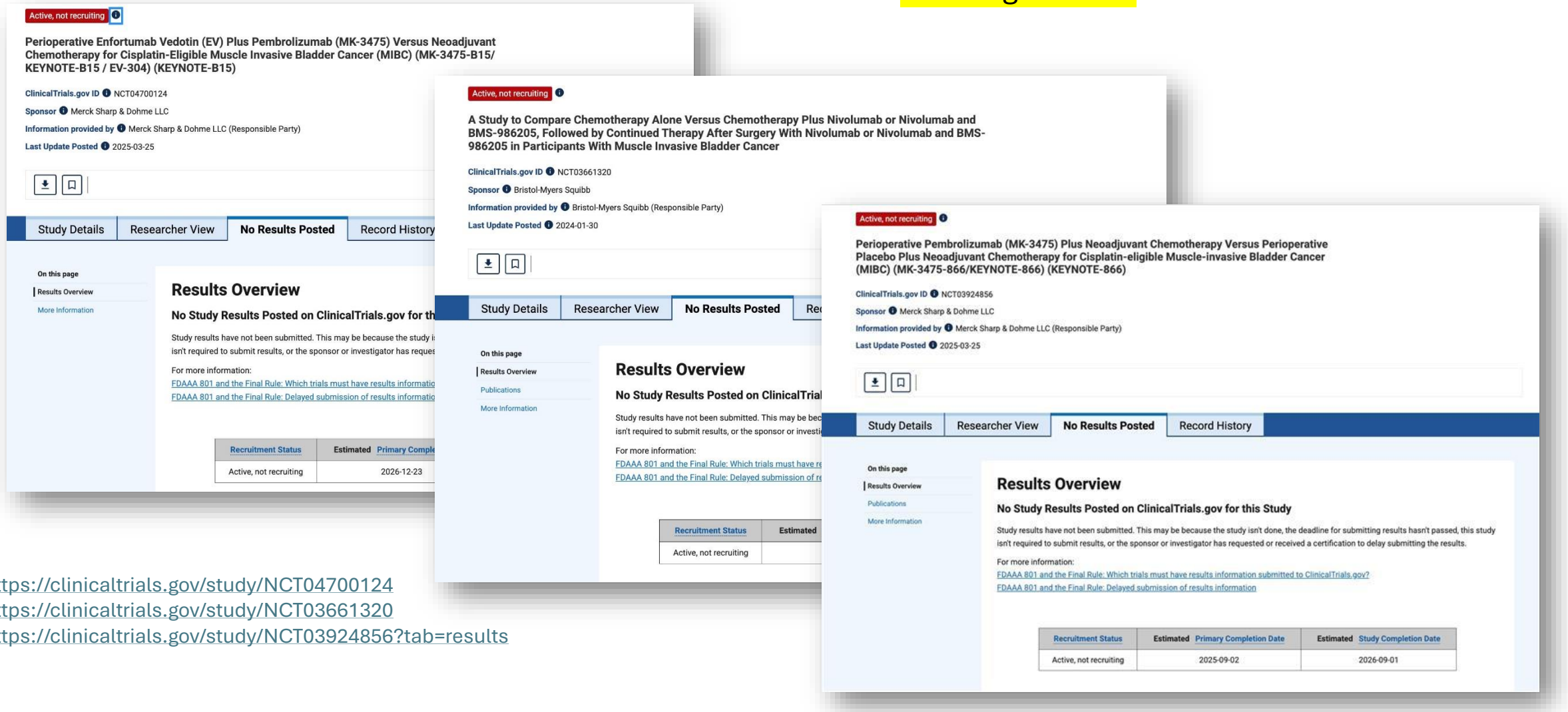
IO therapies are being assessed in both **cis-eligible** and **cis-ineligible** patients to address the **unmet need in the neoadjuvant setting**

*PD-L1 inhibitor; †PD-1 inhibitor; ‡CTLA-4 inhibitor.
CTLA-4=cytotoxic T-lymphocyte antigen 4; EV=enfortumab vedotin; IDO=indoleamine-pyrrole 2,3-dioxygenase; IO=immuno-oncology; MIBC=muscle-invasive bladder cancer; PD-1=programmed cell death protein 1; PD-L1=programmed death-ligand 1; RC=radical cystectomy; SoC=standard of care.
References are included in the slide notes.

Chỉ định của Durvalumab chưa được phê duyệt trong điều trị ung thư bàng quang tại Việt Nam. Vui lòng tham khảo thông tin kê toa cụ thể của thuốc được phê duyệt tại Việt Nam trước khi sử dụng

Các TNLS KEYNOTE 866, KEYNOTE-B15/EV-304, ENERGIZE còn chưa công bố kết quả

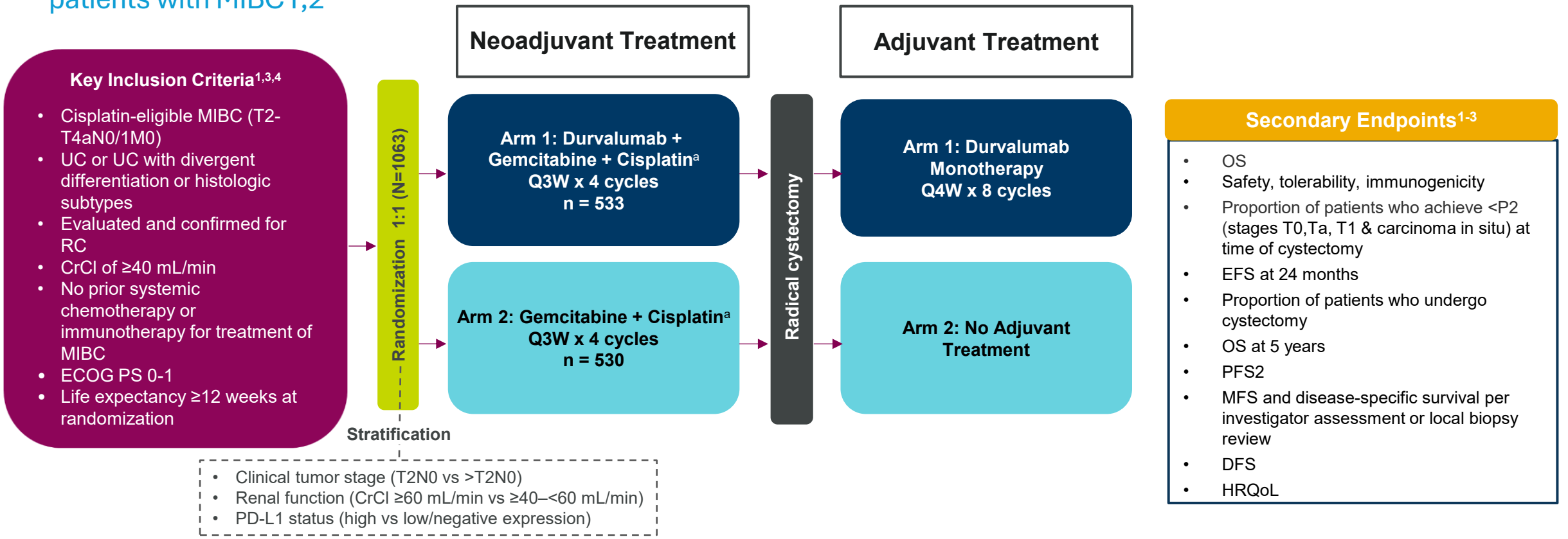
Awaiting results..



https://clinicaltrials.gov/study/NCT04700124
https://clinicaltrials.gov/study/NCT03661320
https://clinicaltrials.gov/study/NCT03924856?tab=results

NIAGARA: Thiết kế nghiên cứu[1-4]

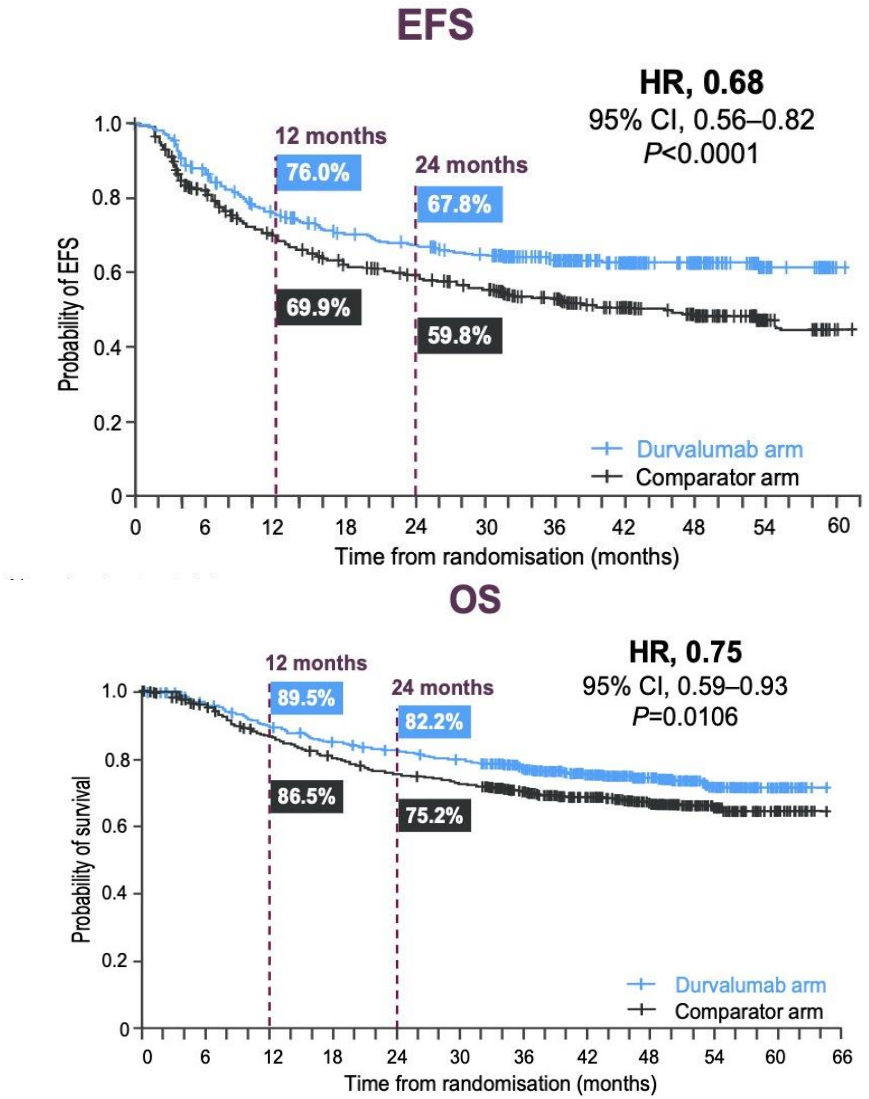
Phase III, randomised, open-label study of durvalumab plus chemotherapy vs. chemotherapy alone for cis-eligible patients with MIBC1,2

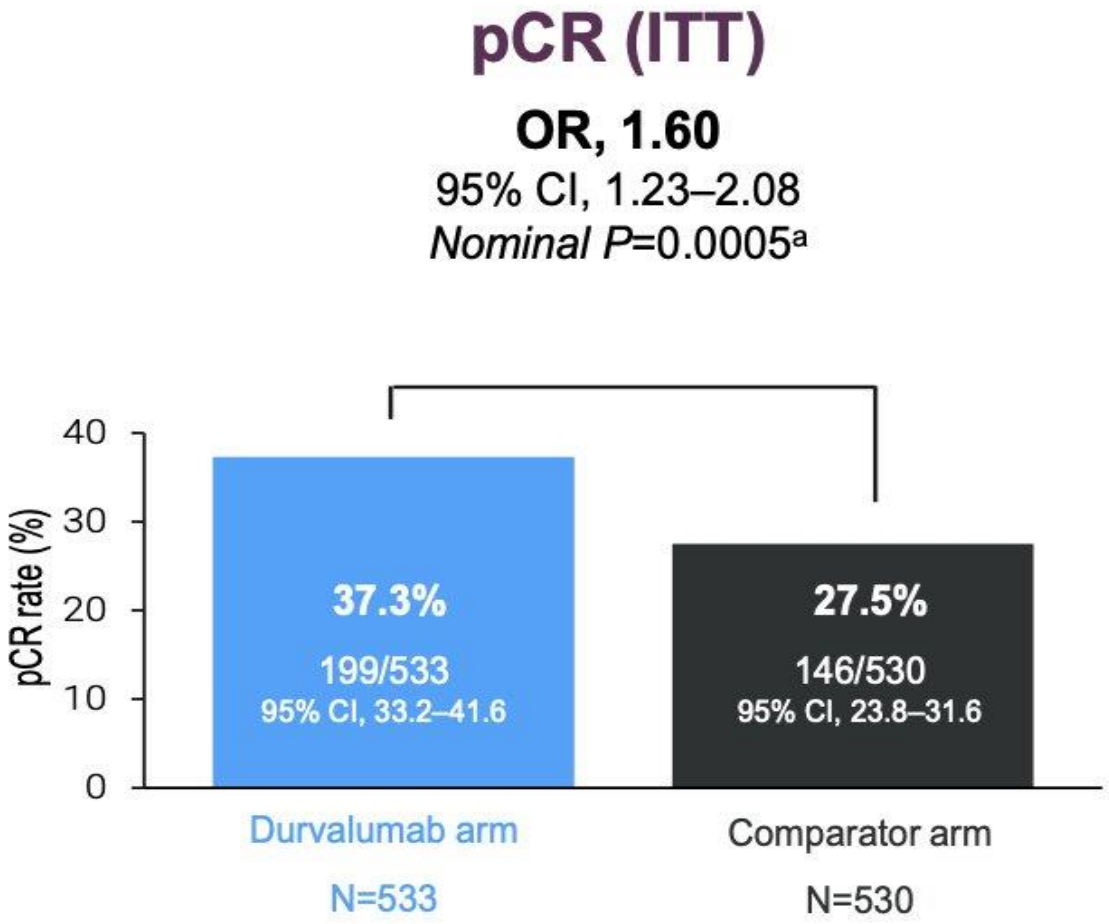


[a]Gemcitabine + Cisplatin dosing: CrCl ≥60 mL/min: cisplatin 70 mg/m^2 + gemcitabine 1000 mg/m^2 Day 1, then gemcitabine 1000 mg/m^2 Day 8, Q3W for 4 cycles; CrCl ≥40–<60 mL/min: Split dose cisplatin 35 mg/m^2 + gemcitabine 1000 mg/m^2 Day 1 and 8, Q3W for 4 cycles. [b]Evaluated by BICR or central pathology review (if a biopsy was required for a suspected new lesion). [c]Evaluated by blinded central pathology review.
BICR = Blinded Independent Central Review; CrCl = creatinine clearance; DFS = disease-free survival; ECOG PS = European Cooperative Oncology Group performance score; EFS = event-free survival; HRQoL = health-related quality of life; MFS = metastasis-free survival; MIBC = muscle-invasive bladder cancer; OS = overall survival; pCR = pathologic complete response; PD-L1 = programmed cell death ligand-1; PFS2 = second progression-free survival; Q3W = every 3 weeks; Q4W = every 4 weeks; RC = radical cystectomy; TNM = Tumor, Node, Metastasis; UC = urothelial carcinoma.
1. Study NCT03732677. ClinicalTrials.gov website. 2. Powles T et al. Poster presented at: ASCO-GU Virtual Meeting; Feb 11-13, 2021. TPS505. 3. Powles T, et al. Presented at: ESMO Congress; September 13-17, 2024; Barcelona, Spain. Abs#LBA5. 4. Powles T, et al. *N Engl J Med.* 2024.

Chỉ định của Durvalumab chưa được phê duyệt trong điều trị ung thư bàng quang tại Việt Nam. Vui lòng tham khảo thông tin kê toa cụ thể của thuốc được phê duyệt tại Việt Nam trước khi sử dụng

NIAGARA: Kết quả





N Engl J Med. 2024 Nov 14;391(1):1773-1786.

Chỉ định của Durvalumab chưa được phê duyệt trong điều trị ung thư bàng quang tại Việt Nam. Vui lòng tham khảo thông tin kê toa cụ thể của thuốc được phê duyệt tại Việt Nam trước khi sử dụng

NIAGARA: DFS

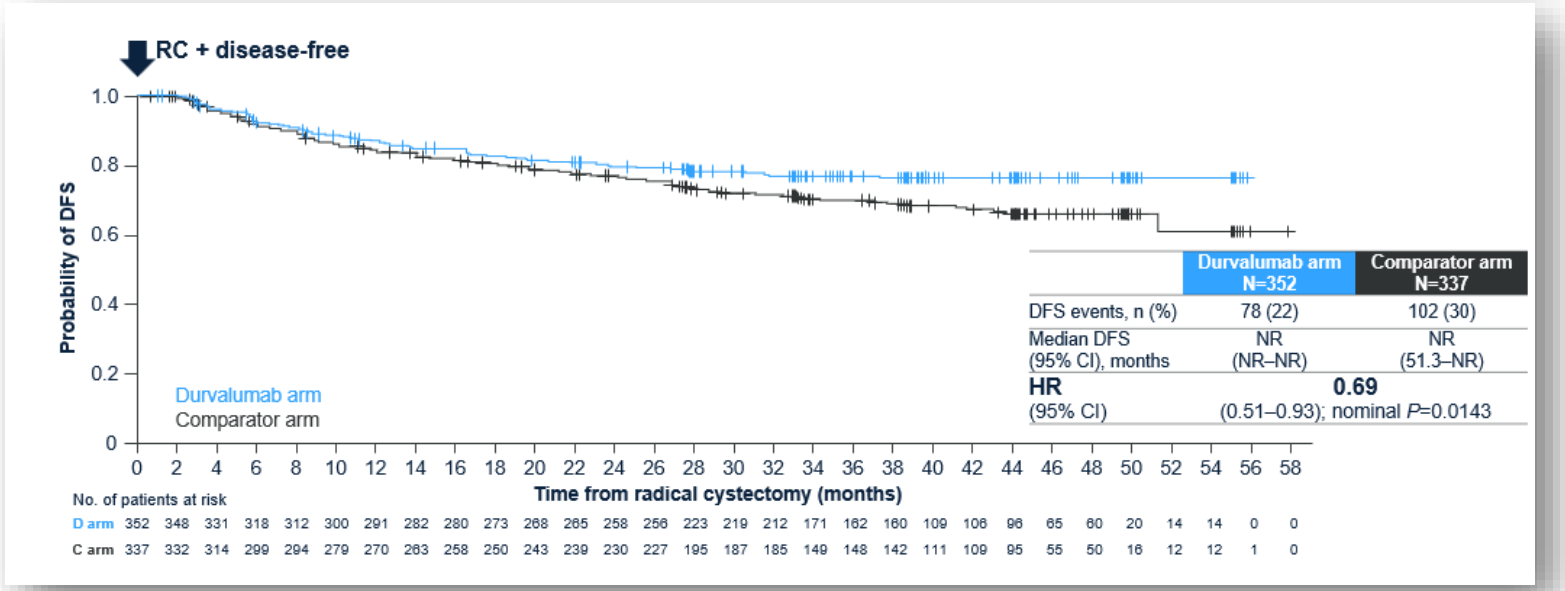
Phân tích DFS cung cấp góc nhìn sâu sắc hơn về kết quả điều trị ở nhóm bệnh nhân trải qua phẫu thuật cắt bỏ bàng quang tận gốc. Trong số đó, có 469 bệnh nhân (88%) ở nhóm điều trị bằng Durvalumab và 441 bệnh nhân (83%) ở nhóm đối chứng.

Kết quả:

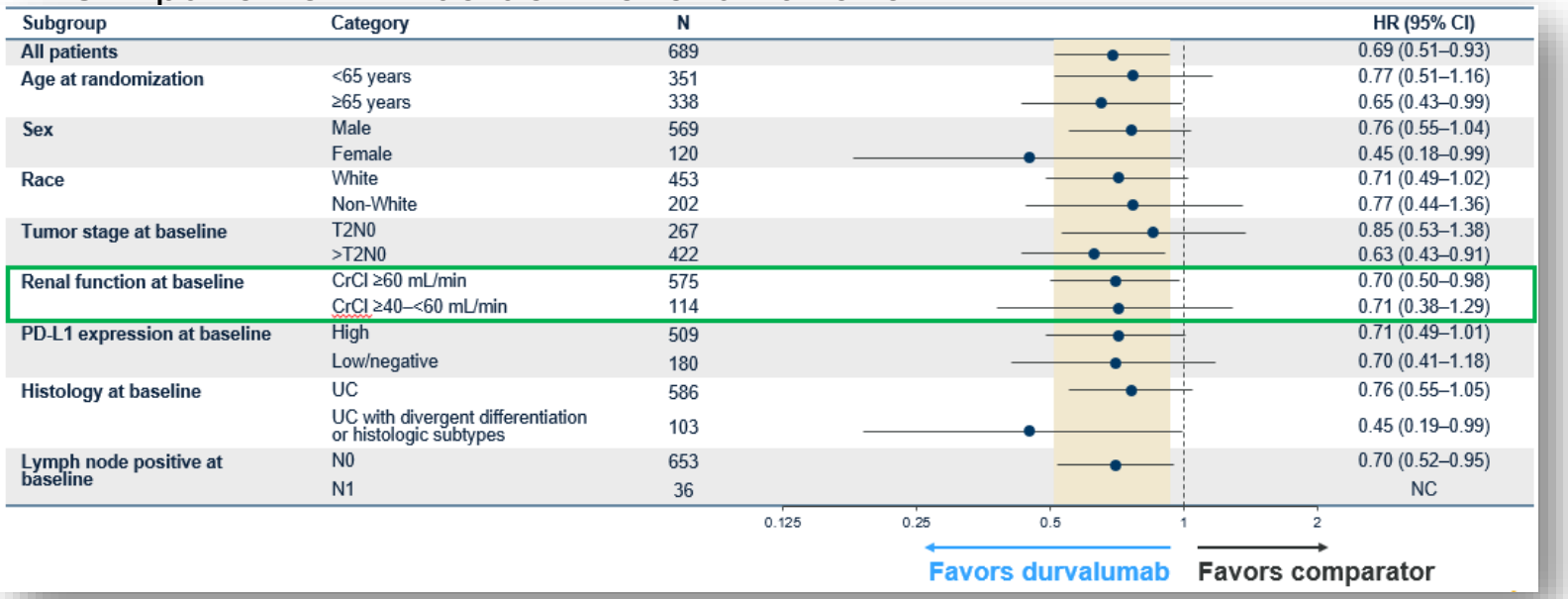
- Durvalumab quanh phẫu thuật giúp giảm 31% nguy cơ bệnh tái phát hoặc tử vong sau khi cắt bỏ bàng quang tận gốc
- Lợi ích DFS quan sát thấy ở nhóm bệnh nhân có chức năng thận ở mức biên (CrCl ≥40–<60 mL/min)

Chỉ định của Durvalumab chưa được phê duyệt trong điều trị ung thư bàng quang tại Việt Nam. Vui lòng tham khảo thông tin kê toa cụ thể của thuốc được phê duyệt tại Việt Nam trước khi sử dụng

DFS in patients who underwent RC



DFS in patients with borderline renal function



International Guidelines – Bladder Cancer

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2025
Bladder Cancer

NCCN Guidelines Index
Table of Contents
Discussion

PRINCIPLES OF SYSTEMIC THERAPY

Neoadjuvant Chemotherapy (preferred for bladder)	Perioperative/Sandwich Therapy
Preferred regimen • DDMVAC (dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin) with growth factor support for 3–6 cycles[1,2] **Useful in certain circumstances** • Gemcitabine and cisplatin for 4 cycles[3,4]	**Preferred regimen** • Gemcitabine + cisplatin + durvalumab prior to cystectomy, then durvalumab after cystectomy[5] (for bladder cancer only) (category 1)

Adjuvant Therapy	
No previous platinum-based neoadjuvant therapy (pT3, pT4a, pN+)	**Previous platinum-based neoadjuvant therapy (ypT2–ypT4a or ypN+)**
Preferred regimen • DDMVAC with growth factor support for 3–6 cycles[1,2] **Other recommended regimens** • Gemcitabine and cisplatin for 4 cycles[3,4] • Nivolumab[6] • Pembrolizumab[7]	**Other recommended regimen** • Nivolumab[6] • Pembrolizumab[7]

EMA Recommends Extending Indications for Durvalumab

New indication concerns a neoadjuvant and adjuvant treatment of patients with muscle invasive bladder cancer

Date: 17 Jul 2025

Topics: Immunotherapy

Tumor Sites: Urothelial Cancer

European Association of Urology

FDA approves durvalumab for muscle invasive bladder cancer

On March 28, 2025, the Food and Drug Administration approved durvalumab (Imfinzi, AstraZeneca) with gemcitabine and cisplatin as neoadjuvant treatment, followed by single agent durvalumab as adjuvant treatment following radical cystectomy, for adults with muscle invasive bladder cancer (MIBC).

Full prescribing information for Imfinzi will be posted on Drugs@FDA.

7.1.5 ***Summary of evidence and guidelines for neoadjuvant therapy***

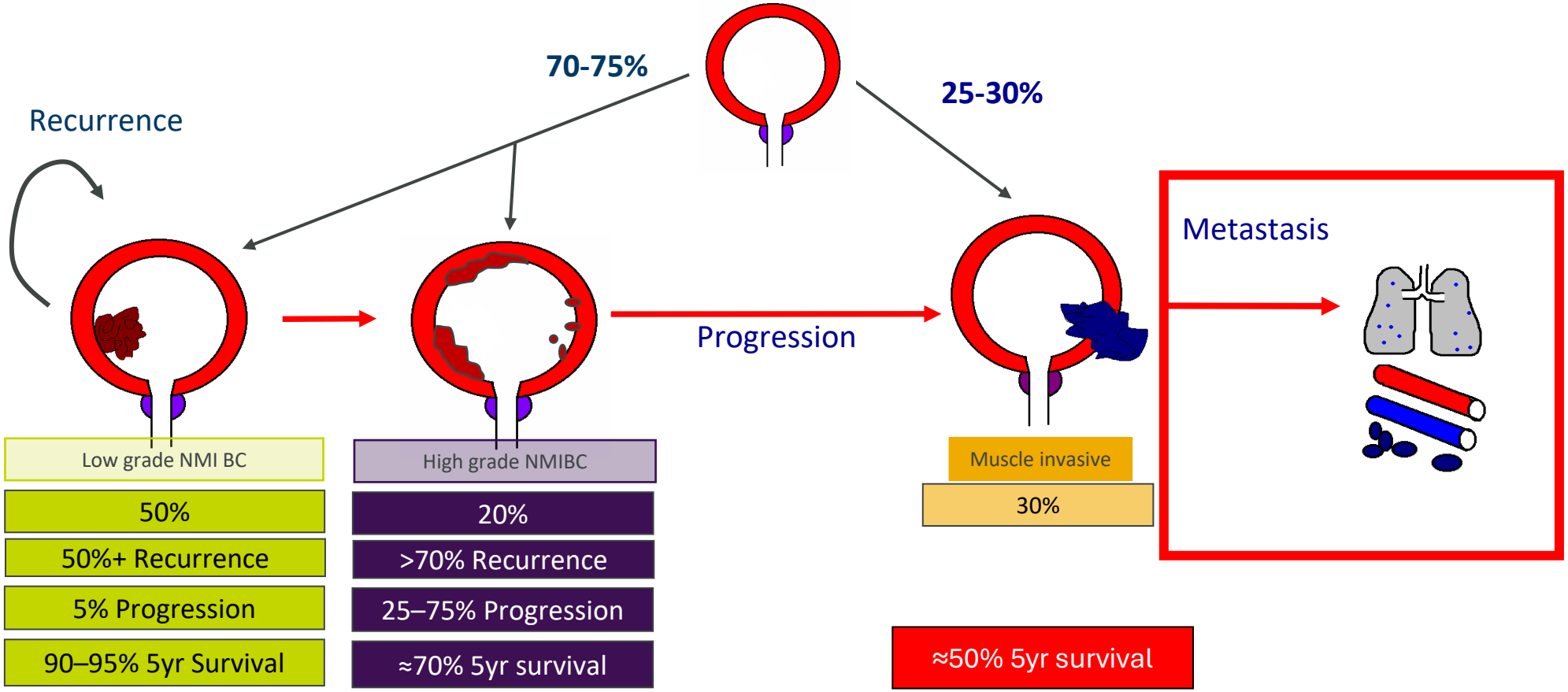
Summary of evidence	LE
Neoadjuvant cisplatin-containing combination chemotherapy improves OS (8% at five years).	1a
Neoadjuvant treatment may have a major impact on OS in patients who achieve ypT0 or ≤ ypT2.	2a
Peri-operative durvalumab plus neoadjuvant gemcitabine and cisplatin improves EFS and OS compared to neoadjuvant gemcitabine and cisplatin alone.	1b
Neoadjuvant immunotherapy with checkpoint inhibitors alone has demonstrated promising results.	-
There are still no reliable tools available to select patients who have a higher probability of benefitting from NAC. In the future, genomic markers in a personalised medicine setting might facilitate the selection of patients for NAC and differentiate responders from non-responders.	-

Chỉ định của Durvalumab chưa được phê duyệt trong điều trị ung thư bàng quang tại Việt Nam. Vui lòng tham khảo thông tin kê toa cụ thể của thuốc được phê duyệt tại Việt Nam trước khi sử dụng

Quản lý và điều trị giai đoạn di căn

Khoảng 5% các trường hợp mắc UTBQ được phát hiện ở giai đoạn tiến xa/ di căn

Tế bào ung thư thường di căn theo đường máu hoặc đường bạch huyết, dẫn đến các triệu chứng nghiêm trọng tùy thuộc vào vị trí di căn.



Marko Babjuk. European Urology 76 (2019) 639 – 657

Các liệu pháp điều trị toàn thân đóng vai trò chính trong điều trị mUC[1–6]

Bao gồm liệu pháp hóa trị và liệu pháp miễn dịch.

Lựa chọn điều trị được phân loại dựa trên tình trạng đủ điều kiện sử dụng platinum và số bước điều trị trước đó.

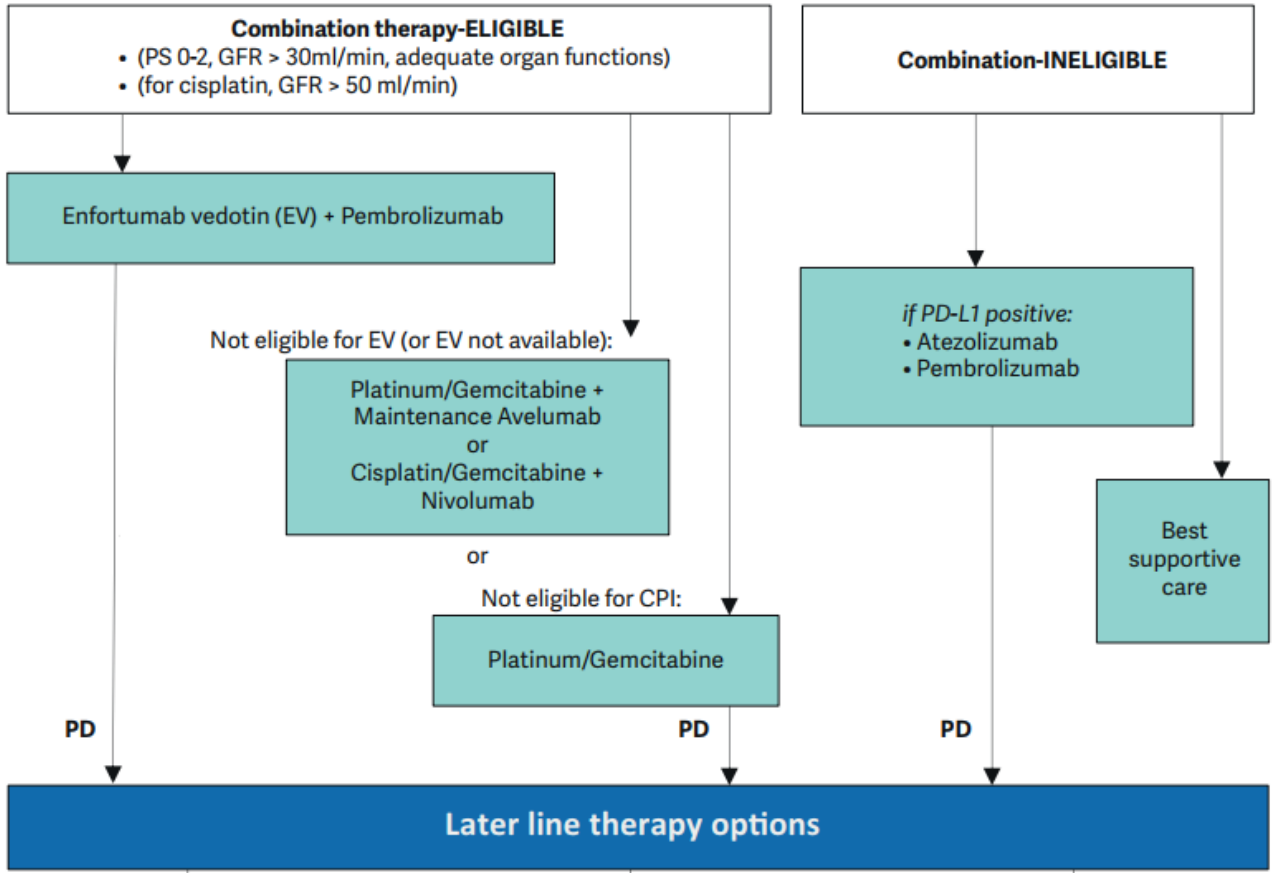
Việc lựa chọn điều trị bước 1 không phụ thuộc vào điều kiện sử dụng hóa trị có chưa platinum của bệnh nhân.

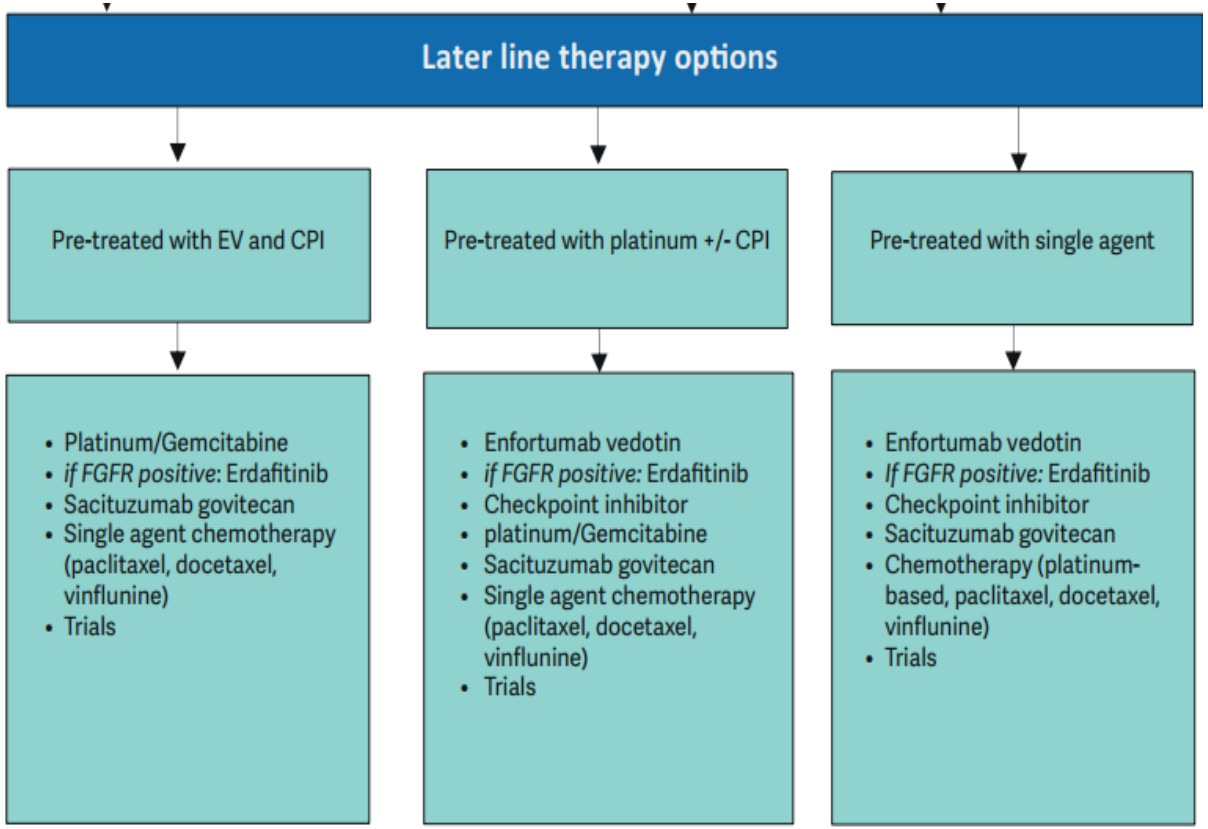
1L=first line; IO=immuno-oncology; UC=urothelial cancer.

1. NCCN Clinical Practice Guidelines in Oncology. Bladder Cancer. v3.2022; 2. Bellmunt J, et al. *Ann Oncol*. 2014;25(suppl 3): iii40–iii48; 3. Powles T, et al. *Ann Oncol*. 2022;33(3):244–258; 4. Bellmunt J, et al. *Cancer Treat Rev*. 2017;54:58–67; 5. FDA. FDA approves new, targeted treatment for bladder cancer. Available from: https://www.fda.gov/news-events/press-announcements/fda-approves-new-targeted-treatment-bladder-cancer. Accessed January 2023; 6. EMA. Tecentriq. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/tecentriq. Accessed January 2023.

Lưu đồ điều trị ung thư bàng quang di căn

Điều trị bước 1



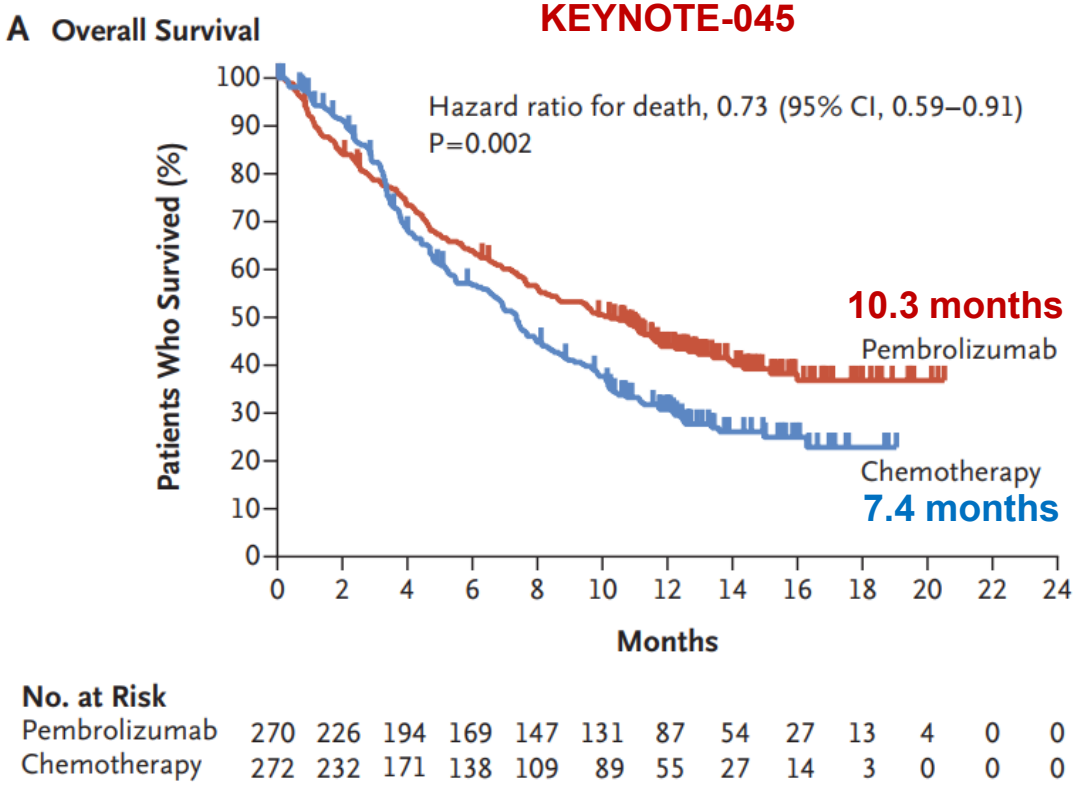


EAU guidelines on Muscle-invasive and Metastatic Bladder Cancer 2024

2nd line therapy – Tiến triển sau hóa trị

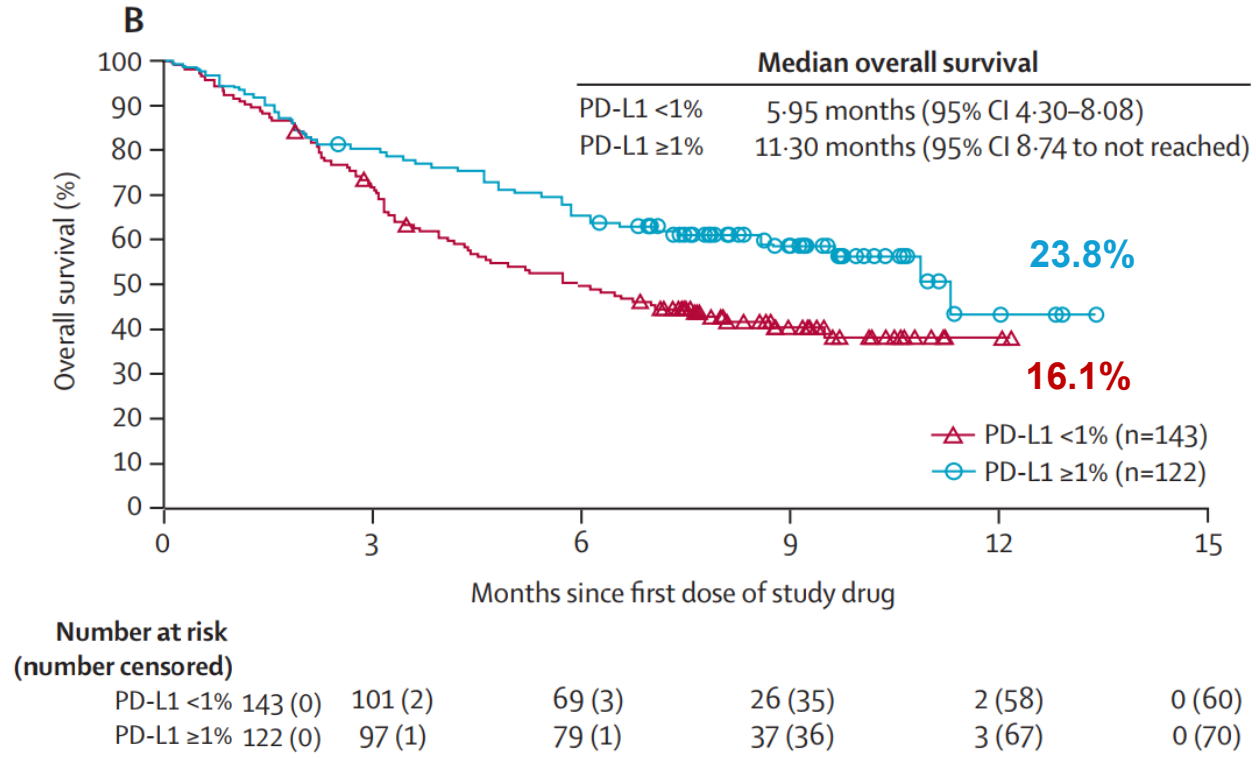
PD-1

KEYNOTE-045



Pembrolizumab: giảm nguy cơ tử vong 27%

CheckMate-275

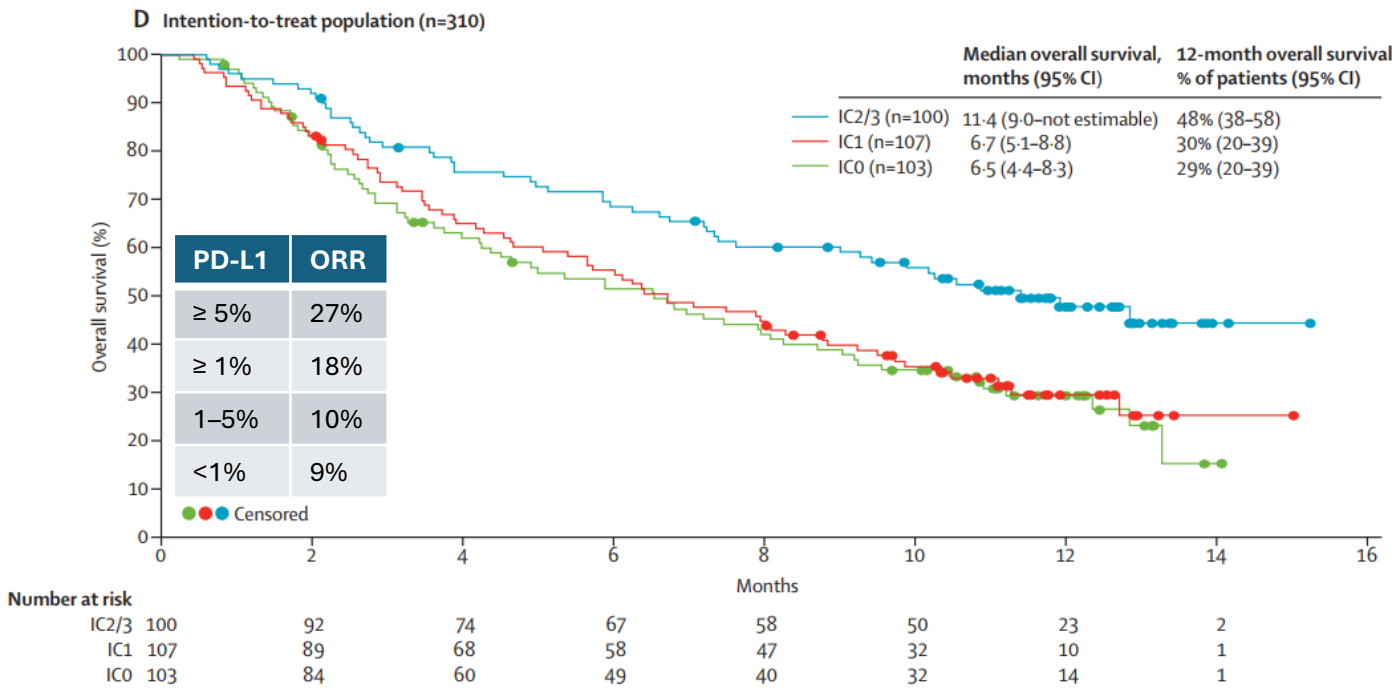


Nivolumab: tỉ lệ đáp ứng 19.6%

1. Bellmunt J et al. N Engl J Med. 2017 March 16;376(11):1015-26 2. Sharma P. et al. The Lancet Oncology. 2017;18(3):312-322

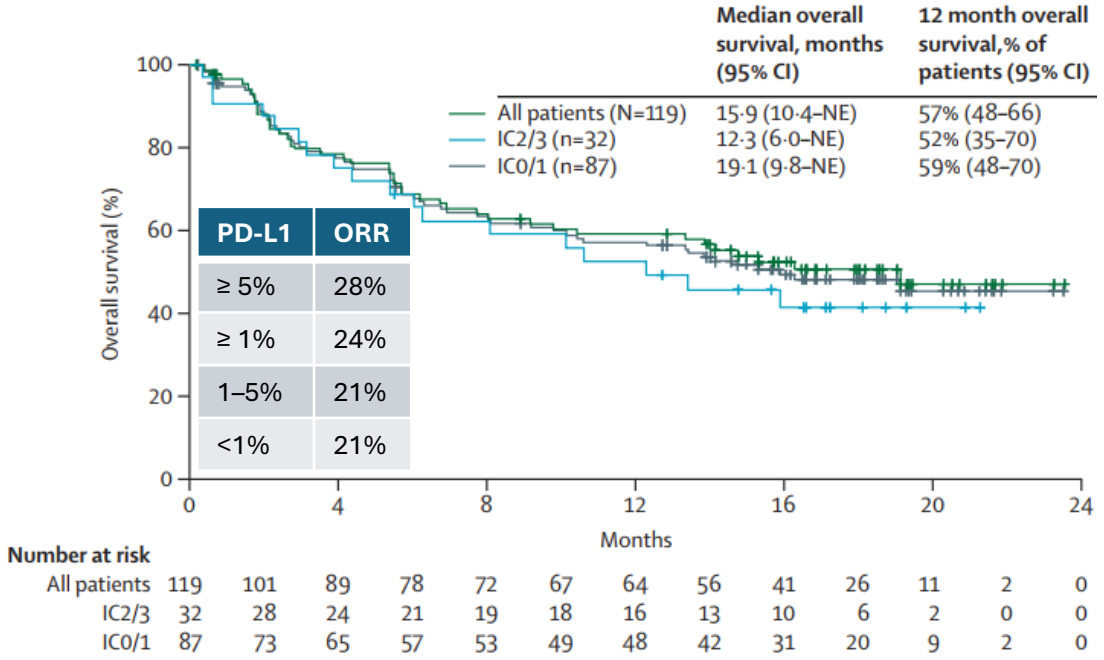
2nd line therapy – Tiến triển sau hóa trị

PD-L1 **IMvigor210** **Atezolizumab**



Tỉ lệ đáp ứng 15%

1st line – ineligible cisplatin



Tỉ lệ đáp ứng 23%

1. Rosenberg JE et al. The Lancet. 2016;387(10031):1909-1920 2. Balar AV. et al. The Lancet. 2017;389(10064):67-76.

Kết luận

- Primary treatment is currently radical cystectomy plus neoadjuvant cisplatin-based chemotherapy
- A large unmet need exists as utilization neoadjuvant chemotherapy is low
- IO therapies are currently being assessed in the neoadjuvant setting to address this unmet need
- Perioperative (“Sandwich”) Therapy: Adding Durvalumab to Gemcitabine and Cisplatin (GemCis) in the perioperative setting has been shown to improvepCR, EFS and OS (category 1 recommendation/NCCN guidelines)