

Bladder preservation for everyone? ¿Preservación de la vejiga para todos?

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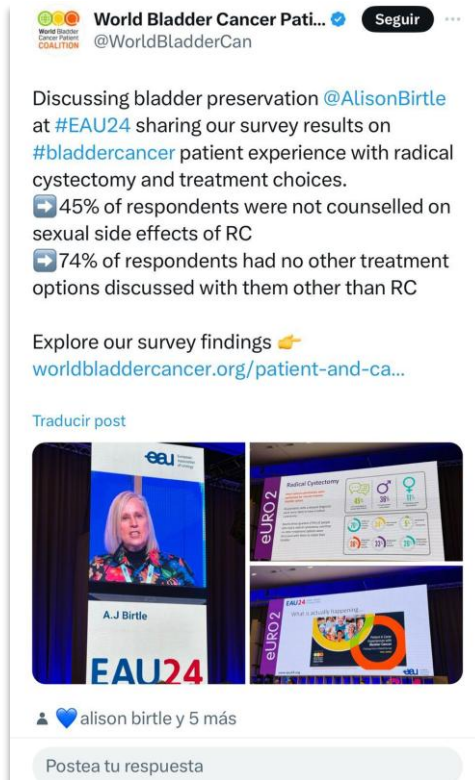
Hospital Universitario Vithas La Milagrosa

Profesor Titular de la Universidad Europea de Madrid

Profesor de la Universidad Alfonso X El Sabio

Are we doing Bladder Preservation for Everyone??????

- 74% of patients were not offered a treatment alternative other than radical cystectomy.
- 45% were not informed about the sexual side effects of cystectomy.

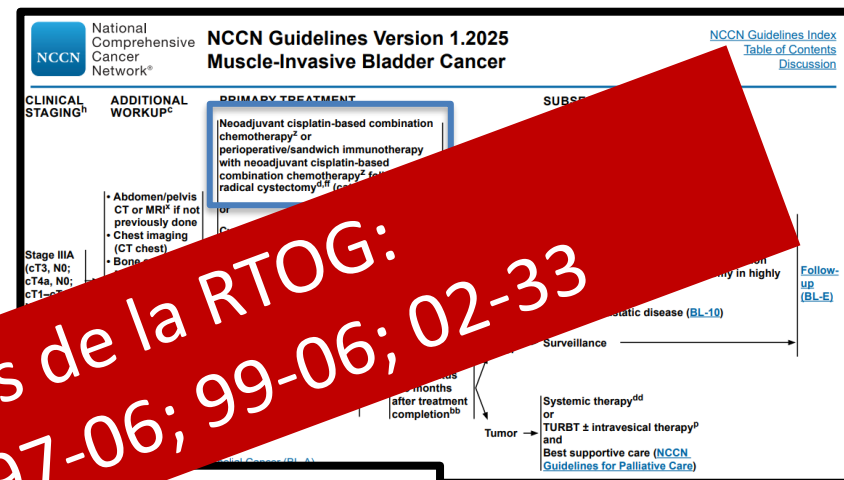
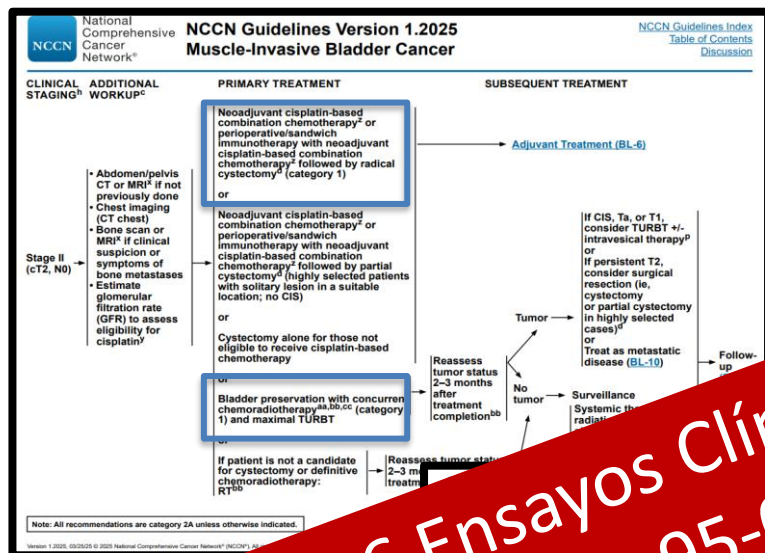


Alison Birtle. EAU . 2024.

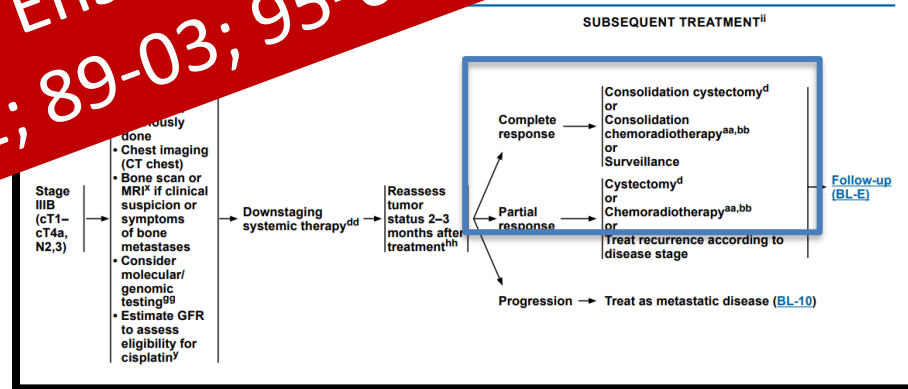


<https://worldbladdercancer.org/patient-and-carer-experiences-with-bladder-cancer/>

Clinical Guidelines for TMT and Cystectomy



6 Ensayos Clínicos de la RTOG:
88-02; 89-03; 95-06; 97-06; 99-06; 02-33



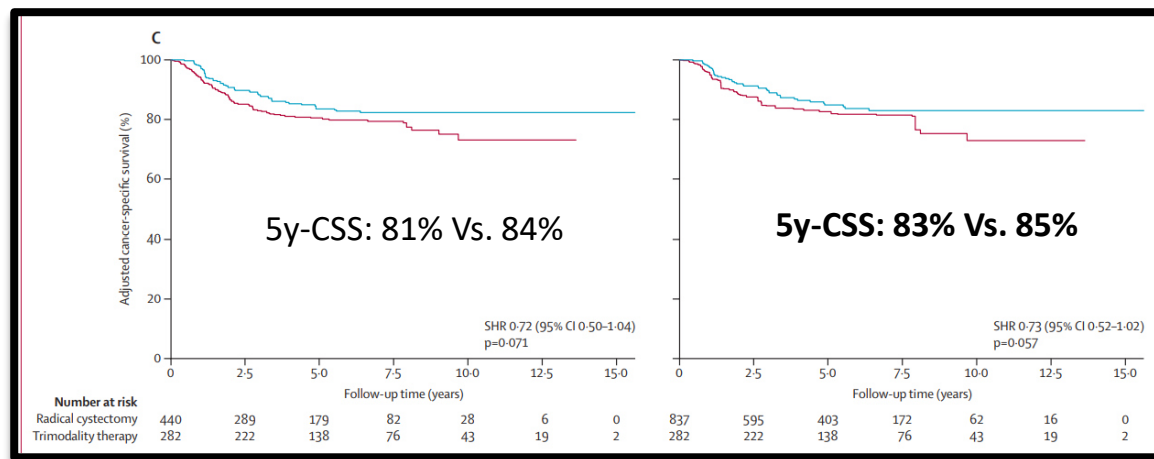
Radical cystectomy versus trimodality therapy for muscle invasive bladder cancer: a multi-institutional propensity score matched and weighted analysis

N=1119

	Before matching			After 3:1 matching		
	Radical cystectomy (n=440)	Trimodality therapy (n=282)*	p value	Radical cystectomy (n=837)	Trimodality therapy (n=282)*	p value
Age, years	71.2 (63.7-77.2)	71.6 (64.0-78.9)	0.22	71.4 (66.0-77.1)	71.6 (64.0-78.9)	0.76
Sex			0.31			0.65
Female	92 (21%)	68 (24%)		213 (25%)	68 (24%)	
Male	348 (79%)	214 (76%)		624 (75%)	214 (76%)	
Carcinoma in situ			0.096			0.51
No	324 (74%)	223 (79%)		646 (77%)	223 (79%)	
Yes	116 (26%)	59 (21%)		191 (23%)	59 (21%)	
Clinical T-stage			0.0024			0.91
T2	362 (82%)	255 (90%)		755 (90%)	255 (90%)	
T3-4	78 (18%)	27 (10%)		82 (10%)	27 (10%)	
BMI			0.014			0.40
<30 kg/m ²	340 (77%)	192 (69%)		600 (72%)	192 (69%)	
≥30 kg/m ²	100 (23%)	86 (31%)		237 (28%)	86 (31%)	
Missing	0	4		0	4	
Hydronephrosis			<0.0001			0.35
No	339 (77%)	255 (90%)		740 (88%)	255 (90%)	
Yes	101 (23%)	27 (10%)		97 (12%)	27 (10%)	
Neoadjuvant or adjuvant chemotherapy			<0.0001			0.42
No	259 (60%)	123 (44%)		340 (41%)	123 (44%)	
Yes	176 (40%)	159 (56%)		492 (59%)	159 (56%)	
Missing	5	0		5	0	
Smoking history			0.57			0.91
Never smoked	115 (26%)	69 (24%)		201 (24%)	69 (24%)	
Current or former smoker	321 (74%)	213 (76%)		632 (76%)	213 (76%)	
Missing	4	0		4	0	
ECOG status			0.59			0.57
0	189 (75%)	218 (77%)		392 (76%)	218 (77%)	
1 or 2	62 (25%)	64 (23%)		127 (24%)	64 (23%)	
Missing	189	0		318	0	

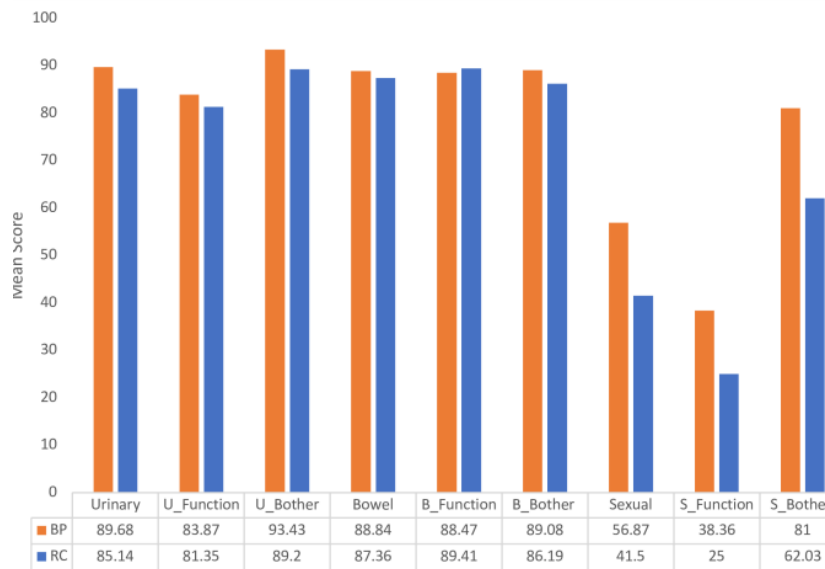
Data are median (IQR) or n (%). ECOG=Eastern Cooperative Oncology Group. *All patients in the trimodality therapy cohort received concurrent radiotherapy. †Of the 282 trimodality therapy patients, 3:1 matching, nine could only be matched to two radical cystectomy patients, therefore resulting in a total of 837 matched radical cystectomy patients, instead of 846.

Table: Baseline characteristics before and after matching



➤ This multi-institutional study provides the best evidence to date showing similar oncological outcomes between radical cystectomy and trimodality therapy for select patients with muscle-invasive bladder cancer.

Prospective Comparative Study of Quality of Life in Bladder Cancer Patients Undergoing Cystectomy or Bladder Preservation



- Overall, bladder cancer survivors have good quality-of-life outcomes.
- There are no differences in urinary and bowel domains with radiotherapy and surgery
- Sexual bother scores are better with radiotherapy compared to radical cystectomy
- Quality-of-life should be central to the decision-making process

Quality of life after radical treatment for muscle invasive bladder cancer: A systematic review and meta-analysis

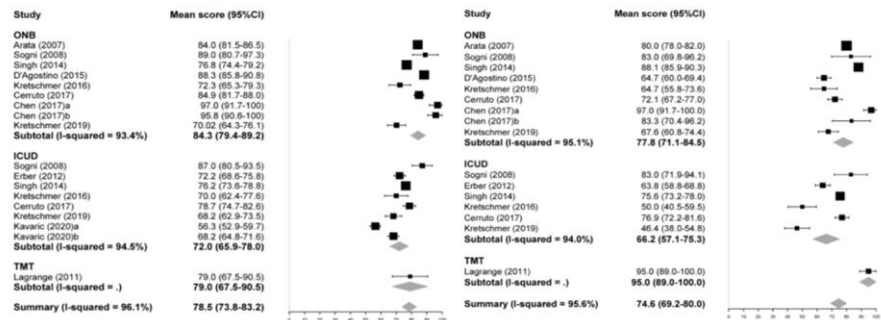


Fig. 3. EORTC QLQ C30 results for Orthotopic nebladder (ONB), Ileal Conduit Urinary Diversion (ICUD) or Trimeral therapy(TMT) in terms of Emotional Functioning (Panel A) or Role Functioning (Panel B).

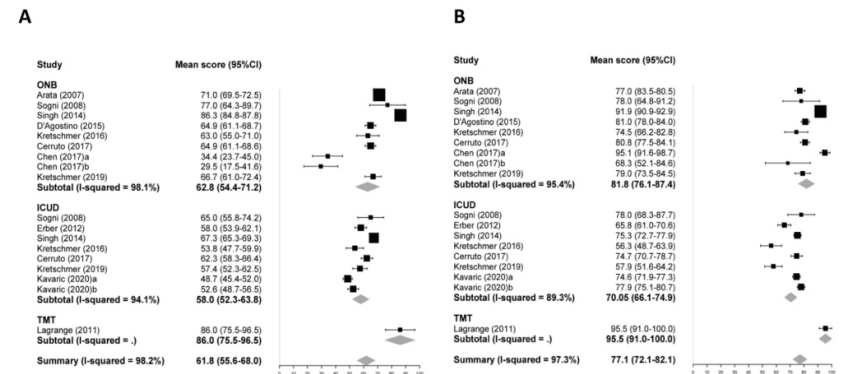


Fig. 2. EORTC QLQ C30 results for Orthotopic nebladder(ONB), Ileal Conduit Urinary Diversion (ICUD) or Trimeral Therapy(TMT) in terms of Global Health Score (Panel A) or Physical functioning (Panel B).

No direct comparison with TMT is available, but data suggest advantage of this approach when compared to both reconstructive scenarios.

Radical cystectomy

Factors that may favor RC

Poor bladder function
IBD or previous RT
Diffuse CIS
Multifocal tumor

Favorable prognostic factors for RC and TMT

High PS
Unifocal cT2 stage
No hydronephrosis
No multifocal CIS

Trimodal therapy

Unfavorable prognostic factors for TMT (and *RC)

Multifocal tumor
Diffuse CIS
*Poor PS
*Poor renal function
(cisplatin ineligible)
*Hydronephrosis
*T3–4

Factors that may favor TMT

High surgical risk
Desire to preserve bladder

(Caveats: comparative data limited/absent; tailor treatment toward each patient)

TMT: Radiotherapy

Choudhury A. Lancet Oncol 2021



Hypofractionated radiotherapy in locally advanced bladder cancer: an individual patient data meta-analysis of the BC2001 and BCON trials



Ananya Choudhury*, Nuria Porta*, Emma Hall, Yee Pei Song, Ruth Owen, Ronald MacKay, Catharine M L West, Rebecca Lewis, Syed A Hussain, Nicholas D James†, Robert Huddart†, Peter Hoskin†, on behalf of the BC2001 and BCON investigators

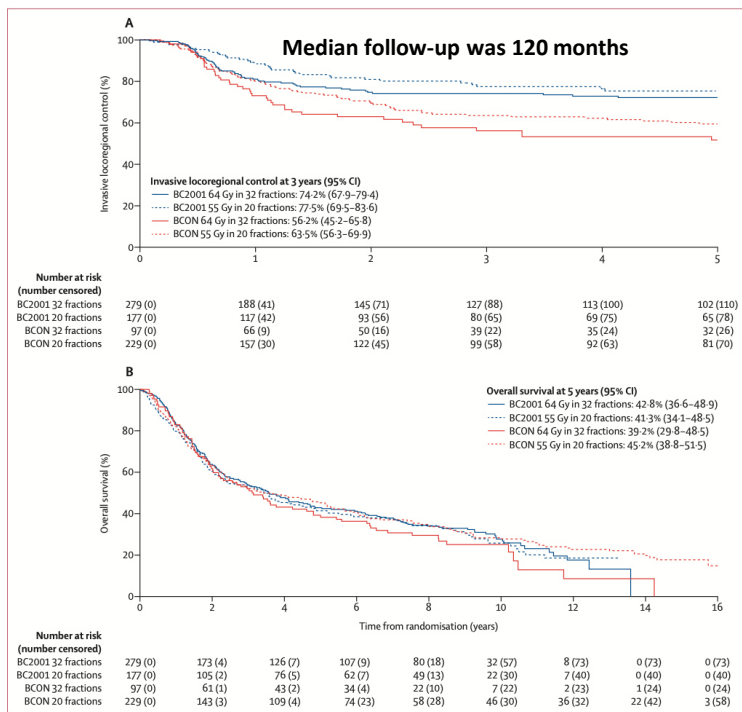


Figure 2: Kaplan-Meier estimates of observed invasive locoregional control (A) and observed overall survival (B) by trial and fractionation group

	64 Gy in 32 fractions (n=278)	55 Gy in 20 fractions (n=295)
2-year late toxicity		
Rectum	7 (3%)	17 (6%)
Bladder	66 (24%)	74 (25%)
Rectum or bladder	69 (25%)*	82 (28%)†
5-year late toxicity		
Rectum	8 (3%)	21 (7%)
Bladder	86 (31%)	88 (30%)
Rectum or bladder	89 (32%)‡	97 (33%)§

LENT-SOMA urinary and rectal dysfunction subscales were recorded up to 5 years after radiotherapy in the BC2001 and BCON trials. LENT-SOMA=Late Effects Normal Tissue Task Force-Subjective, Objective, Management, Analytic. *Four patients with both. †Nine patients with both. ‡Five patients with both. §12 patients with both.

Table 2: LENT-SOMA grade 3–4 bladder or rectum toxicity after the end of treatment by fractionation groups

55 Gy in 20 fractions should be adopted as a standard of care for bladder preservation in patients with locally advanced bladder cancer

TMT: Concomitant Chemotherapy



National
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NCCN Guidelines Version 1.2024 Bladder Cancer

[NCCN Guidelines Index](#)
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PRINCIPLES OF SYSTEMIC THERAPY

Radiosensitizing Chemotherapy Regimensⁱ
<u>Preferred regimens</u> • Cisplatin^h alone^{35,36} • Low-dose gemcitabine³⁷⁻³⁹ • 5-FU and mitomycin⁴⁰
<u>Other recommended regimen</u> • Cisplatin and 5-FU^{37,41} • Cisplatin and paclitaxel^{37,42}
<u>Useful in certain circumstances (not generally used for curative-intent chemoradiotherapy for organ preservation)</u> • Taxane (docetaxel or paclitaxel) (category 2B) • 5-FU (category 2B) • Capecitabine (category 3)

*RTOG 02-33; RTOG 95-06; RTOG 99-06; RTOG 09-26; BC2011; RTOG 0712; BCON

Clinical Studies of TMT in MIBC

Estudio	Esquema de tratamiento	Medida de resultado primaria	Estado
ARTIA-Vesica NCT05295992	Radioterapia adaptativa diaria	Toxicidad	Reclutamiento
HIRACOM NCT5453682	CT (cisplatino) + hypo-IMRT (64 Gy en 32 fx)	PFS a 2 años	Reclutamiento
HyBla_RCT NCT05397262	CT (cisplatino) + hypo-IMRT (56-64 Gy en 20 fx vol. riesgo alto) y 40-44 Gy vol. riesgo bajo Hipertermia 1-2/semanas en 10 sesiones + RT (50,4 Gy en 28 fx + boost 5,4 Gy (R0) o 9 Gy (R1/2) + CT (cisplatino + 5 FU)	OS	Reclutamiento
ARTIA-Bladder NCT05700227	Radioterapia diaria adaptativa + CT	Toxicidad	Reclutamiento
RAIDER NCT02447549	WBRT; SART; DART	Toxicidad	Activo, no reclutando
NCT01104350	RT + Gemcitabina RT dosis: 23,4 Gy/1,8 Gy × 13 fx (total 68,4 Gy) 27 Gy/1,8 Gy × 15 fx (total 72 Gy) 30,6 Gy/1,8 Gy × 17 fx (total 75,6 Gy)	Dosis máxima tolerada	Activo, no reclutando
GETUGV04 NCT01495676	RT (45 Gy pelvis y 63 Gy vejiga a 1,8 Gy/fx) + Cisplatino Cisplatino + gemcitabina	PFS	Activo, no reclutando

These trials include adaptive radiation techniques, dose escalation, hypofractionation and different sensitizing agents



Ongoing studies of TMT with immune checkpoint inhibitors

Estudio	Esquema de tratamiento	1. ^{er} End-point	Estado
Quimiorradioterapia + inmunoterapia			
ANZUP 1502 NCT02662062	RT (64 Gy en 32 fx) + cisplatino (35 mg/m ²) + pembrolizumab (200 mg)	Seguridad	Activo, no reclutando
MK3475 NCT02621151	Pembrolizumab pembrolizumab (200 mg cada 3 semanas × 3 ciclos)	BIDFS a 2 años	Activo, no reclutando
KEYNOTE 992 NCT04241185	Brazo A: RT (64 Gy o 55 Gy) + CT (cisplatino 35 mg/m ² o 5FU 500 mg/m ² + MMC 12 mg/m ² Brazo B: gemcitabina 27 mg/m ²) ± pembrolizumab (400 mg cada 6 semanas)	BIDFS	Reclutamiento
SWOG/NRG 1806 NCT03775265	Atezolizumab 6 semanas por 6 meses)		Reclutamiento
CRIMI NCT03844256	Nivolumab+Ipi ipilimumab + nivolumab		Reclutamiento
ML-39576 NCT03620435	RT (50 Gy) + atezolizumab	Seguridad	Completado
Bladderspar	Atezolizumab 1200 mg / 3 semanas por 12 meses		Reclutamiento
INSPIRE NCT04216290	RT + CT + durvalumab (3 ciclos)	Respuesta clínica completa	Reclutamiento
SunRIse-2 NCT04658862	Durva+Cetrelimab+TAR partir de la semana 24/12 semanas durante 3 años Brazo B: CTRT (cisplatino o gemcitabina) + RT (64 Gy o 55 Gy solo vejiga)		Reclutamiento
RADIOTERAPIA + IMMUNOTERAPIA NUTRA NCT03421652	Nivolumab nivolumab (240 mg cada 2 semanas)	es	Activo, no reclutando
IMMUNOPRESERVE NCT03702179	Durva+Tremilumumab 4 semanas)		Activo, no reclutando
ATEZOBLADDER PRESERVE NCT04186013	Atezolizumab F (C	ológica	Activo, no reclutando

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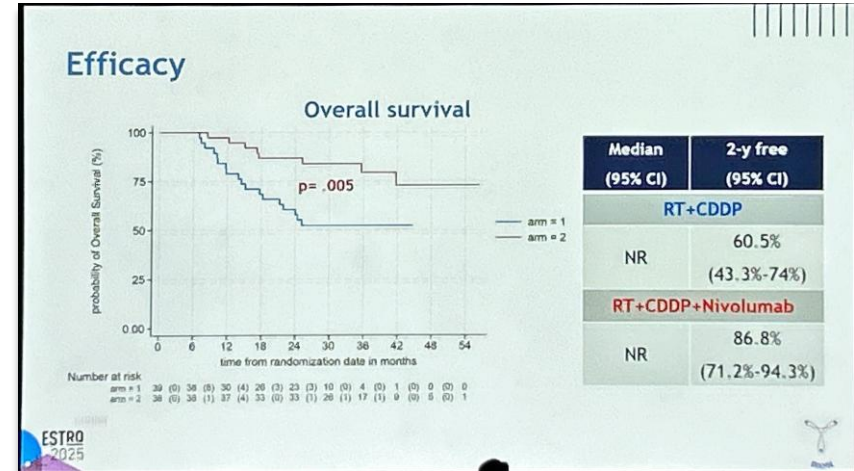
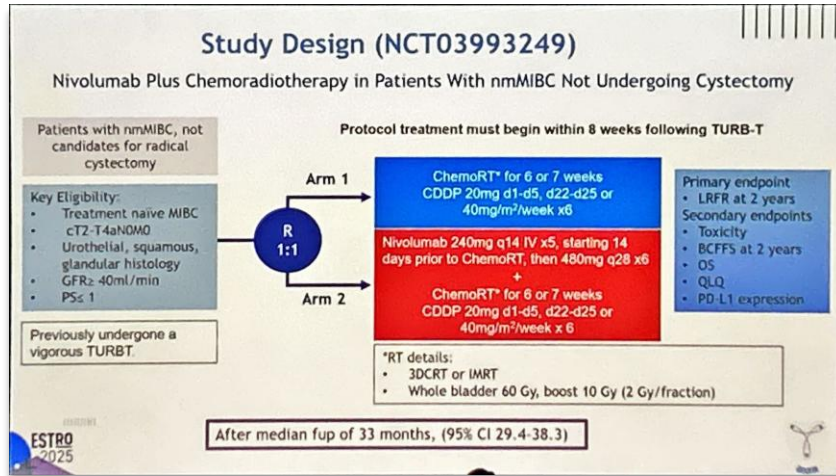
www.elsevier.es/actasuro

ARTÍCULO DE REVISIÓN

Terapia trimodal para el cáncer de vejiga: ¿es ahora el estándar para la enfermedad músculo-invasiva?

M. López Valcárcel^{a,*}, M. Barrado Los Arcos^b, M. Ferri Molina^c,
I. Cienfuegos Belmonte^d, V. Duque Santana^e, P. Gajate Borau^f,
J. Fernández Ibiza^g, M. Álvarez Maestro^h, P. Sargosⁱ, F. López Campos^j y F. Couhago^k

Nivolumab + TMT: RCT Phase II (NCT03993249)

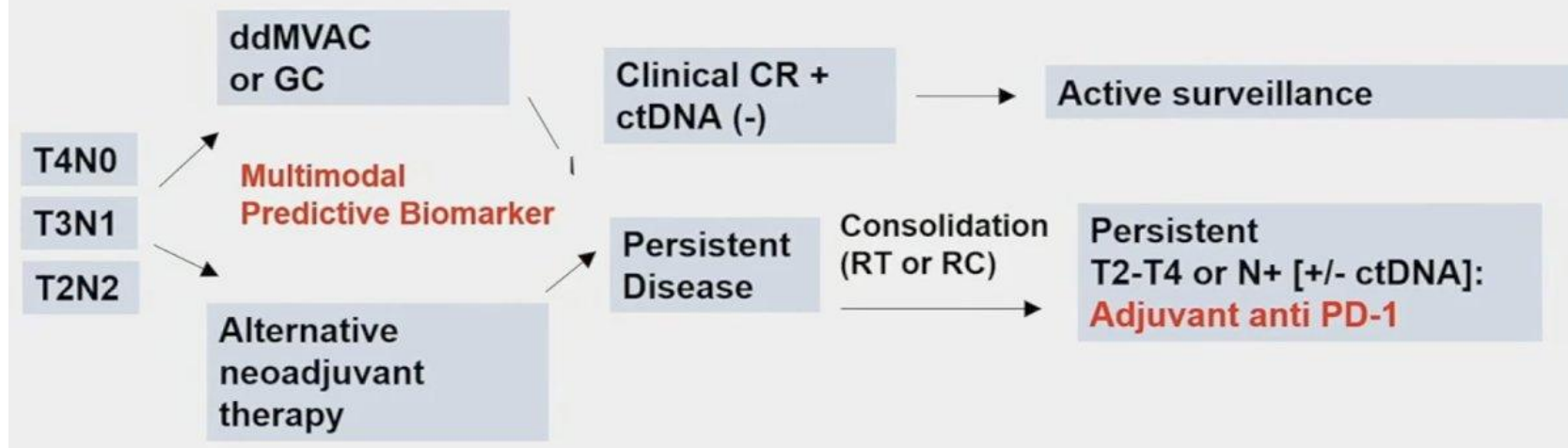


The addition of Nivolumab to chemoradiotherapy significantly improved BCFFs and OS in patients with high-risk MIBC. The combination therapy led to higher rates of adverse events, particularly thyroid immune-related dysfunction.

A New Era in the Perioperative Management of Muscle Invasive Bladder Cancer

Kates MR. ASCO GU 2024

Future Paradigms in cis-eligible MIBC



C O N C L U S I O N S

- **Ni preservación de vejiga para todos, ni cistectomía para todos!!!!**
- Los casos deben valorarse en comité multidisciplinar, y los pacientes deben poder visitar al urólogo , al oncólogo médico y al **oncólogo radioterápico** para hablar de las distintas opciones terapéuticas y que el paciente pueda participar en la decisión final de tratamiento.
- Los candidatos ideales para TMT incluyen pacientes con estadio cT2 unifocal, sin hidronefrosis, ni CIS multifocal concomitante, y que presentan una buena función urinaria basal.
- Si bien el estadio cT3-4a, la hidronefrosis y el CIS son factores de mal pronóstico, su presencia no es contraindicación absoluta para TMT
- Cuando sea posible, se debe realizar una TURBT máxima, antes de iniciar el TMT.

Muchas gracias



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