

Intravesical drug-delivery systems in BCG-naïve disease: Evidence and limitations

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- Dirección de Compra Publica Innovadora Andalucía



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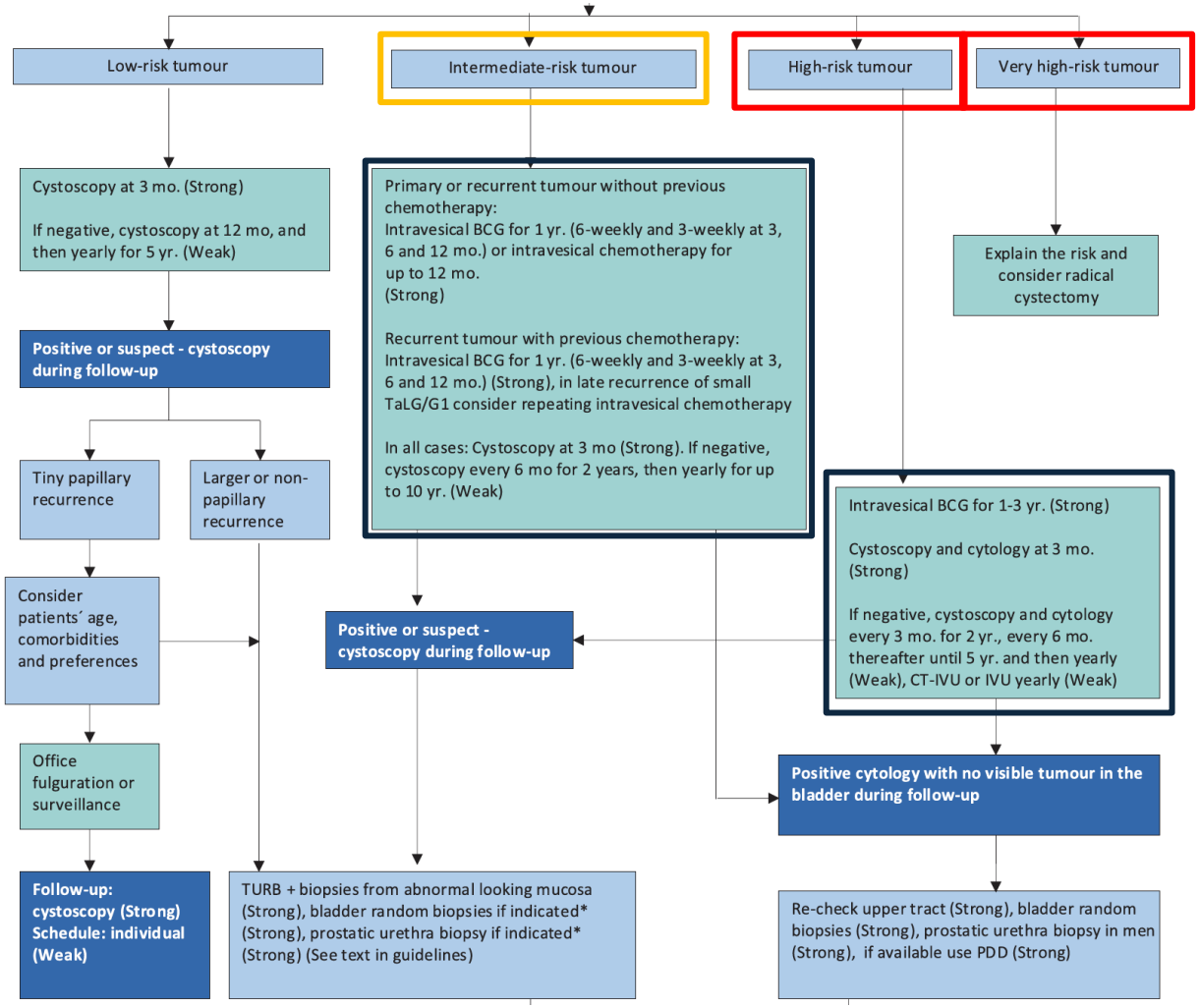
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BCG naive population



Risk group	
Low Risk	• A primary, single, TaT1 LG/G1 tumour < 3 cm in diameter without CIS in a patient ≤ 70 years • A primary Ta LG/G1 tumour without CIS with at most ONE of the additional clinical risk factors
Intermediate Risk	• Patients without CIS who are not included in either the low-, high-, or very high-risk groups
High Risk	• All T1 HG/G3 without CIS, EXCEPT those included in the very high-risk group • All CIS patients, EXCEPT those included in the very high-risk group
	Stage, grade with additional clinical risk factors: • Ta LG/G2 or T1 G1, no CIS with all three risk factors • Ta HG/G3 or T1 LG, no CIS with at least two risk factors • T1 G2 no CIS with at least one risk factor
Very High Risk	**Stage, grade with additional clinical risk factors:** • Ta HG/G3 and CIS with all three risk factors • T1 G2 and CIS with at least two risk factors • T1 HG/G3 and CIS with at least one risk factor • T1 HG/G3 no CIS with all three risk factors



Age

≤ 70 years	> 70 years

Tumor Status

Primary	Recurrent

Number of Tumors

Single	Multiple

Maximum Tumor Diameter

< 3 cm	≥ 3 cm

Stage

Ta	T1

Concomitant CIS

No	Yes

Select Classification System

Either the WHO 1973, the WHO 2004/2016, or both grading classification systems can be selected.

WHO Grade 2004/2016

LMP-LG	HG

WHO Grade 1973

G1	G2	G3

Calculate

Results

Probability of progression after TURBT without induction or maintenance BCG

	BASED ON WHO 2004/2016 Intermediate Risk	BASED ON WHO 1973 High Risk
at 1 year	1.0%, 0.50%-2.0%	3.8%, 2.6%-5.7%
at 5 years	4.9%, 3.4%-7.0%	11%, 8.1%-14%
at 10 years	8.5%, 5.6%-13%	14%, 10%-19%

Probability of Progression and 95% Confidence Interval

Reset

Share result



Age

≤ 70 years	> 70 years

Tumor Status

Primary	Recurrent

Number of Tumors

Single	Multiple

Maximum Tumor Diameter

< 3 cm	≥ 3 cm

Stage

Ta	T1

Concomitant CIS

No	Yes

Select Classification System

Either the WHO 1973, the WHO 2004/2016, or both grading classification systems can be selected.

WHO Grade 2004/2016

LMP-LG	HG

WHO Grade 1973

G1	G2	G3

Calculate

Results

Probability of progression after TURBT without induction or maintenance BCG

	BASED ON WHO 2004/2016 Very High Risk	BASED ON WHO 1973 High Risk
at 1 year	16%, 10%-26%	3.8%, 2.6%-5.7%
at 5 years	40%, 29%-54%	11%, 8.1%-14%
at 10 years	53%, 36%-73%	14%, 10%-19%

Probability of Progression and 95% Confidence Interval

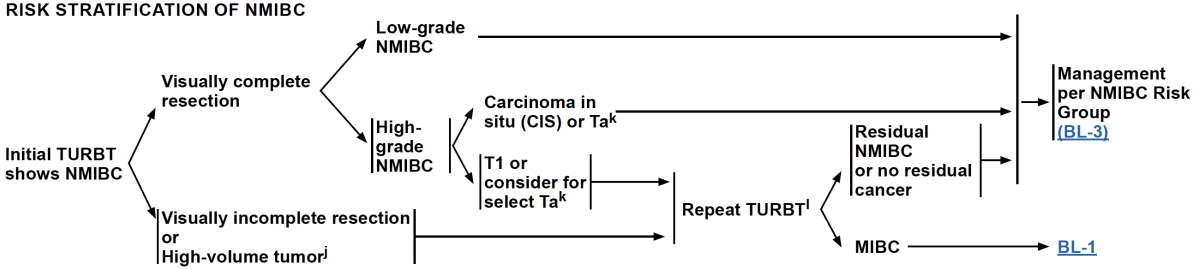
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BCG naive population

RISK STRATIFICATION OF NMIBC



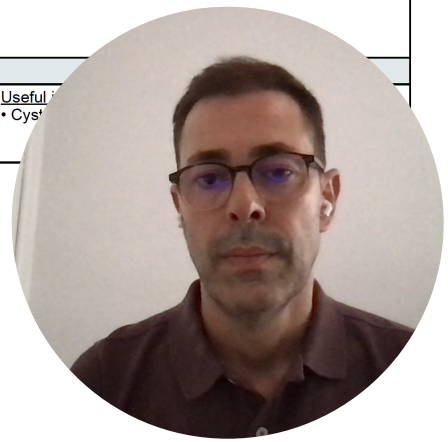
Risk Stratification for Non–Muscle-Invasive Bladder Cancer*

Low Risk[m]	Intermediate Risk[n]	High Risk[m]
• Papillary urothelial neoplasm of low malignant potential • Low grade urothelial carcinoma ▸ Ta and ▸ ≤3 cm and ▸ Solitary	• Baseline intermediate risk eligibility factors ▸ Ta low grade tumor that is any one of the following: ◊ recurrent ◊ multifocal ◊ ≥3 cm ▸ Any T1 low grade (G1–G2) tumor ▸ Any Ta G2 tumor, regardless of recurrence status • Patients are then further stratified by the number of adverse risk factors ▸ Multifocal tumors (>1 lesion) ▸ Early recurrence (<1 year) ▸ Frequent recurrence (>1 recurrence/year) ▸ Tumor size ≥3 cm ▸ Failure of prior intravesical therapy • Intermediate risk subgroups ▸ Lower risk: 0 risk factors ▸ Intermediate risk: 1–2 factors ▸ Higher risk: ≥3 factors	• High grade urothelial carcinoma ▸ CIS or ▸ T1 or ▸ >3 cm or ▸ Multifocal • Very high risk features (any): ▸ BCG unresponsive[o,p] ▸ Certain histopathologic subtypes[q] ▸ Lymphovascular invasion ▸ Prostatic urethral invasion

*Within each of these risk strata an individual patient may have more or fewer concerning features that can influence care.

MANAGEMENT PER NMIBC RISK GROUP

Preferred	Other recommended	Useful in certain circumstances
BCG naïve high-risk NMIBC		
• BCG induction followed by maintenance therapy[s,u]	• Intravesical chemotherapy[s] • Clinical trial	• BCG + Durvalumab • Cystectomy
BCG unresponsive NMIBC, CIS +/- Ta/T1 papillary		
• Cystectomy[v] • Clinical trial	• BCG + Nogapendekin alfa inbakicept-pmln • Gemcitabine intravesical system • Intravesical multi-agent chemotherapy[s] • Nadofaragene firadenovec-vncg	• Pembrolizumab • Intravesical single-agent chemotherapy[s] (category 2B)
BCG unresponsive NMIBC, Ta/T1 papillary only without CIS		
• Cystectomy[v] • Clinical trial	• BCG + Nogapendekin alfa inbakicept-pmln • Gemcitabine intravesical system • Intravesical multi-agent chemotherapy[s] • Nadofaragene firadenovec-vncg • Intravesical single-agent chemotherapy[s] (category 2B)	• Pembrolizumab (category 2B)
BCG exposed high-risk NMIBC		
• Repeat BCG induction (particularly if initial BCG course inadequate)[s] • Clinical trial	• Intravesical multi-agent chemotherapy[s] • Intravesical single agent chemotherapy[s]	• Cyst



VOLUME 34 · NUMBER 16 · JUNE 1, 2016

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Definitions, End Points, and Clinical Trial Designs for Non–Muscle-Invasive Bladder Cancer: Recommendations From the International Bladder Cancer Group

Ashish M. Kamat, Richard J. Sylvester, Andreas Böhle, Joan Palou, Donald L. Lamm, Maurizio Brausi, Mark Soloway, Raj Persad, Roger Buckley, Marc Colombel, and J. Alfred Witjes

Table 2. Summary of Clinical Trial Design Elements for NMIBC According to Risk Category

	NMIBC Population			
	High Risk		Intermediate Risk	
Element	BCG Naive	BCG Failure	BCG Naive	Low Risk
Patient eligibility				
Inclusion criteria	▪ Histologically confirmed T1 and/or high-grade tumors and/or CIS ▪ Never treated with BCG immunotherapy	▪ Depends on type of BCG failure (Table 5)	▪ Histologically confirmed multiple and/or recurrent low-grade Ta tumors ▪ Never treated with BCG immunotherapy	▪ Histologically confirmed solitary, primary low-grade Ta tumor < 3 cm in diameter
Exclusion criteria	▪ Stage ≥ T2 tumors ▪ Previous treatment with intravesical BCG therapy ▪ Life expectancy < 5 years ▪ WHO performance status 3 or 4	▪ Stage ≥ T2 tumors ▪ Low-grade Ta recurrence after BCG therapy ▪ Recurrence > 1 year after last BCG instillation ▪ Life expectancy < 5 years ▪ WHO performance status 3 or 4	▪ Primary, solitary, low-grade Ta tumor < 3 cm in diameter ▪ Stage T1 or high-grade tumors or CIS ▪ Stage ≥ T2 tumors ▪ Previous treatment with intravesical BCG therapy ▪ Life expectancy < 5 years ▪ WHO performance status 3 or 4	▪ Multiple and/or recurrent low-grade Ta tumors > 3 cm ▪ Stage T1 or high-grade tumors or CIS ▪ Stage ≥ T2 tumors ▪ Previous treatment with adjuvant intravesical therapy ▪ Life expectancy < 5 years ▪ WHO performance status 3 or 4
Baseline evaluations	Document: ▪ Patient demographics ▪ Cytology results ▪ Presence or absence of CIS ▪ Tumor stage and grade and number and size of tumors ▪ Details and dates of: – Initial TURBT – Previous therapies (immediate postoperative chemotherapeutic instillation, adjuvant intravesical therapy, PDD) ▪ Mandatory: – Appropriate upper-tract evaluation – Bladder biopsies for CIS ▪ Recommended: – Repeat TURBT if initial resection incomplete or if no muscle in the specimen – Bladder biopsies for papillary disease only when cytology positive or when exophytic tumor has a nonpapillary appearance	Document: ▪ Patient demographics ▪ Cytology results ▪ Presence or absence of CIS ▪ Tumor stage and grade and number and size of tumors ▪ Details and dates of: – Initial TURBT – Type of BCG schedule administered before failure (including induction and maintenance: instillations per course, schedule of instillations and duration) – Timing of recurrence ▪ Mandatory: – Appropriate upper-tract evaluation – Bladder biopsies for CIS ▪ Recommended: – Repeat TURBT if initial resection incomplete or if no muscle in the specimen – Bladder biopsies for papillary disease only when cytology positive or when exophytic tumor has a nonpapillary appearance	▪ Patient demographics ▪ Cytology results ▪ Tumor stage and grade and number and size of tumors ▪ Details and dates of: – Initial TURBT – Previous therapies (immediate postoperative chemotherapeutic instillation) ▪ Mandatory: – Appropriate upper-tract evaluation ▪ Recommended: – Repeat TURBT if initial resection incomplete or if no muscle in the specimen – Bladder biopsies for papillary disease only when cytology positive or when exophytic tumor has a nonpapillary appearance	▪ Patient demographics ▪ Cytology results ▪ Tumor stage and grade and size of tumor ▪ Details and dates of: – Initial TURBT – Immediate postoperative chemotherapeutic instillation (if provided) ▪ Recommended: – Repeat TURBT if initial resection incomplete or if no muscle in the specimen – Bladder biopsies for papillary disease only when cytology positive or when exophytic tumor has a nonpapillary appearance – Appropriate upper-tract evaluation
Study design	▪ Randomized superiority trial (preferred) ▪ Randomized noninferiority trial	▪ Randomized superiority trial with investigator-choice comparator ▪ Single-arm trial	▪ Randomized superiority trial (preferred) ▪ Randomized noninferiority trial	▪ Ran (no like
Comparator or control arm	▪ Full-dose BCG induction plus maintenance (minimum 1 year; standard of care) ▪ Intravesical chemotherapy (6-12 months) in patients not eligible for BCG	Investigator choice may include valrubicin, gemcitabine, mitomycin, thermochemotherapy, BCG plus IFN, and taxanes	▪ Full-dose BCG induction plus maintenance (1 year) for higher-risk intermediate-risk disease ▪ Intravesical chemotherapy for 6-12 months for lower-risk intermediate-risk disease	TURBT chemo



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Table 2. Summary of Clinical Trial Design Elements for NMIBC According to Risk Category (continued)

Element	NMIBC Population: High Risk — BCG Naive	NMIBC Population: High Risk — BCG Failure	NMIBC Population: Intermediate Risk — BCG Naive	NMIBC Population: Low Risk
Primary end point	▪ Time to recurrence or RFS (for papillary disease) ▪ CR rate and duration of response (for CIS)	▪ Freedom from high-risk recurrence at 1 year (for papillary disease) ▪ CR at 6 months (for CIS)	▪ Time to recurrence or RFS	▪ Time to recurrence or RFS
Secondary	▪ Time to progression ▪ Disease worsening ▪ Disease-specific survival ▪ OS ▪ Toxicity ▪ QOL	▪ Freedom from high-risk recurrence at 6 months and at 2 years (for papillary disease) ▪ CR at 12 months (for CIS) ▪ Time to progression ▪ Disease worsening ▪ Disease-specific survival ▪ OS ▪ Toxicity ▪ QOL	▪ Time to progression ▪ Disease worsening ▪ Disease-specific survival ▪ OS ▪ Toxicity ▪ QOL	▪ Toxicity
Study duration	Minimum 2 years: 1 year of active treatment followed by a minimum of 1 year of monitoring and follow-up	Minimum 2 years: 1 year of active treatment followed by a minimum of 1 year of monitoring and follow-up	Minimum 2 years: 1 year of active treatment followed by a minimum of 1 year of monitoring and follow-up	Minimum 2 years: 1 year of active treatment followed by a minimum of 1 year of monitoring and follow-up
Patient follow-up and monitoring	Mandatory: ▪ Cystoscopy every 3 months ▪ Cytology every 3 months for CIS ▪ Appropriate upper-tract evaluation at end of study Recommended: ▪ Cytology every 3 months for papillary disease	Mandatory: ▪ Cystoscopy every 3 months ▪ Cytology every 3 months for CIS ▪ Appropriate upper-tract evaluation at end of study Recommended: ▪ Cytology every 3 months for papillary disease	Mandatory: ▪ Cystoscopy every 3 months ▪ Appropriate upper-tract evaluation at end of study Recommended: ▪ Cytology every 3 months	Mandatory: ▪ Cystoscopy every 3 months, then every 6 months Recommended: ▪ Cytology every 3 months
Clinically meaningful magnitude of effect	▪ Absolute difference of 10% in the percentage of patients with recurrence at 2 years	BCG refractory or unresponsive CIS: ▪ Initial CR rate of 50% at 6 months ▪ Durable response rate of 30% at 12 months and 25% at 18 months BCG refractory or unresponsive papillary disease: ▪ Recurrence-free rate of 30% at 12 months and 25% at 18 months	▪ Absolute difference of 10% in the percentage of patients with recurrence at 2 years	▪ Absolute difference of 6% in the percentage of patients with recurrence at 2 ye
Sample size	150 recurrences per 450 patients	▪ CIS: 20 CR per 40 patients ▪ Papillary: 10 recurrence-free patients per 33 patients	BCG control: ▪ 150 recurrences per 450 patients ▪ Chemotherapy control: ▪ 250 recurrences per 500 patients	110 re

Abbreviations: BCG, bacillus Calmette-Guérin; CIS, carcinoma in situ; CR, complete response; IFN, interferon; NMIBC, non–muscle-invasive bladder cancer; OS, overall survival; QO
free survial; TURBT, transurethral resection of the bladder tumor.



EMDA, HIVEC–COMBAT y RITE–Synergo

Aplicación y dispositivos para potenciar la quimioterapia intravesical

Característica	EMDA [1,2]	HIVEC–COMBAT [2]	RITE–Synergo [3,4]
Mecanismo	Transporte del fármaco mediante corriente eléctrica	Hipertermia conductiva por solución calentada	Hipertermia del tejido por radiofrecuencia
Dispositivo	Physionizer Generador de corriente	COMBAT BRS Calentador y bomba	Synergo Generador RF de 915 MHz
Sonda y accesorios	Electrodo intravesical y electrodos cutáneos abdominales	Sonda de recirculación y circuito cerrado con tubuladuras	Sonda con antena RF y sensores térmicos. Circuito de recirculación
Aplicación de energía	Campo eléctrico Sin hipertermia terapéutica programada	Calentamiento externo del líquido, que transfiere calor a la pared vesical	La antena calienta el tejido. La solución recircula y se enfría
Sesión habitual*	≈20 mA 30 minutos	≈43 °C (solución) 60 minutos	≈42–44 °C (tejido) 60 minutos
Fármaco más estudiado	**Mitomicina C**	**Mitomicina C**	**Mitomi**

*Parámetros orientativos. Varían según el protocolo y la versión del dispositivo.



REFERENCIAS

[1] Estudio mecanístico de EMDA, 2016. PMCID: PMC5012313. [2] Cancers. 2025;17(3):453. doi:10.3390/cancers17030453.

[3] Synergo Medical. Technology (fabricante). [4] Overview of bladder heating technology, 2016. PMCID: PMC4968693.

EMDA e HIVEC: visión global de principales estudios

Comparaciones únicamente descriptivas.

Estudio	Esquema de tratamiento	Población: CVNMI	Diseño y N	Resultados principales	Conclusión crítica
Di Stasi 2003 [1]	**EMDA–MMC / MMC / BCG** 6 sem. ± reinducción + mantenimiento según RC	Alto riesgo, CIS multifocal; 98 con T1 concomitante	ECA multicéntrico N=108 36 / 36 / 36	**RC 6 m: 58% / 31% / 64%** **EMDA vs MMC: p=0,012** Recurrencia: 35 / 19,5 / 26 m*	**Mejor RC vs MMC pasiva.**
Di Stasi 2006 [2]	**BCG + EMDA vs BCG** (2 BCG + 1 EMDA) ×3 + mantenimiento distinto	Alto riesgo T1 ± CIS	**ECA, 4 centros** N=212 107 / 105	**ILE mediano: 69 vs 21 m** (p=0,0012). Seguim.: 88 m Progresión: 9,3% vs 21,9%	**Beneficio de la secuencia.**
HIVEC-HR Guerrero-Ramos 2022 [3]	**HIVEC: 6 sem. + 6 meses vs BCG: inducción + mantenimiento 1 año**	Alto riesgo papilar Sin CIS	ECA piloto fase II N=50 25 / 25	**SLR 24 m: 86,5% vs 71,8%** **(p=0,184).** SLP: 95,7% vs 71,8%; señal según análisis	**Señal favorable a HIVEC.** **Pocos eventos: no prueba equivalencia/superioridad.**
Sachan 2024 [4]	**HIVEC / MMC / BCG** Todos: 6 sem. + mensual 12 meses	Riesgo intermedio Bajo grado Tras RTU completa	**ECA, un centro** N=135; análisis 45 / 45 / 42	**Recidiva: 17,8% / 20% / 9,5%** (p=0,375). Seguim.: 26 m Necrosis: 22,2 / 11,1 / 4,8%	**Sin ventaja de HIVEC.**
Melgarejo-Segura 2025 [5]	**HIVEC vs EMDA–MMC** Ambos: 6 semanales + 6 mensuales	Riesgo intermedio o alto Sin CIS	Prospectivo No aleatorizado N=121: 67 / 54	**SLE 36 m: 62,4% vs 67%** (p=0,4). Seguim.: 38,6 m IC95%: 49–73% / 52–78%	**Sin diferencia detectada.**
Michael 2026 [6]	**Gemcitabina / HIVEC / BCG** Gem./HIVEC: 6 sem. + 1 año BCG: esquema SWOG	Intermedio/alto 84% alto riesgo Sin terapia previa	ECA abierto N=100 50 / 25 / 25	**SLR 12 m: 94% / 84% / 92%** (p=0,675). Sin progresión Gemcitabina mejor tolerada	**Cierre precoz**, p[illegible]sos. No demues[illegible] inferiorid[illegible]
Del Giudice 2026 [7]	**BCG / BCG + EMDA–MMC (secuencia Di Stasi) / cistectomía inicial**	Alto/muy alto riesgo	**Retrospectivo** N=1.178; 2 centros 852 / 249 / 77	**Ninguna asociación fue significativa**	**No p[illegible]** **conc[illegible]**

*Mediana hasta recurrencia. RC: respuesta completa. ILE/SLE: intervalo/supervivencia libre de enfermedad. SLR/SLP: supervivencia libre de recurrencia/progresión.

ECA: ensayo aleatorizado. NS: no significativo. m: meses. HIVEC: MMC con COMBAT. Cifras en orden de tratamientos. Seguimiento: mediana.

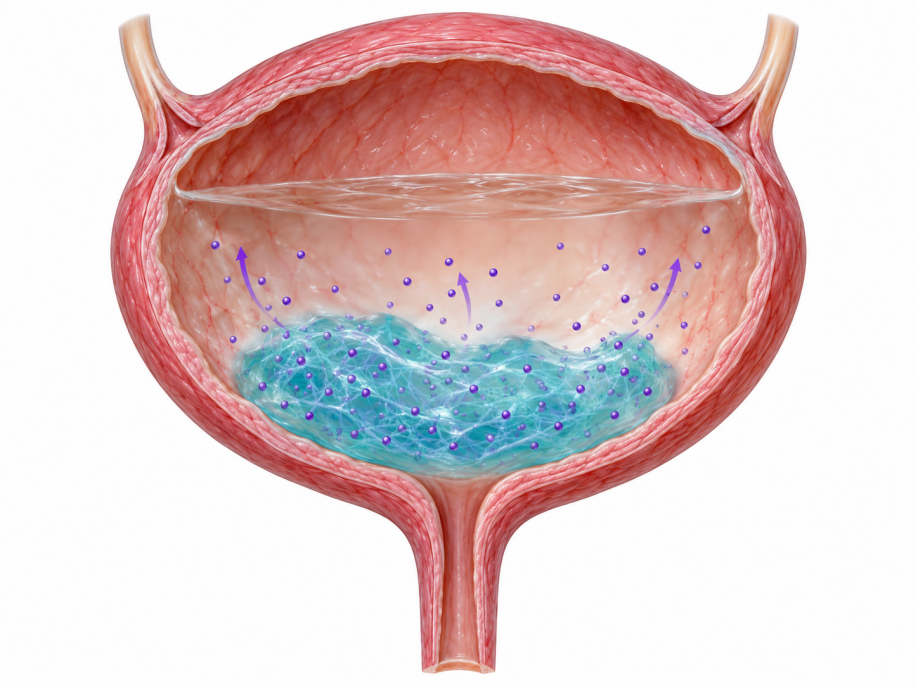


Fuentes [1–7]: Di Stasi 2003, Di Stasi 2006, Guerrero-Ramos 2022, Sachan 2024, Melgarejo-Segura 2025, Michael 20[illegible]e 2026.

Nuevas tecnologías de liberación intravesical

Mayor permanencia del fármaco en la vejiga

Hidrogeles y matrices poliméricas



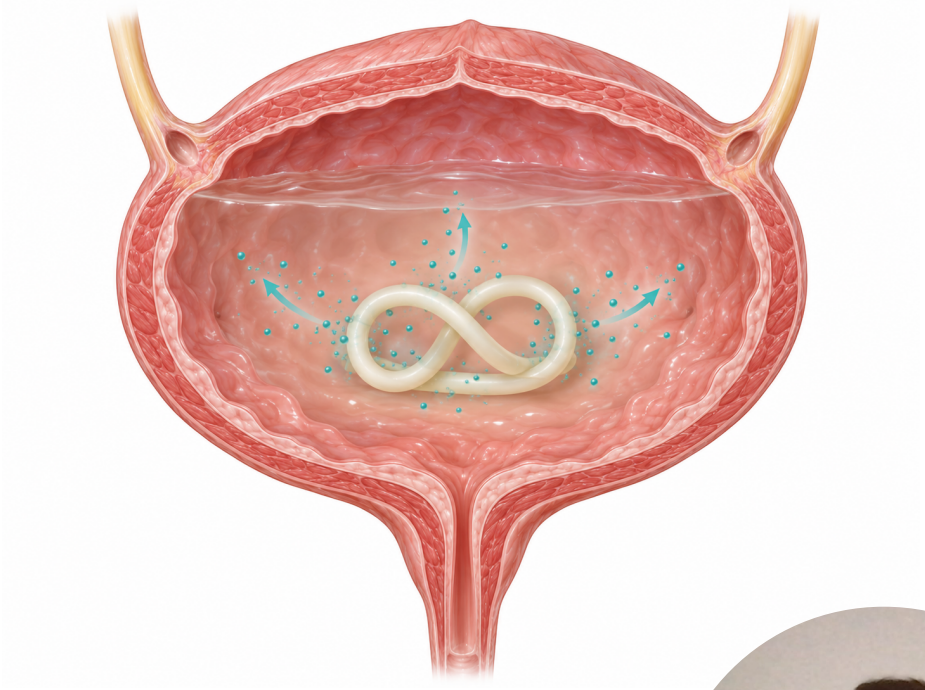
Depósito que libera el fármaco

MMC: hidrogel termorreversible

Gem/Doce: matriz polimérica en investigación

ADCs: hidrogeles experimentales

Dispositivos TAR-200 / TAR-210

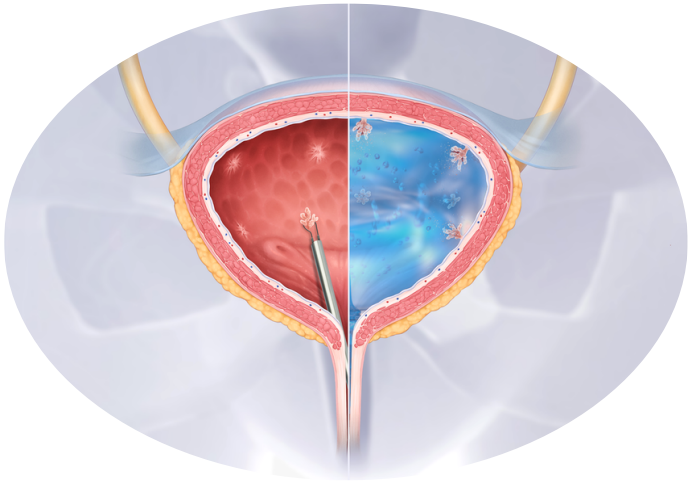


Tubo flexible con liberación

TAR-200: gemcitabi

TAR-210: erdafitinib





UGN 102 Late Studies Program

Study Population = Low-Grade Intermediate-Risk Non-Muscle Invasive Bladder Cancer (LG-IR-NMIBC)
Target Dose = 75 mg instilled into the bladder via urinary catheter once weekly for 6 weeks

ENVISION (n=240)
Pivotal Phase 3 Trial
Recurrent Only

Primary: **CRR** at 3 months
Key Secondary:
- **DOR**[a] after 3-month CR

Other Endpoints:
- QoL

Follow-up = At least 18 months after 3-month CR

OPTIMA II (n=63)
Phase 2b POC Trial
Recurrent & Newly Diagnosed

Primary: **CRR** at 3 months
Secondary:
- **DOR**[a] after 3-month CR
- QoL

Follow-up = 9 months after 3-month CR

ATLAS (n=282)
Supportive Phase 3 RCT
Recurrent & Newly Diagnosed

Primary: DFS[b]
Secondary:
- **CRR** at 3 months
- **DOR**[a] after 3-month CR
- QoL

Follow-up = At least 12 months after 3-month CR

Key Inclusion Criteria	Key Exclusion Criteria
• LG-NMIBC (Ta) histologically confirmed by cold cup biopsy at screening or within 8 weeks before screening • History of LG-NMIBC requiring treatment with TURBT (ENVISION only) • Intermediate risk disease, defined as having 1 or 2 of the following – Presence of multiple tumors – Solitary tumor >3 cm – Early or frequent recurrence (≥1 occurrence of LG-NMIBC within 1 year of the current diagnosis) • Negative voiding cytology for HG disease within 8 weeks (ENVISION) or 6 weeks (ATLAS) before screening	• Received BCG treatment for UC in the past 1 year • History of HG papillary bladder cancer in the past 2 years • History of CIS in the past 2 years (ENVISION) or 5 years (ATLAS) • Clinically significant urethral stricture that would preclude passage of a urethral catheter • Any condition that would prohibit normal voiding • Past or current muscle invasive bladder cancer (i.e., T2, T3, T4) or metastatic UC • Current tumor stage of T1 • Concurrent UTUC • IVCT in the past 2 years (ENVISION) or any history (ATLAS) except for a single dos TURBT

BCG=Bacillus Calmette-Guérin; CIS=carcinoma in situ; HG=high-grade; IVCT=intravesical ch
LG=low-grade; NMIBC=non-muscle invasive bladder cancer; TURBT=transurethral rese
UC=urothelial carcinoma; UTUC=upper tract urothelial carcinoma.



Study Population = Low-Grade Intermediate-Risk Non-Muscle Invasive Bladder Cancer (LG-IR-NMIBC)
Target Dose = 75 mg instilled into the bladder via urinary catheter once weekly for 6 weeks

ENVISION (n=240)
Pivotal Phase 3 Trial
Recurrent Only

Primary: **CRR** at 3 months
Key Secondary:
- **DOR**[a] after 3-month CR

Other Endpoints:
- QoL

Follow-up = At least 18 months after 3-month CR

OPTIMA II (n=63)
Phase 2b POC Trial
Recurrent & Newly Diagnosed

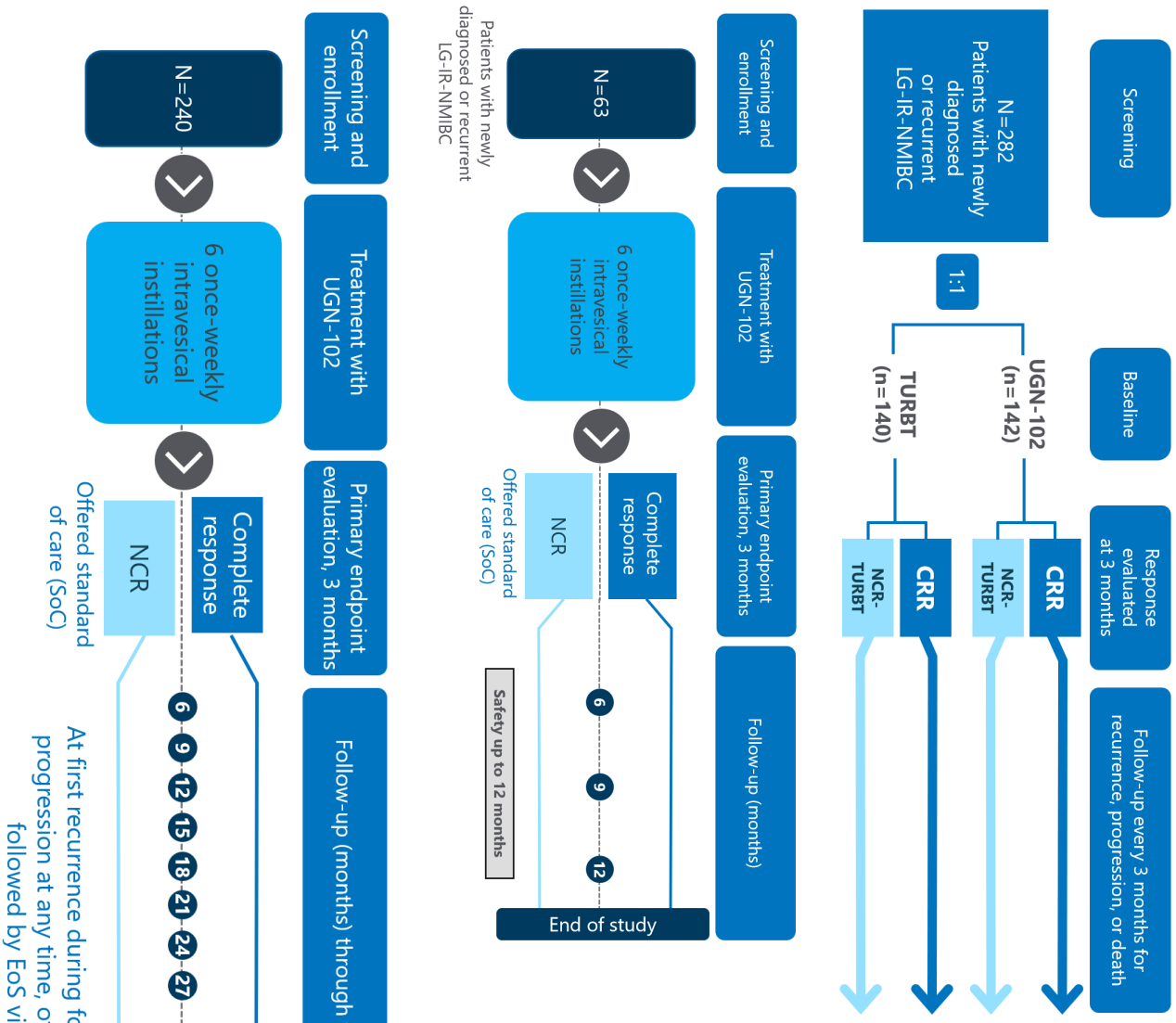
Primary: **CRR** at 3 months
Secondary:
- **DOR**[a] after 3-month CR
- QoL

Follow-up = 9 months after 3-month CR

ATLAS (n=282)
Supportive Phase 3 RCT
Recurrent & Newly Diagnosed

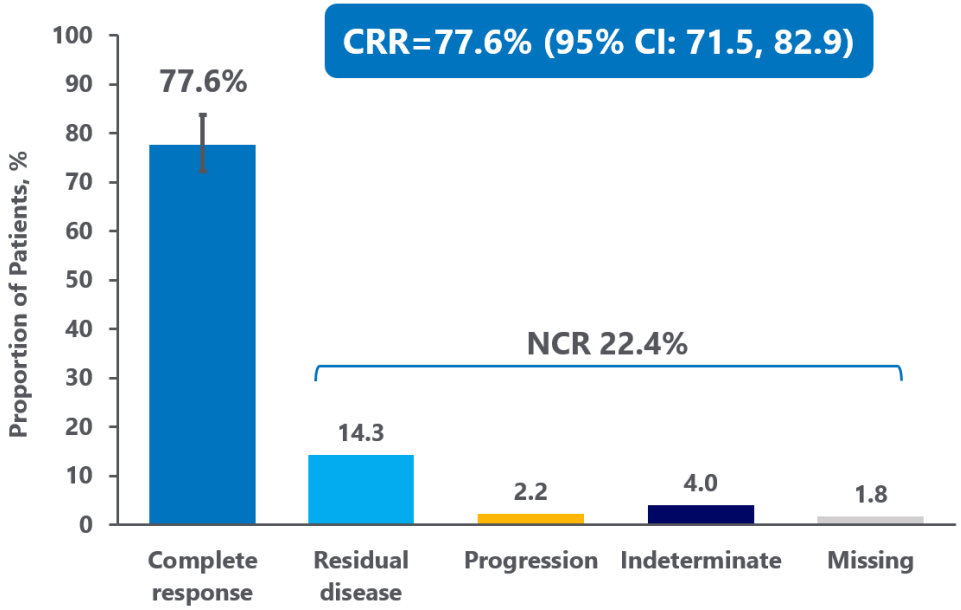
Primary: DFS[b]
Secondary:
- **CRR** at 3 months
- **DOR**[a] after 3-month CR
- QoL

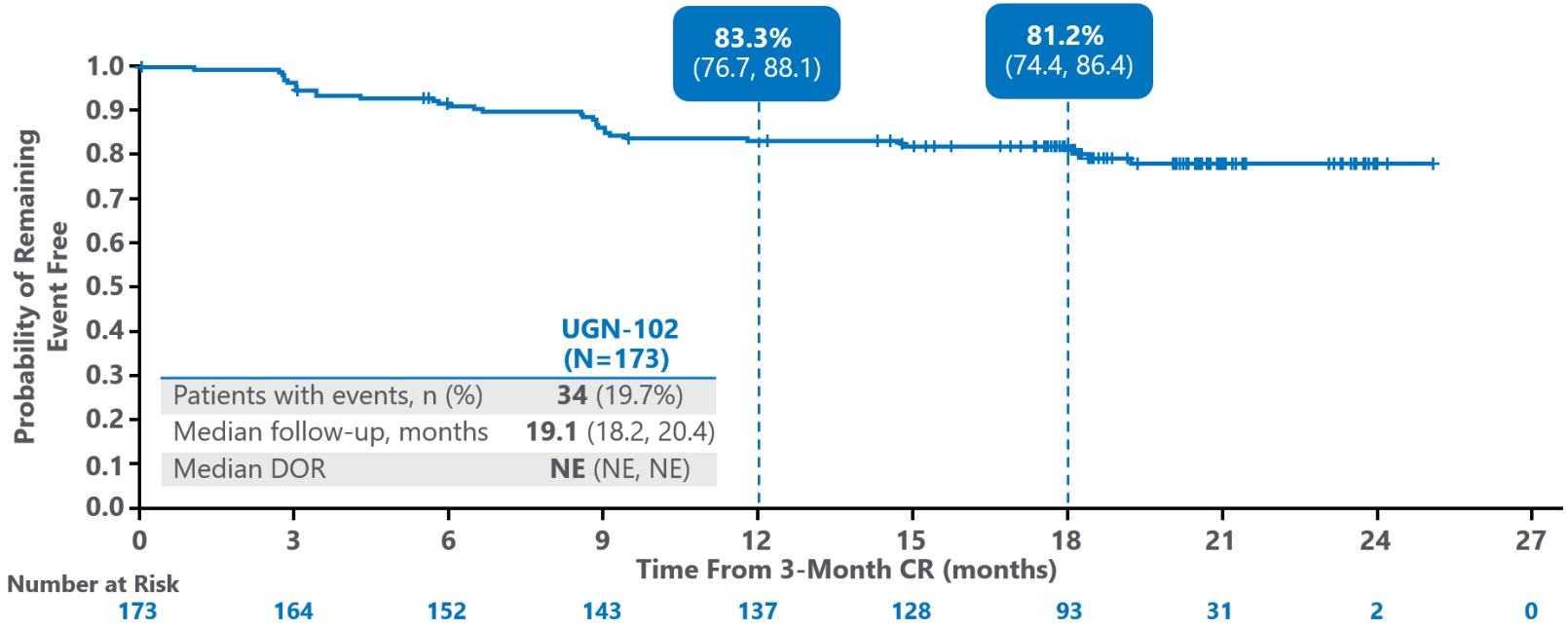
Follow-up = At least 12 months after 3-month CR





UGN 102 ENVISION







UGN-102 / ZUSDURI: aprobación y reservas de la FDA

Mitomicina intravesical en hidrogel RTGel

APROBACIÓN

12 junio 2025

Adultos con CVNMI recurrente, bajo grado y riesgo intermedio

RESERVAS SOBRE LA EVIDENCIA

ENVISION sin grupo control

Actividad antitumoral demostrada. Incertidumbre al atribuir la duración de respuesta al tratamiento.

Comparación con RTU no concluyente

ATLAS no sustentaba superioridad en eficacia. Tampoco se demostró mayor seguridad ni menos RTU a largo plazo.

Seguimiento tras la aprobación

Compromiso de completar ENVISION y actualizar la duración de respuesta. Informe final previsto para julio de 2028.

La aprobación para esta indicación no acredita superioridad frente a la RTU



FDA/UroGen para ODAC, 21/05/2025 (pp. 38, 55–56) y carta FDA ND

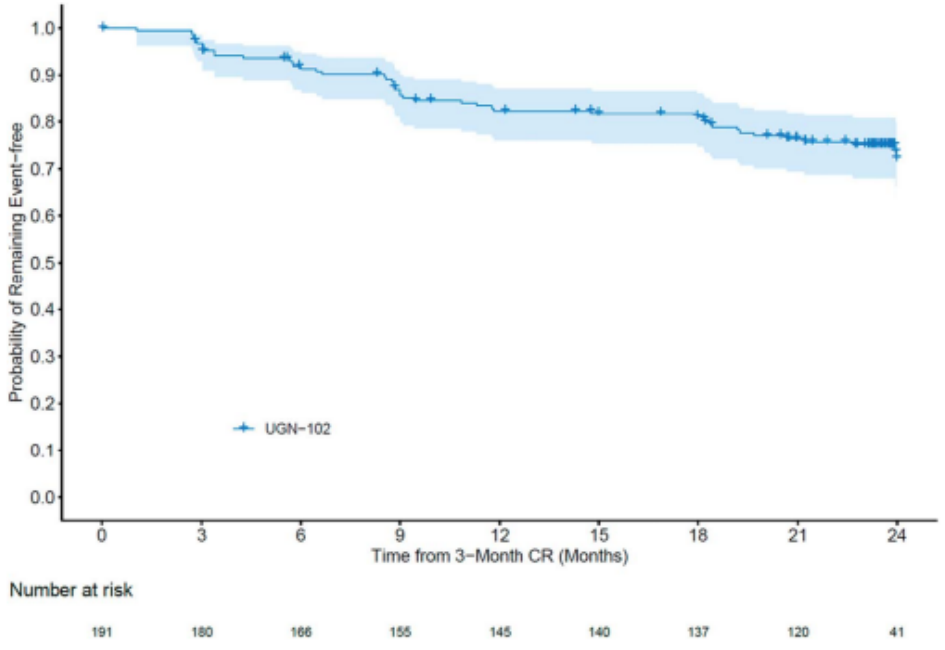
ENVISION 2026: duración de respuesta a 24 meses

Fase III, un brazo. CVNMI recurrente de bajo grado y riesgo intermedio (N=240)
6 instilaciones semanales de 75 mg, sin mantenimiento. RC al mes 3: 80% (191/240)

RESPONDEDORES AL MES 3 (n=191)

72% sin eventos a 24 meses tras RC

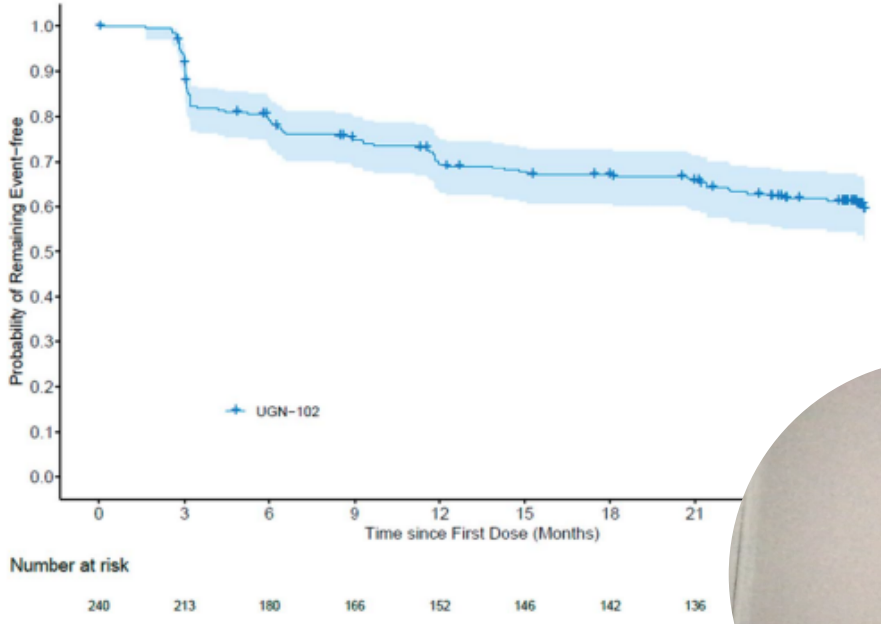
Kaplan–Meier, IC95% 64–79. Mediana de duración no estimable.



TODOS LOS TRATADOS (N=240)

Supervivencia libre de enfermedad

Análisis exploratorio post hoc desde la primera dosis.





Sin comparador: no demuestra superioridad frente a RTU. Seguridad: disuria 23%, retirada del tratamiento por EA 2,9%.

Prasad SM et al. J Urol. 2026;216:194–205.. Figuras 1 y 4. Corte de datos: [illegible]/2025.

Extended dwell time as a gel

As the temperature of the formulation rises to body temperature, it converts to gel form.

The formulation is then intended to dwell in the target organ for several hours while providing sustained exposure of the active drug.



UGN 103 UTOPIA

FIGURE 1. STUDY DESIGN

UTOPIA is a Phase 3, single-arm, multicenter study evaluating the efficacy and safety of UGN-103 (a novel formulation of UGN-102) as treatment for recurrent LG-IR-NMIBC

30 sites in Europe and the US

99 patients with LG-IR-NMIBC

Key inclusion criteria:
- ✓ Adults (≥18 years) with biopsy-confirmed Ta LG NMIBC (at screening or within 8 weeks of screening) able to provide informed consent
- ✓ History of at least one prior episode of NMIBC
- ✓ IR disease with one or two of the following:
  - a. Multiple tumors
  - b. Solitary tumor >3 cm
  - c. Early or frequent recurrence

Key exclusion criteria:
- ✗ Prior IVCT within 2 years, except single dose immediately after TURBT
- ✗ Received BCG treatment for UC within the previous 1 year
- ✗ History of HG bladder cancer (papillary or CIS) in the past 2 years
- ✗ Concurrent UTUC
- ✗ Current T1 tumor stage
- ✗ Pregnancy/lactation

Primary endpoint:
- CR rate (defined as the proportion of patients with no detectable disease at 3 months after the first instillation)

Secondary endpoints:
- Durability of response:
  - DoR (defined as the time from the date of evidence of CR at the 3-month Visit to the earliest date of recurrence or progression, or death due to any cause)
  - DCR rate at scheduled disease assessment timepoints (defined as the proportion of patients who achieved CR at the 3-month Visit and maintained CR up to that follow-up disease assessment)
- Safety and tolerability
- Pharmacokinetics (subgroup)

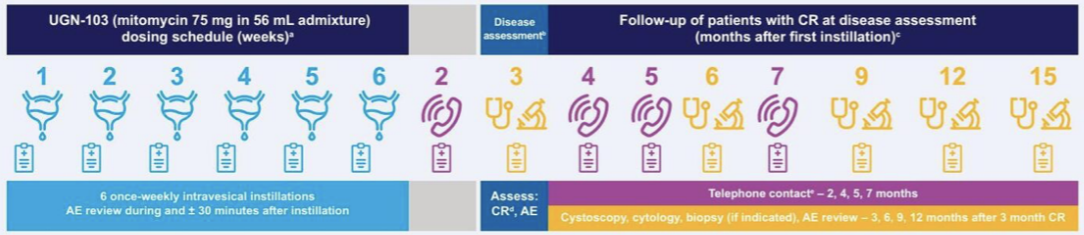
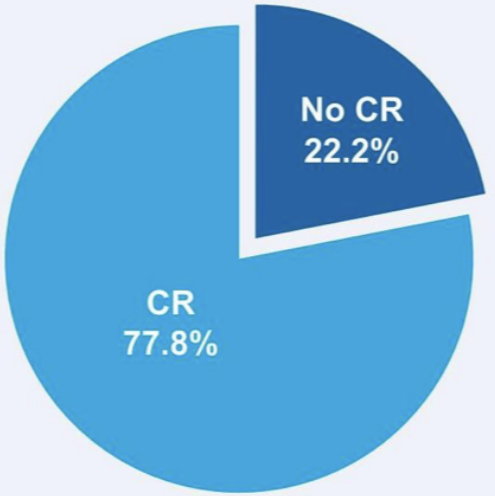
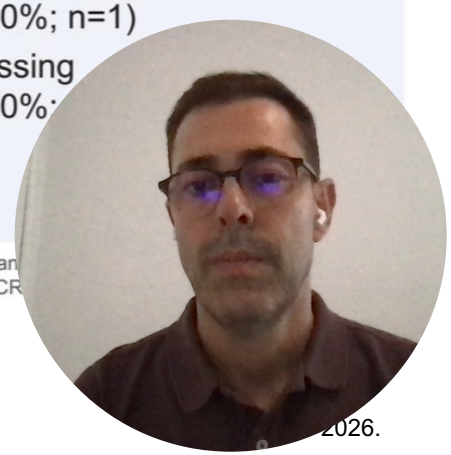


FIGURE 2: SUMMARY OF RESPONSE RATE AT 3-MONTH DISEASE ASSESSMENT (ITT POPULATION)



No CR subcategories:
- Residual disease (16.2%; n=16)
- Progression to HG disease (4.0%; n=4)
- Indeterminate (1.0%; n=1)
- Missing (1.0%;

Any missing or indeterminate responses are considered as NCR in this an
CR, complete response; HG, high grade; ITT, intent-to-treat; NCR, non-CR



2026.

UTOPIA / UGN-103: reformulación y evidencia clínica

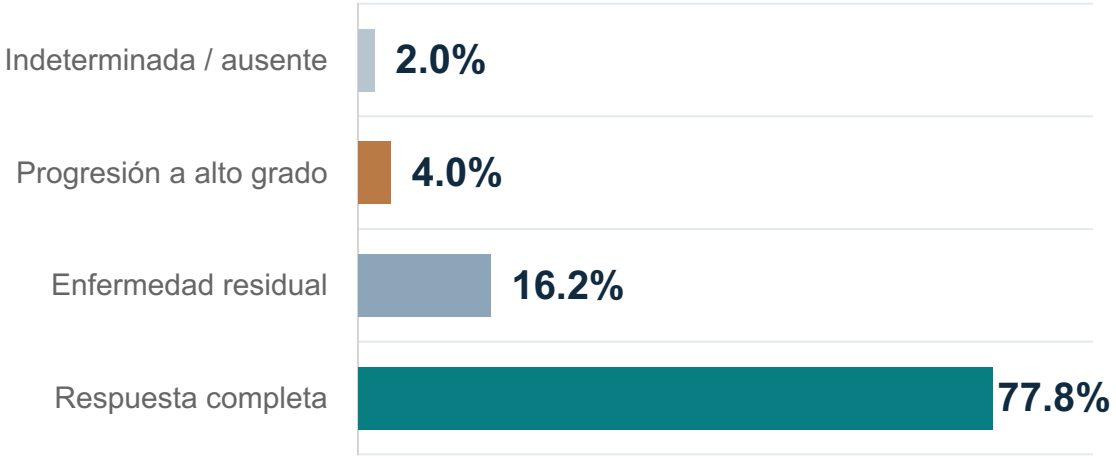
Mitomicina liofilizada de medac + RTGel. Busca simplificar fabricación y reconstitución.

NDA presentada el 17/08/2026 según UroGen.

Fase III, un brazo, N=99. CVNMI recurrente de bajo grado y riesgo intermedio. 75 mg semanales × 6.

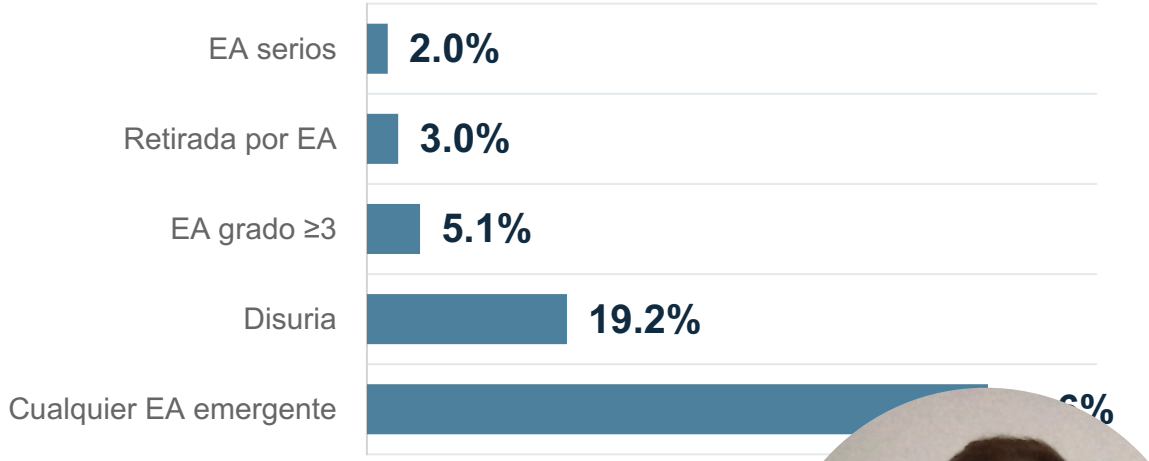
RESPUESTA AL MES 3

RC 77,8% (77/99), IC95% 68,3–85,5



SEGURIDAD

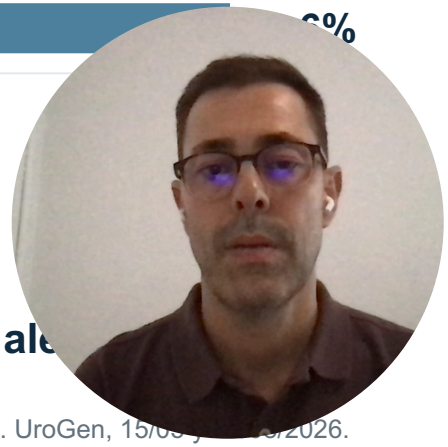
Porcentaje de pacientes (N=99)



Actualización posterior: DoR a 6 meses 94,5% (IC95% 86,1–97,9)

Estimación Kaplan–Meier entre respondedores. Comunicado del promotor del 15/05/2026.

Actividad consistente con UGN-102, sin demostrar equivalencia ni superioridad. Falta comparación ale



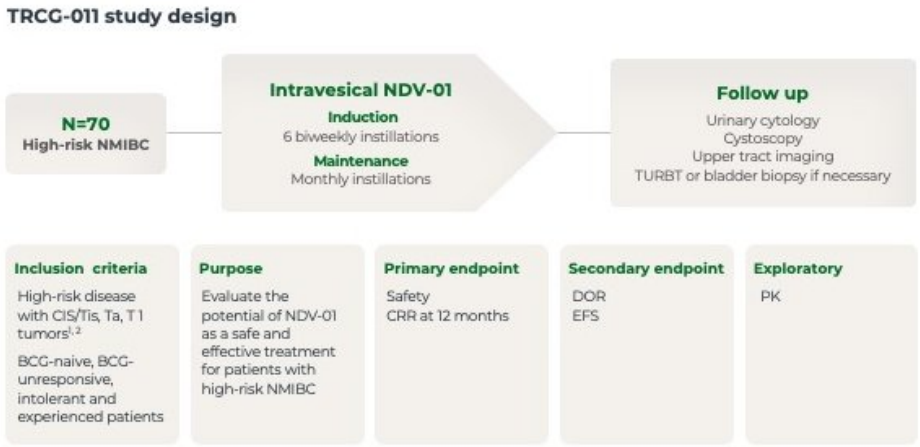
Fuentes: Srivastava et al., póster ASCO 2026 (corte 03/09/2025). UroGen, 15/05 y [illegible]/2026.

NDV-01: respuesta completa a 9 meses

SUO 2025. TRCG-011, prospectivo, abierto y sin comparador

CVNMI de alto riesgo, con o sin BCG previa. 36 tratados en el corte comunicado.

DISEÑO Y TRATAMIENTO

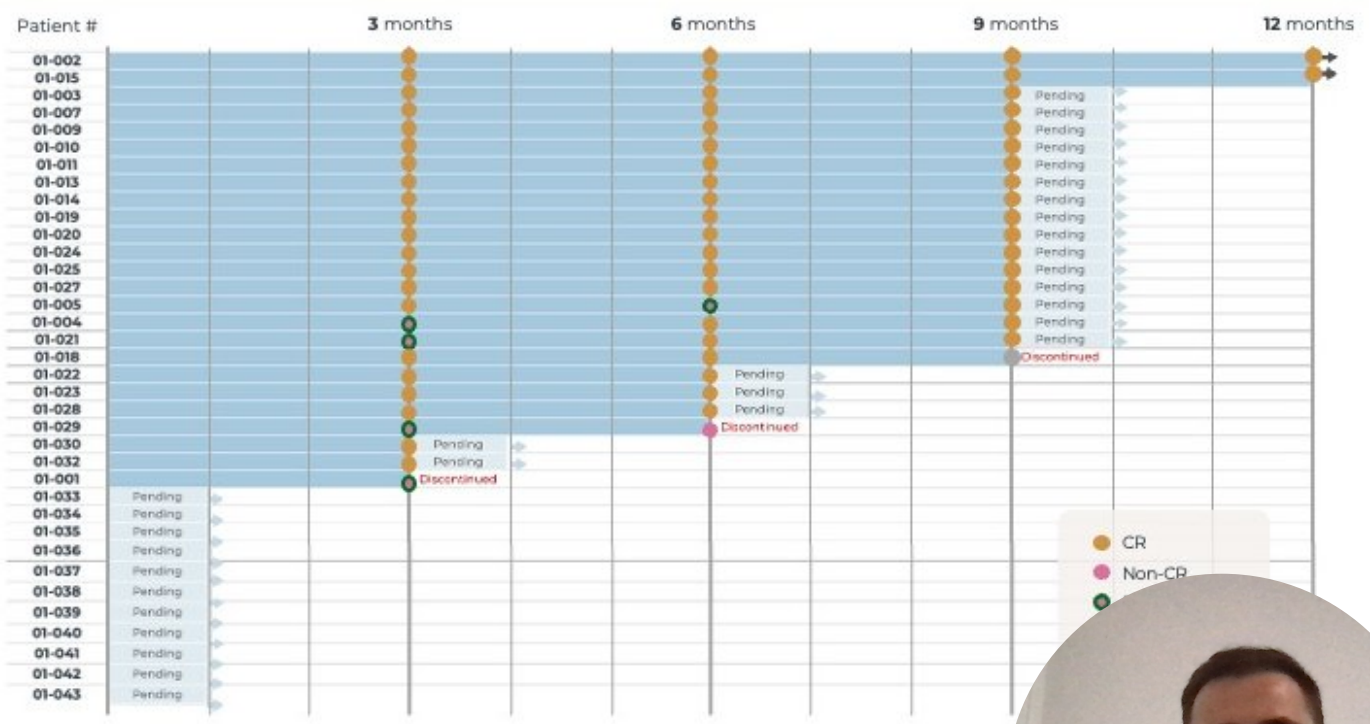


6 instilaciones cada 2 semanas

Mantenimiento mensual hasta el mes 12.
Posible reinducción si no hay RC al mes 3.

Seguridad: EA relacionados 22/36 (61%).
Sin EA relacionados de grado 3 ni retiradas por toxicidad comunicados.

EVOLUCIÓN INDIVIDUAL DE LA RESPUESTA



84% (21/25)
Mes 3

87% (20/23)
Mes 6

85
Mes

Señal preliminar: denominadores variables y cohorte heterogénea. No demuestra superioridad frente a Gem/Doce conven



Fuente: Lotan [illegible] 2025.

BOOST: fase III adyuvante de NDV-01

AUA 2026. REL-NDV01-301, aleatorizado, multicéntrico y abierto

Riesgo intermedio tras RTU. N previsto = 276. Sin resultados clínicos en esta comunicación.

DISEÑO DEL ENSAYO

Pivotal Phase 3, multicenter, open-label study

Cohort 1: Adjuvant Intermediate-Risk NMIBC

JOHNS HOPKINS MEDICINE

Registrational Randomized study of TURBT + NDV-01 vs. TURBT in IR NMIBC

Inclusion Criteria
- IR NMIBC
- IBCG risk factors ≥ 1

Primary Endpoint
- DFS*
- Safety

Secondary Endpoint
- HG-RFS
- PFS
- QOL

Study design

Cohort 1 (Registrational; N=276)

TURBT within 12 weeks (+/- single-dose peri-operative chemotherapy)

Intravesical NDV-01
Induction
6 biweekly instillations
+ maintenance

Observation
Option to have Induction with NDV-01 with recurrence

Follow up to 24 months
Urinary cytology
Cystoscopy
Upper tract imaging
TURBT or bladder biopsy if necessary

*DFS = time from randomization to the date of the first documented recurrence/progression.

Stratification Factors:
- LG vs. HG
- Single-dose peri-operative chemotherapy: yes vs. no

DFS: Disease Free Survival; IR: Intermediate Risk; HG-RFS: High Grade Recurrence Free Survival; PFS: Progression Free Survival; QOL: Quality of Life Metrics; TURBT: Transurethral resection of bladder
IBCG: International Bladder Cancer Group; LG: Low grade; HG: High grade

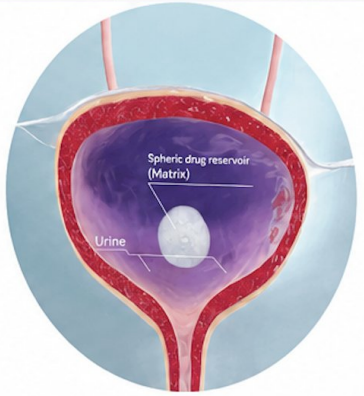
5

Fuente: Kates M. AUA 2026. UroToday, Chavarriaga J.

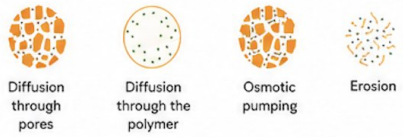
MATRIZ Y LIBERACIÓN DEL FÁRMACO

NDV-01 - Sustained-Release Intravesical Gem/Doce

JOHNS HOPKINS MEDICINE

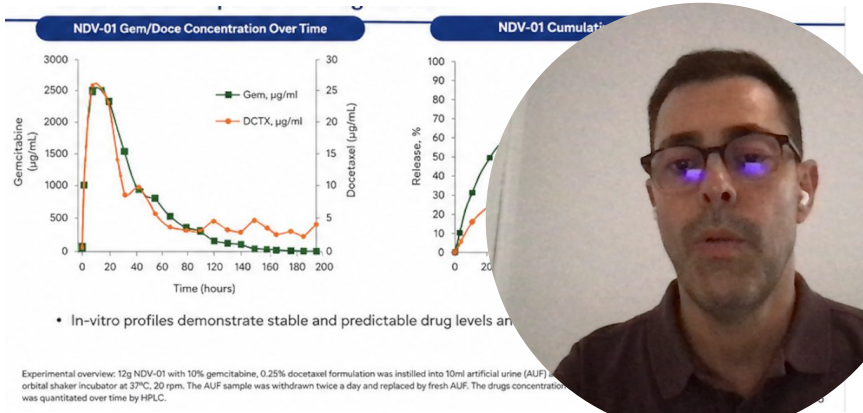


Bladder-targeted matrix enables prolonged tumor exposure to the cytotoxic drug combination via multiple delivery modalities



5

Gemcitabina 1.000 mg + docetaxel 40 mg



Curvas in vitro, no resultados de eficacia clínica

Thermo-sensitive Hydrogel System Enables Sustained Intravesical Delivery of Antibody–Drug Conjugates for Effective Treatment of Non–Muscle-Invasive Bladder Cancer

PRESENTER:
Shi Fu

The Second Affiliated Hospital of Kunming Medical University

BACKGROUND:

Antibody–drug conjugates (ADC) have achieved remarkable success in the treatment of bladder cancer. However, intravesical administration of ADC for non–muscle-invasive bladder cancer (NMIBC) remains limited due to drug instability, short residence time, frequent instillations, and high treatment costs.

MATERIALS & METHODS:

We developed a novel intravesical ADC delivery system based on a thermo-sensitive ALG-NIPAM hydrogel, which is injectable in liquid form at 25 °C and rapidly forms a gel at 37 °C. A Transwell co-culture system was used to mimic the sustained drug release process. The structural stability of the encapsulated monoclonal antibody was evaluated by UV spectroscopy, SDS-PAGE, SEC-HPLC, DLS. HIC-HPLC were used to assess drug–antibody ratio stability, while LC-MS/MS were used to evaluate payload deconjugation. Antitumor activity of disitamab vedotin (DV) encapsulated in ALG-NIPAM hydrogel was assessed in vitro and in vivo.

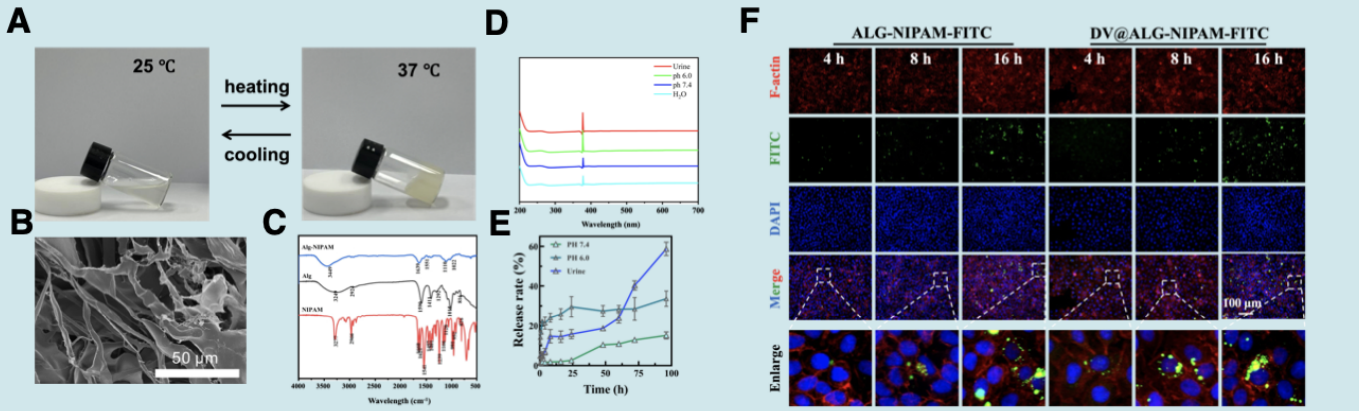


Figure 1. A. Reversible sol-gel phase transition process of ALG-NIPAM hydrogel at 25°Cand 37°C. **B.** SEM images of ALG-NIPAM. **C.** FTIR images of ALG, ALG-NIPAM and DV@ALG-NIPAM. **D.** UV-Vis spectrum of released DV in Urine, ultra-pure water, PBS buffer solution with a pH of 6.0 and 7.4. **E.** Percentages of released DV from DV@ALG-NIPAM over time in the urine, pH 6.0 and 7.4 medium (n=5). **F.** The cellular uptake of ALG-NIPAM and DV@ALG-NIPAM into 5637 cells by fluorescence imaging.

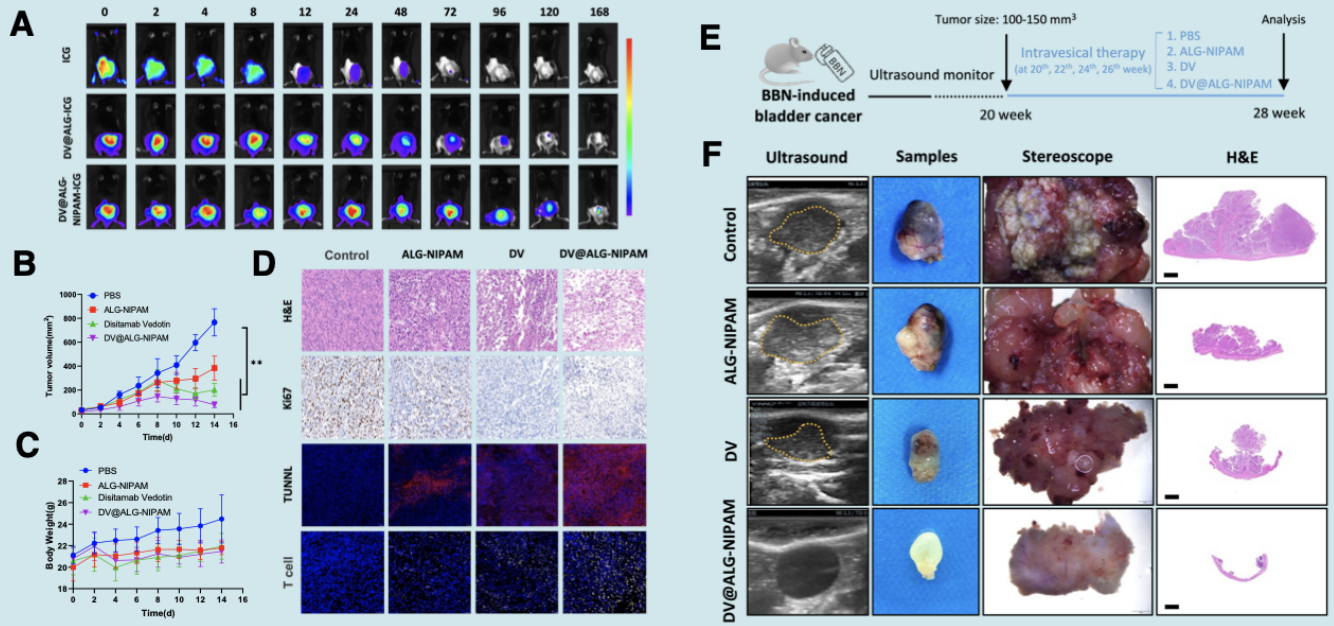


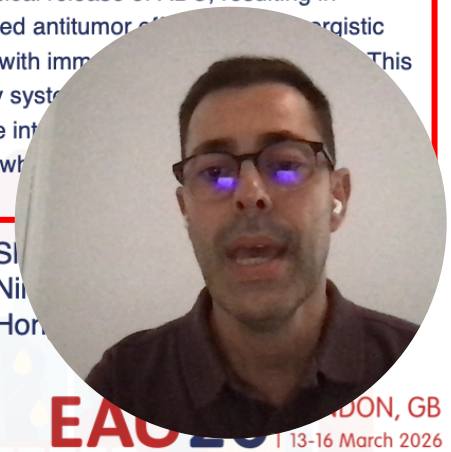
Figure 2. A. The accumulation of ICG in tumor at 0, 2, 4, 8, 12, 24, 48, 72, 96, 120, and 168h post-injection. **B.** The tumor growth curve of CDX tumor bearing mice with different treatments. **C.** The body weight of CDX-bearing mice with different treatments. **D.** H&E, Ki-67, TUNEL and CD8 staining of tumor in CDX tumor. **E.** Schematic illustration of intravesical instillation treatment in the BBN-induced bladder cancer mouse model. **F.** Ultrasound, sample, stereoscopic and H&E images of bladder tumor in mice under different treatments.

RESULTS:

The hydrogel system preserved antibody stability and affinity without inducing aggregation, conformational changes and payload deconjugation in different pH solutions and urine. In urine, drug release peaked at 96 h. FITC-labeled assays showed comparable internalization of DV@ALG-NIPAM and free DV by HER2-positive cells, with uptake increasing over time. DV@ALG-NIPAM exerted antitumor effects against HER2-positive cells equivalent to free DV but with more sustained activity. DV@ALG-NIPAM induced stronger and more durable immunogenic cell death compared to free DV. In vivo, intravesical instillation of DV@ALG-NIPAM in the BBN mice significantly reduced tumor burden relative to free DV. Tumor fluorescence signals persisted for 168 hours in the hydrogel group versus only 8 hours with free DV. Pathological assessment confirmed smaller tumors in the hydrogel group, with no significant differences in body weight or organ toxicity between groups.

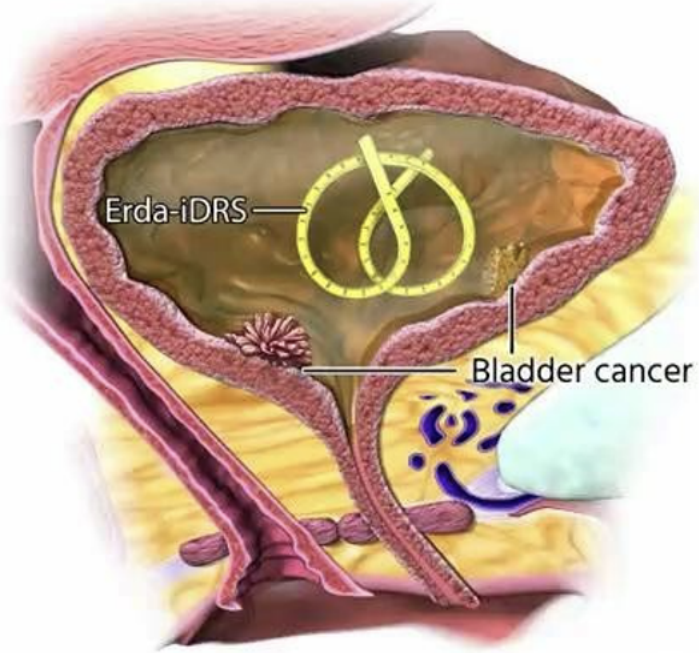
CONCLUSIONS:

We report a novel thermo-sensitive hydrogel system that enables sustained and stable intravesical release of ADC, resulting in enhanced antitumor [illegible]rgistic effects with imm[illegible]This delivery syst[illegible] improve int[illegible] cancer wh[illegible] costs.



First-in-Human, Open-Label, Multicenter Phase 1 Study of Erda-iDRS in *FGFR*-Altered IR NMIBC and HR NMIBC

Erda-iDRS (TAR-210) is an intravesical drug-releasing system designed to provide sustained delivery of erdafitinib to the bladder in 3-month treatment cycles, aiming to limit systemic toxicities



Erda-iDRS is inserted using a urinary placement catheter in a brief in-office procedure



Study Design

NCT05316155

Molecular Eligibility

Flexible molecular eligibility strategy used to detect *FGFR* alterations:

- Local or central fresh/archival **tissue-based** testing by NGS or PCR

—or—

- Central **urine cell-free DNA** NGS testing

Cohort 1 (HR NMIBC)

- Recurrent, high-grade Ta/T1, papillary only, no CIS
- BCG-experienced[a] and not undergoing radical cystectomy
- TURBT with complete resection of all visible disease prior to treatment

Cohort 3 (IR NMIBC)

- Recurrent, history of low-grade only Ta/T1 disease
- **Visible target lesions** prior to treatment (ablation design)

Part 1: Dose Escalation

BOIN[1,2]

- **TAR-210-D** ~4 mg/day
- **TAR-210-B** ~2 mg/day

- Erda-iDRS placement every 3 months

Parts 2 and 3: Dose Expansion

RP2D

- **TAR-210-D** ~4 mg/day
- **TAR-210-C** ~3 mg/day
- **TAR-210-B** ~2 mg/day

- Expansion of all 3 dose levels

Primary End Point

- Safety

Secondary End Points

- PK: plasma and urine concentrations of erdafitinib
- RFS (**Cohort 1**)
- CR rate and duration (**Cohort 3**)[b]

- Treatment for up to 12 months
- Response was assessed every 3 months[c]

Clinical cutoff: Nov 3, 2025

BCG, bacillus Calmette-Guérin; BOIN, Bayesian optimization interval; CIS, carcinoma in situ; CR, complete response; NGS, next-generation sequencing; PCR, polymerase chain reaction; PK, pharmacokinetics; RFS, recurrence-free survival; RP2D, recommended phase 2 dose; TURBT, transurethral resection of bladder tumor.

[a]BCG-experienced is defined as 5 of 6 induction doses with or without maintenance or intolerant of BCG.

[b]CR was defined as absence of malignant tumors by cystoscopy with negative urine cytology.

[c]Response assessments were every 3 months in year 1 and year 2, then every 6 months in year 3.

1. Liu S, Yuan Y. *J R Stat Soc Ser C Appl Stat*. 2015;64:507-523. 2. Yuan Y, et al. *Clin Cancer Res*. 2016;22:4291-4301.

Presented by A Vilaseca at the 41st Annual EAU Congress; March 13-16, 2026; London, UK



Patient Characteristics and Treatment Exposure

Characteristic	Cohort 1 (HR NMIBC) (N=26)	Cohort 3 (IR NMIBC) (N=62)
Median age, years (range)	72.5 (37-90)	68.5 (41-89)
Male, n (%)	19 (73.1)	48 (77.4)
Race, n (%)		
White	21 (80.8)	38 (61.3)
Asian	5 (19.2)	24 (38.7)
Tumor stage, n (%)		
Ta	21 (80.8)	60 (96.8)
T1	5 (19.2)	2 (3.2)
Tumor grade, n (%)		
Low grade	0	62 (100)
High grade	26 (100)	0
Number of tumors, n (%)[a]		
1	13 (50.0)	31 (50.8)
2	2 (7.7)	12 (19.7)
3	4 (15.4)	5 (8.2)
4	4 (15.4)	5 (8.2)
≥5	3 (11.5)	8 (13.1)

Characteristic	Cohort 1 (HR NMIBC) (N=26)	Cohort 3 (IR NMIBC) (N=62)
ECOG performance status, n (%)		
0	17 (65.4)	52 (83.9)
1	6 (23.1)	7 (11.3)
2	3 (11.5)	3 (4.8)
Prior cancer treatment, n (%)		
Surgery or procedure	26 (100)	62 (100)
Intravesical BCG	26 (100)	14 (22.6)
Intravesical chemotherapy	6 (23.1)	33 (53.2)
Systemic therapy	1 (3.8)	0
Prior TURBT or other ablative procedure, n (%)[b]		
1	0	14 (22.6)
2	1 (3.8)	18 (29.0)
3	10 (38.5)	9 (14.5)
4	6 (23.1)	10 (16.1)
≥5	9 (34.6)	11 (17.7)

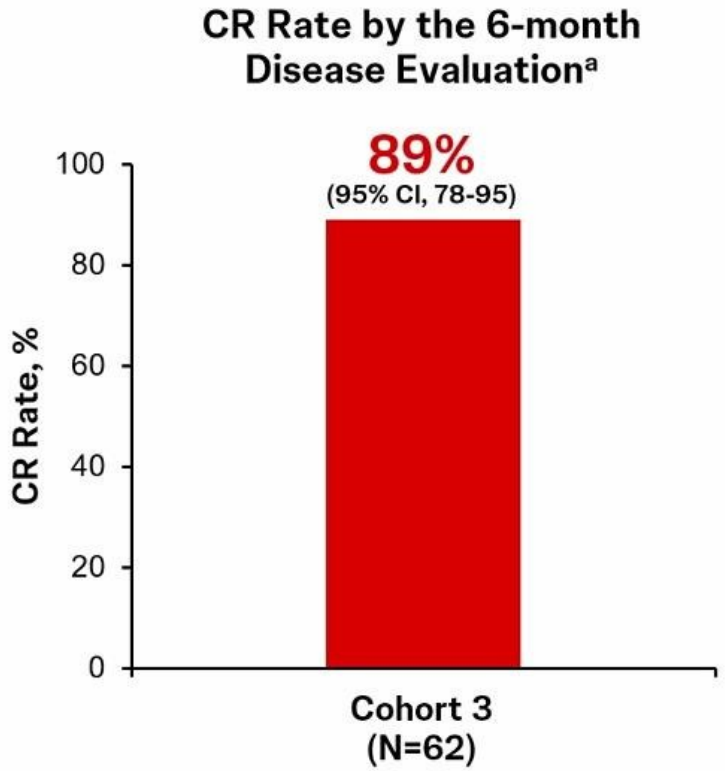
- Median treatment duration was 11.9 months (range, 3-15) in Cohort 1 and 11.8 months (range, 0.1-15) in Cohort 3

[a]In Cohort 1, number of tumors prior to required TURBT (n=26). In Cohort 3, number of tumors at time of screening cystoscopy (n=61 patients with available data).
[b]Surgeries/procedures were counted only once on a given date and included the following: TURBT, fulguration, cauterization, or laser photoablation.

Presented by A Vilaseca at the 41st Annual EAU Congress; March 13-16, 2026; London, UK



Erda-iDRS Showed a High CR Rate as Ablative Therapy in Patients With IR NMIBC



	Cohort 3 (n=55)
Median CR duration (95% CI)[a]	**18 months** (14-25)
Median follow-up in responders (range)[a]	18 months (15-21)

- 81% of patients had achieved CR at the 3-month disease evaluation
- 49% of responders were in ongoing follow-up and remained in CR at the clinical data cutoff

[a]Kaplan-Meier estimate.

Presented by A Vilaseca at the 41st Annual EAU Congress; March 13-16, 2026; London, UK



MoonRISe-2: Phase 2 Study of Erda-iDRS as Ablative Treatment in Recurrent IR NMIBC

Key eligibility criteria

- Adults (aged ≥18 years)
- Histologically confirmed **recurrent IR NMIBC**, defined as Ta LG/grade 1 *or* Ta LG/grade 2
  - Must have visible disease (≥5 mm) in the bladder and must have not undergone complete/debulking resection or other ablative procedure of bladder tumors following current diagnosis
- Must submit tissue and urine for *FGFR* testing
- Must have **≥1 IBCG risk factor**
  - Multiple Ta LG tumors
  - Solitary LG tumor ≥3 cm
  - Early recurrence (<1 year)
  - Frequent recurrences (>1 per year)
  - Recurrence after prior adjuvant intravesical treatment

→

Erda-iDRS
(N =140)
Q12W for ~1 year[a]

Primary end point

- Overall CR rate[b]

Secondary end points

- Duration of CR (key)
- CR at 3 months (key)
- TURBT-free survival
- Safety and tolerability
- Patient-reported outcomes

NCT05316155

- MoonRISe-2 is a phase 2 expansion of the first-in-human study in recurrent IR NMIBC
- Response to treatment will be assessed based on cystoscopic visualization (Q12W) and biopsy (if needed)
- The study began in April 2025. Enrollment is complete, with 140 patients enrolled at 52 sites across 7 countries



LG, low-grade; Q12W, every 12 weeks.
[a]4 cycles in absence of disease worsening, recurrence, or unacceptable toxicity and if in CR after cycle 2.
[b]Overall CR rate is defined as negative cystoscopy or positive cystoscopy with a biopsy that is negative for malignancy. If urine cytology is performed, findings that are negative for malignancy or atypical urothelial cells are considered compatible with CR. Patients with non-CR/non-progressive disease at the end of cycle 1may continue with an additional cycle of erda-iDRS treatment; if patients do not achieve a CR at the end of cycle 2 (around week 24), they should discontinue treatment.

Presented by CM Pieczonka at the 121st AUA Annual Meeting; May 15-18, 2026; Washington, DC, USA

Patient Baseline Characteristics

Characteristics	Erda-iDRS (N=140)
Age, years, median (range)	73.0 years (43-93)
Sex, male, n (%)	104 (74.3%)
Race, White, n (%)[a]	109 (77.9%)
Recurrent disease, n (%)	140 (100%)
ECOG PS 0, n (%)	118 (84.3%)
Any individual tumors >3 cm, n (%)[b]	12 (8.6%)
No. of lesions, n (%)[c]	
1-3	90 (65.2%)
≥4	48 (34.8%)

Characteristics	Erda-iDRS (N=140)
Sum of lesion(s) longest axes, n (%)[c]	
5 to <10 mm	38 (27.5%)
≥10 to <30 mm	71 (51.4%)
≥30 to <50 mm	16 (11.6%)
≥50 mm	13 (9.4%)
Sum of lesion sizes, median (range), mm[c]	14.5 mm (5-190 mm)
Prior intravesical therapy, n (%)[d]	58 (41.4%)
BCG	26 (18.6%)
Mitomycin C	20 (14.3%)
Gemcitabine	14 (10.0%)
Epirubicin	
No. of prior cancer-related surgeries, median (range)	
TURBT[e]	
Bladder biopsy[f]	
Fulguration[g]	



Clinical cutoff: April 7, 2026.
ECOG PS, Eastern Cooperative Oncology Group performance status.
[a]Other races included Asian (17.1%), Black or African American (4.3%), and Native Hawaiian or Other Pacific Islander (0.7%). [b]n=139. [c]n=138. [d]Other intravesical therapies included pirarubicin (2.1%), cabergoline (1.4%), cretostimog… grenadenorepvec (0.7%), and doxorubicin (0.7%). [e]n=134. [f]n=32. [g]n=15.

MoonRISe-1 An Open-Label, Multicenter, Randomized Phase 3 Study to Evaluate Efficacy and Safety of TAR-210 Versus Intravesical Chemotherapy in Patients With *FGFR*-altered, Low-Grade Intermediate Risk NMIBC

Key eligibility criteria

- Adults (aged ≥18 years)
- Histologically confirmed **IR NMIBC**:
  - Ta LG/grade 1
    - Recurrent or
    - Primary: Multifocal, or ≥3 cm

    —*or*—
  - Ta LG/grade 2
    - Primary
    - Recurrent
- With **≥1 risk factor**[a]
- *FGFR2/3* alterations by central or local tissue or urine testing

Stratification factors

- Anticipated choice of intravesical chemotherapy
- Newly diagnosed versus recurrent disease
- Cystoscopic assessment method (white light vs photodynamic diagnostics)

1:1
(N≈540)
R

TAR-210
(n≈270)
(Q12W for 1 year)

Investigator's choice of intravesical chemotherapy (n≈270)
MMC or gemcitabine
(QW for 4 to 6 doses [induction]
and maintenance for 6 months to 1 year)

Primary end point

Disease-free survival[b]

Key secondary end points

Time to next treatment

High grade recurrence-free survival

Rate of diagnostic and therapeutic urological interventions

Safety and tolerability

- All visible papillary disease must be fully resected prior to randomization
- Assessments of recurrence or progression include urine cytology, cystoscopy, for cause TURBT or biopsy of bladder lesions, ultras
- The follow-up phase for patients meeting the primary endpoint is up to ≈5 years



LG, low grade; MMC, mitomycin C; QW, every week; Q12W, every 12 weeks; R, randomized; TURBT, transurethral resection of bladder tumor.
[a]Risk factors include multiple Ta LG tumors, tumors >3 cm, early (≤1 year) recurrence, frequent (>1 per year) recurrences, or recurrence after intravesical chemotherapy. [b]Disease-free survival defined as time from randomizatio
first documented recurrence of any-grade NMIBC, disease progression, or death from any cause, whichever occurs first.

Presented by R Li at the 119th AUA Annual Meeting; May 3-6, 2024; San Antonio, TX, USA

MoonRISe-3: Phase 3 Study of TAR-210 vs Intravesical Chemotherapy in Patients With BCG-treated, *FGFR*-altered Papillary-only HR NMIBC

Key eligibility criteria

- Adults (aged ≥18 years)
- Histologically confirmed **papillary-only HR NMIBC**:
  - High-grade Ta
    —or—
    Any T1 (no CIS)
  - Recurrent after BCG
    —or—
    Intolerant of BCG
- ECOG performance status of ≤2
- Susceptible *FGFR* mutation or fusion by urine or tumor tissue testing

Stratification factors

- T stage (high-grade Ta or any T1)
- Prior BCG treatment (BCG unresponsive, experienced, or intolerant)
- Choice of intravesical chemotherapy

1:1
(N≈220)

R

TAR-210
(n≈110)
Q12W for 2 years

Investigator's choice of single-agent intravesical chemotherapy
(n≈110)
MMC or gemcitabine
QW for 6 doses (induction) followed by Q4W for 1-2 years (maintenance)

Primary end point

- Disease-free survival[a]

Key secondary end points

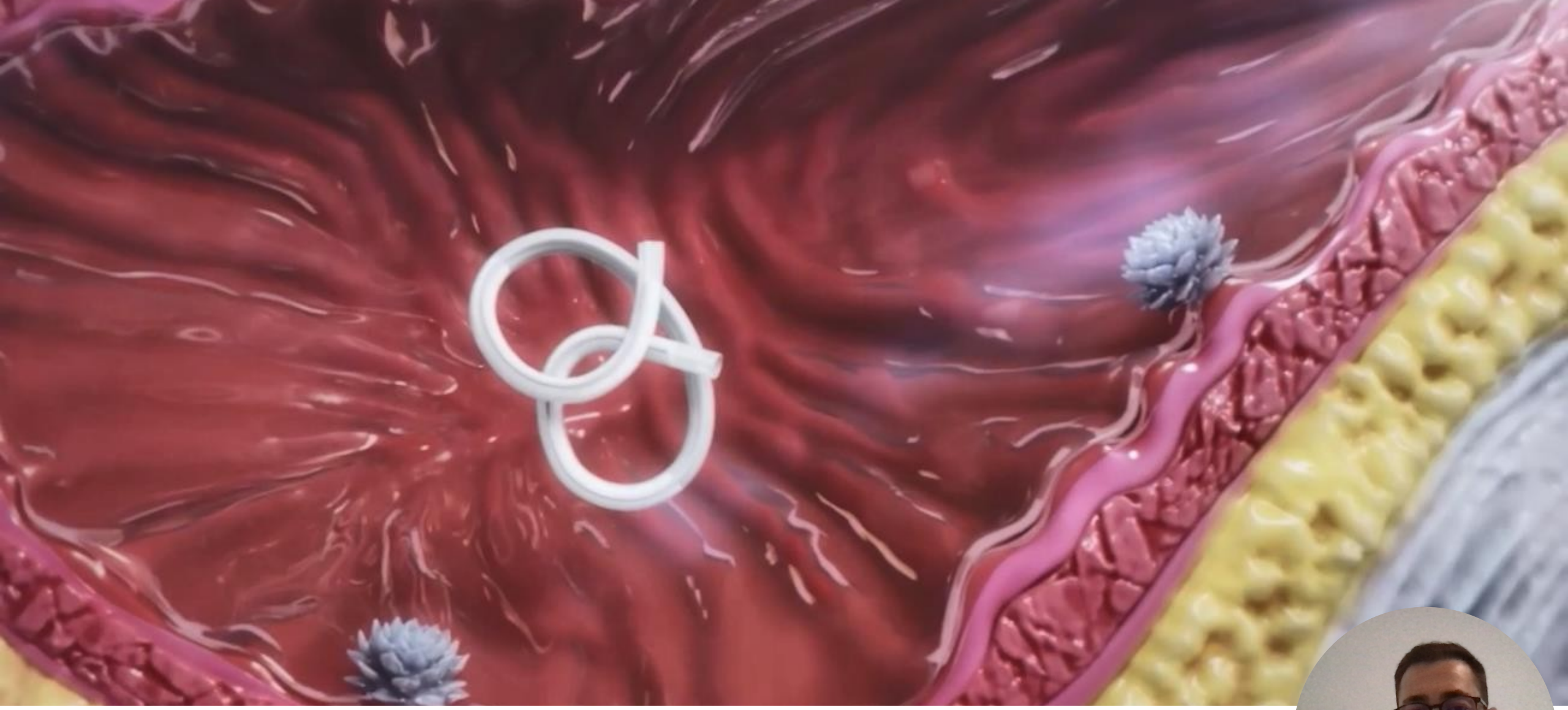
- Recurrence-free survival
- Time to next intervention
- Time to disease worsening
- Time to progression
- Overall survival
- Safety and tolerability



- Assessments of recurrence or progression will be based on central urine cytology, bladder biopsy, and imaging results
- After a positive interim analysis, the IDMC may recommend a crossover option for patients with recurrence in the intravesica arm

[a]Disease-free survival defined as time from randomization to first documented recurrence of HR NMIBC (high-grade Ta, any T1, or CIS), disease progression, or death from any cause, whichever occurs first.
IDMC, independent data monitoring committee; MMC, mitomycin C; NMIBC, non–muscle-invasive bladder cancer; Q12W, every 12 weeks; Q4W, every 4 weeks; QW, every week; R, randomized.

Presented by N Shore at the 120th AUA Annual Meeting; April 26-29, 2025; Las Vegas, NV, USA



TAR-200 is a novel targeted releasing system designed for sustained, local delivery of



SunRISe-3 (NCT05714202) a Phase 3, Open-Label, Multicenter Randomized Study

Key eligibility criteria

- Patients with histologically confirmed HR NMIBC (high grade Ta, any T1, or CIS)
- BCG naive (no prior BCG or last exposure >3 years prior to randomization)

Additional criteria:

- Aged ≥18 years
- ECOG PS of 0, 1, or2
- All visible papillary disease must be fully resected (absent) prior to randomization and documented at baseline cystoscopy
- Local urine cytology at screening must be negative or atypical for high-grade urothelial carcinoma in patients with papillary-only disease
- All adverse events associated with any prior surgery and/or intravesical therapy must have resolved to CTCAE v5.0 grade <2 prior to date of randomization

1:1:1 (N≈1050) R

Group A (n≈350)
TAR-200 + cetrelimab[a]

Group C (n≈350)
TAR-200

Group B (n≈350)
BCG

Primary end point

Event-free survival

Time from randomization to first occurrence of:

- **High-risk disease recurrence**
- **Disease progression[b]**
- **Any-cause death**

For patients with CIS, persistent disease at 6 months is also an EFS event

Secondary end points

- Overall CR rate (CIS only)[c]/duration of CR[d]
- Recurrence-free survival
- Time to progression
- Overall survival
- Cancer-specific survival
- Safety and tolerability
- Patient-reported ou



CR, complete response, CTCAE, Common Terminology Criteria for Adverse Events; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival.
[a]Cetrelimab is an anti–programmed death-1 antibody. [b]Progression is defined as stage increase from Ta to T1 or from CIS to T1 or progression to MIBC (T≥2) or to lymph node (N+) or distant (M+) disease (whichever occurs firs
[c]Proportion of patients with CIS who have no presence of high-risk disease at 6 months. [d]Time from first CR achieved to first evidence of recurrence, progression, or any-cause death, whichever occurs first.

Presented by SS Chang at the 119th AUA Annual Meeting; May 3-6, 2024; San Antonio, TX, USA

Brazos, duración y eficacia de los cuatro ensayos

CVNMI de alto riesgo, BCG-naïve. Duraciones previstas de tratamiento

ESTUDIO	ALEATORIZACIÓN Y TRATAMIENTO	RESULTADOS FRENTE AL CONTROL
ALBAN N = 517	R 1:1 **E** **BCG I+M 12 meses + atezolizumab 12 meses** C BCG I+M 12 meses	**HR EFS 0,98 (IC95% 0,71–1,36)** Sin beneficio demostrado
POTOMAC N = 1.018	R 1:1:1 **E1** **BCG I+M 24 meses + durvalumab 12 meses** **E2** **BCG I 6 semanas + durvalumab 12 meses** C BCG I+M 24 meses	**E1: HR DFS 0,68 (0,50–0,93)** A 3 años: 81,8% vs 77,4% (+4,4 pp) E2: sin superioridad demostrada
CREST N = 1.055	R 1:1:1 **E1** **BCG I+M 24 meses + sasanlimab 24 meses** **E2** **BCG I 6 semanas + sasanlimab 24 meses** C BCG I+M 24 meses	**E1: HR EFS 0,68 (0,49–0,94)** A 3 años: 82,1% vs 74,8% (+7,3 pp) E2: HR 1,16 (0,87–1,55)
SUNRISE-3 N = 1.135	R 1:1:1 **E1** **TAR-200 24 meses + cetrelimab 12 meses*** **E2** **TAR-200 24 meses*** C BCG I+M 24 meses (tercer año opcional)	**Sin resultados publ** Desenlace primario: E1 y E2 frente a BC

I: inducción semanal ×6. M: mantenimiento intermitente. E: experimental. C: control. pp: puntos porcentuales.

HR <1 favorece al experimental. Los desenlaces y las poblaciones difieren: no es una comparación directa entre fármacos.



Fuentes: sesión EAU26 y publicaciones ALBAN, POTOMAC y CREST. SUNRISE-3:

SUNRISE-3: preguntas y respuestas

Fase III, CVNMI de alto riesgo BCG-naïve	Comparación de estrategias
(A) TAR-200 + cetrelimab	Quimioterapia intravesical sostenida + anti-PD-1
(B) BCG: inducción + mantenimiento	Control activo, mantenimiento hasta 2 años, opcional 3
(C) TAR-200 solo	Estrategia local sin inmunoterapia sistémica

1. ¿Puede una estrategia local superar a BCG?

EFS absoluta y durabilidad, separando recurrencia, progresión y muerte.

2. ¿Cuánto aporta añadir cetrelimab?

Beneficio adicional frente a toxicidad inmunitaria. La comparación A–C exige soporte estadístico.

3. ¿En qué pacientes y con qué beneficio neto?

CIS / T1 / Ta, progresión a invasión muscular, supervivencia, síntomas y calidad de vida.

Quedará pendiente: comparación directa con BCG + ICI



NCT05714202. Registro actualizado 25/09/2026: N=1.135, activo sin reclutamiento. Desenlace primario: EFS. Sin resultados publicados

Reflexión Final

Existe una gran interés y desarrollo biotecno-farmacológico en el tratamiento y administración intravesical, mantener un equilibrio entre una correcta **metodología científica** con **beneficio e impacto clínico demostrable** y la **sostenibilidad** del sistema sanitario es fundamental para generar el valor necesario para la incorporación de estas innovaciones en práctica clínica

