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GUARD INTERNATIONAL SYMPOSIUM

GU-Alliance for Research and Development

PRESENCIAL RETRANSMITIDO EN DIRECTO
FACE-TO-FACE AND LIVE STREAMING



16-18 SEPTIEMBRE 2026

Espacio Maldonado, Madrid

Manejo actual del CVNMI de alto riesgo: Manejo intravesical

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Disclosures

None

BCG since 1976, but why?

Efficacy

Tolerable

Manageable toxicity

Intravesical

Unexpensive

Current research landscape in HR NMIBC

Table 1 – Comparative designs of the largest trials assessing novel agents in BCG-naïve high-risk non-muscle invasive bladder cancer

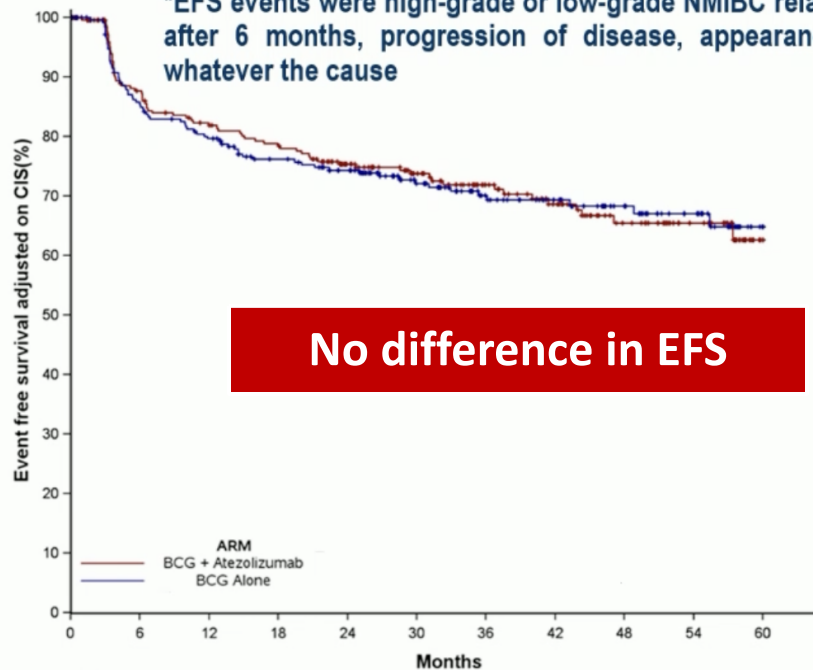
Study title	POTOMAC	ALBAN	KEYNOTE-676 (cohort B)	CREST	SunRISe-3	BRIDGE
Study ID	NCT03528694	NCT03799835	NCT03711032	NCT04165317	NCT05714202	NCT05538663
Intervention	Durv + BCG (I + M) vs Durv + BCG (I) vs BCG (I + M)	Atezolizumab + BCG (I + M) vs BCG (I + M)	Pembro + BCG (M) vs Pembro + BCG (reduced M) vs BCG (I + M)	Sasanlimab + BCG (I + M) vs Sasanlimab + BCG (I) vs BCG (I + M)	TAR-200 vs Cetrelimab + TAR-200 vs BCG (I + M)	Sequential Gem/ Doc vs BCG (I + M)
Administration route	Durvalumab: i.v. BCG: IVS	Atezolizumab: i.v. BCG: IVS	Pembro: i.v. BCG: IVS	Sasanlimab: SC BCG: IVS	Cetrelimab: i.v. TAR-200: IVS BCG: IVS	Gem/Doc: IVS BCG: IVS
BCG M	24 mo	12 mo	18 mo	24 mo	24 mo (optional 36 mo)	36 mo
Participants (n)	1018	516	975	1070	1050	870
Primary EP	DFS	RFS	EFS	EFS	EFS	EFS
Key secondary EPs	OS, QoL, DSS, QoL	PFS, OS, CR, QoL	OS, CRR, RFS, DSS, TTC, DOR, safety/tolerability	OS, CR, duration of CR, TTC, QoL	RFS, OS, MFS, TTC, TTP, safety, QoL	QoL, safety, toxicity, PFS, CFR
BCG strain	OncoTICE	Medac, OncoTICE	OncoTICE	Various, including OncoTICE	BCG Culture	OncoTICE
Current status	Active, NRC	Active, NRC	Recruiting	Active, NRC	Recruiting	Recruiting
eSCD	September 2025	February 2028	October 2028	December 2027	May 2030	October 2030

BCG = bacillus Calmette-Guérin; CFR = cystectomy-free rate; CR = complete response; CRR = complete response rate; DFS: disease-free survival; DOR: duration of response; DSS: disease-specific survival; Durv = durvalumab; EFS = event-free survival; EP = endpoint; eSCD = estimated study completion date; Gem/Doc = gemcitabine + docetaxel; I = induction; i.v. = intravenous; IVS = intravesical; M = maintenance; MFS = metastasis-free survival; NRC = not recruiting; OS = overall survival; Pembro = pembrolizumab; PFS = progression-free survival; QoL = quality of life; RFS = recurrence-free survival; SC = subcutaneous; TTC = time to cystectomy; TTP = time to progression.

ALBAN (Atezolizumab + BCG)

ALBAN – Analysis of EFS* (primary endpoint, ITT population)

*EFS events were high-grade or low-grade NMIBC relapse, persistence of CIS after 6 months, progression of disease, appearance of UTUC, or death whatever the cause



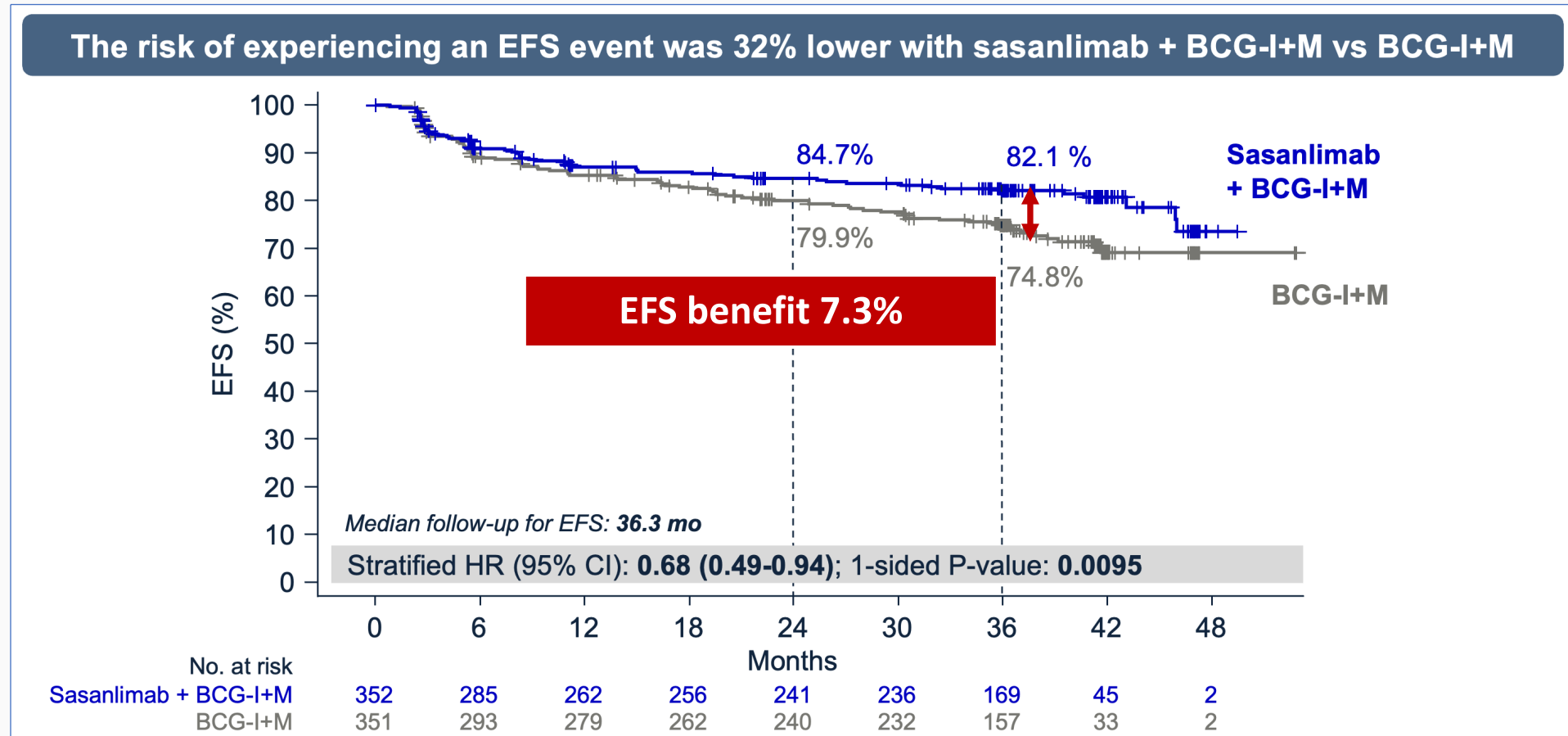
No. at Risk (No. Cumulative Events)												
BCG + Atezolizumab	262 (0)	212 (30)	193 (44)	184 (52)	157 (59)	129 (62)	97 (65)	78 (69)	55 (72)	35 (72)	2 (73)	
BCG Alone	255 (0)	208 (36)	190 (50)	169 (58)	155 (62)	116 (66)	90 (69)	73 (70)	55 (71)	38 (72)	6 (73)	

	BCG + atezolizumab	BCG
EFS events, n / N	73 / 262	73 / 255
Median EFS (95% CI), mo	NE	NE
Adjusted HR (95% CI), mo	0.98 (0.71-1.36); <i>P</i> =0.9106	
<u>Type of events, n (%)</u>		
Local recurrence	62 (84.9%)	60 (82.2%)
Locoregional recurrence	3 (4.1%)	3 (4.1%)
Distant recurrence	1 (1.4%)	2 (2.7%)
UTUC	0 (0.0%)	2 (2.7%)
Death from any cause	7 (9.6%)	6 (8.2%)

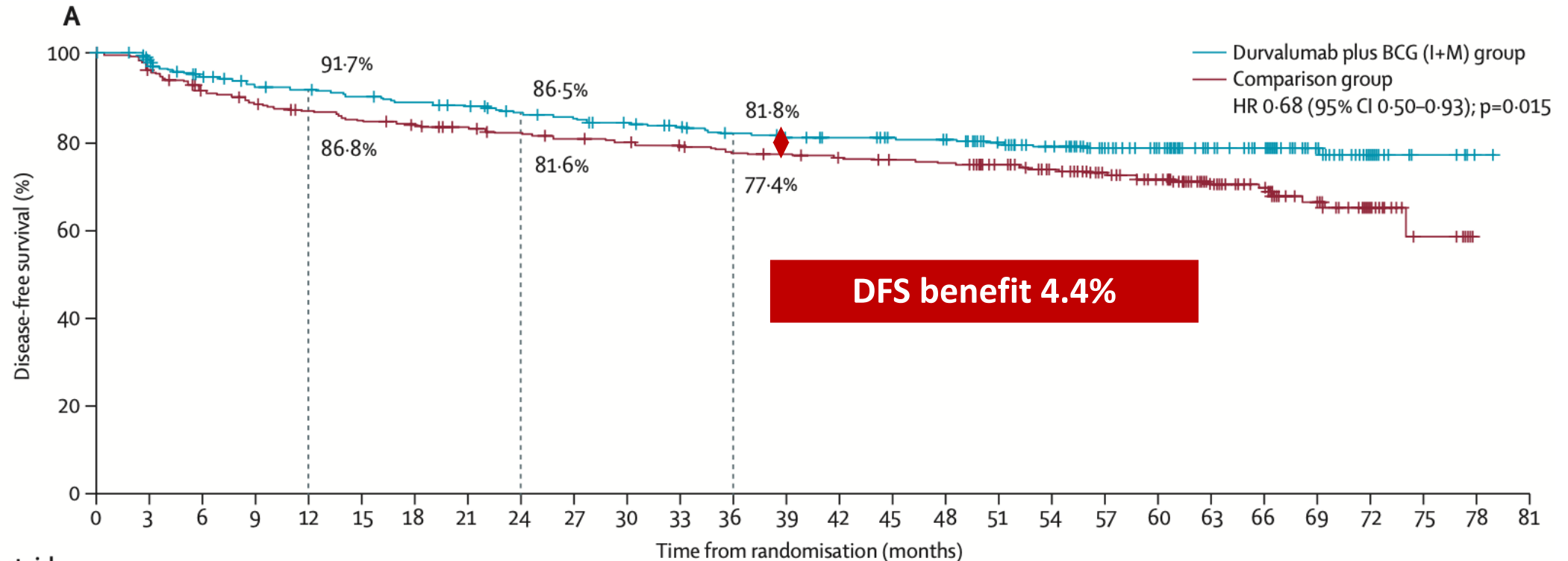
HR was adjusted on the presence of CIS at inclusion

CI, Confidence Interval; CIS, Carcinoma In Situ; EFS, Event-Free Survival; HR, Hazard Ratio; ITT, Intent To Treat; NE not evaluable

CREST (Sasanlimab + BCG)

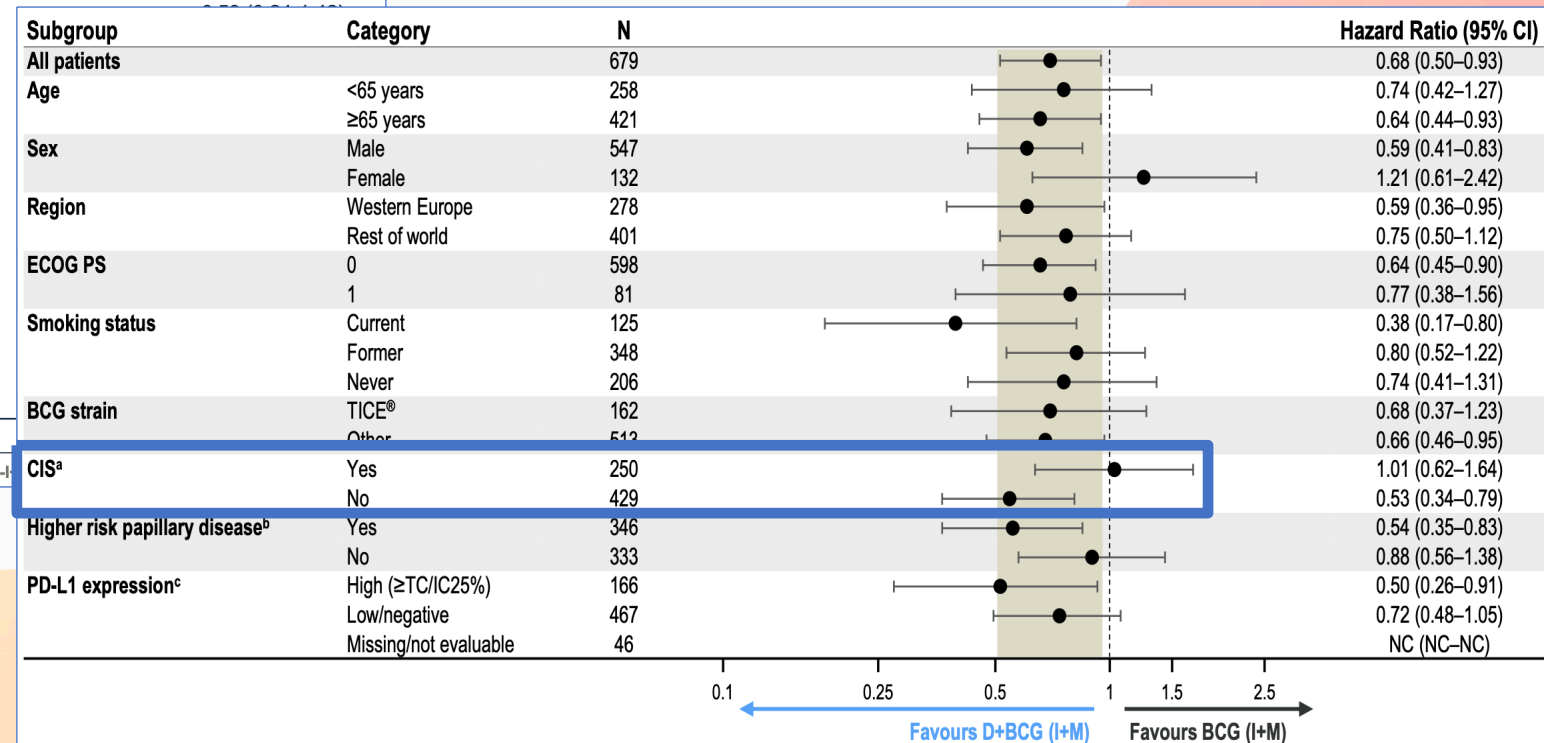
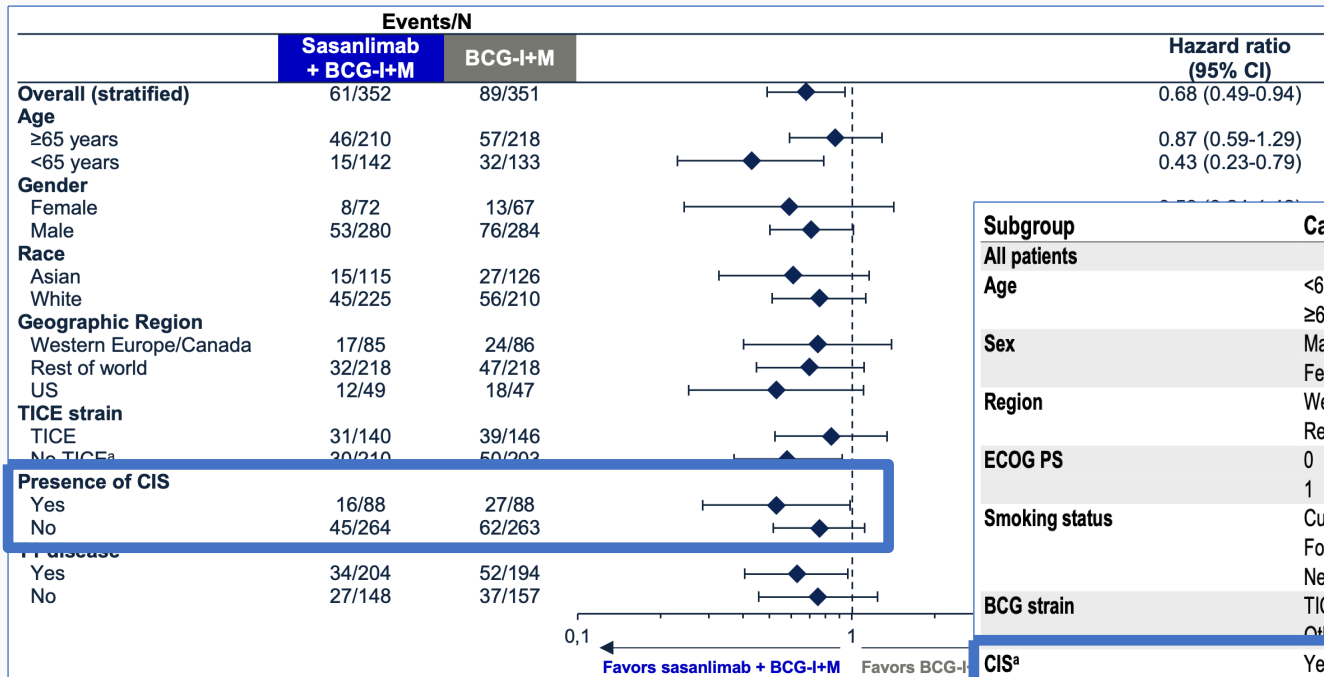


POTOMAC (Durvalumab + BCG)



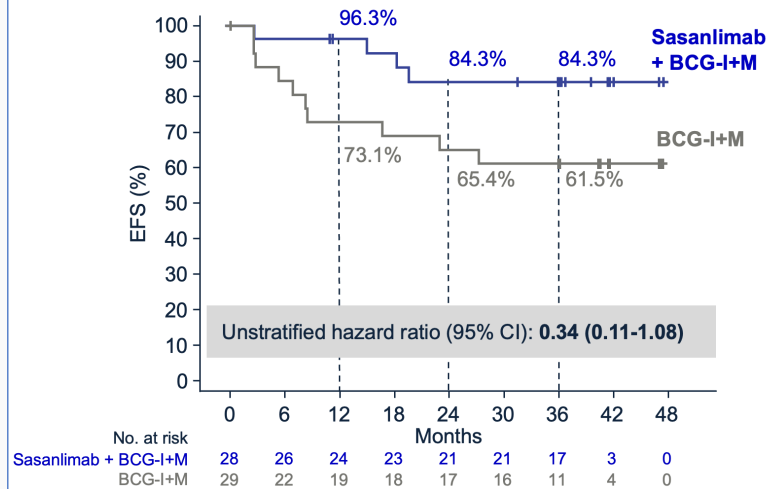
	Number at risk (censored)																											
Durvalumab plus BCG (I+M) group	339	321	304	292	289	283	278	273	262	257	250	245	235	229	226	222	220	204	195	156	145	108	94	57	26	9	1	0
	(0)	(11)	(18)	(22)	(23)	(24)	(25)	(27)	(34)	(35)	(38)	(41)	(47)	(50)	(53)	(57)	(58)	(72)	(79)	(117)	(128)	(165)	(179)	(216)	(246)	(263)	(271)	(271)
Comparison group	340	322	303	292	283	276	271	265	258	254	249	244	237	235	231	227	225	209	196	160	150	101	86	50	20	8	0	0
	(0)	(4)	(8)	(9)	(13)	(13)	(15)	(19)	(21)	(22)	(24)	(27)	(29)	(30)	(32)	(34)	(34)	(49)	(59)	(93)	(100)	(147)	(161)	(194)	(223)	(234)	(241)	(241)

Subgroups: CIS



Subgroups: Very high risk

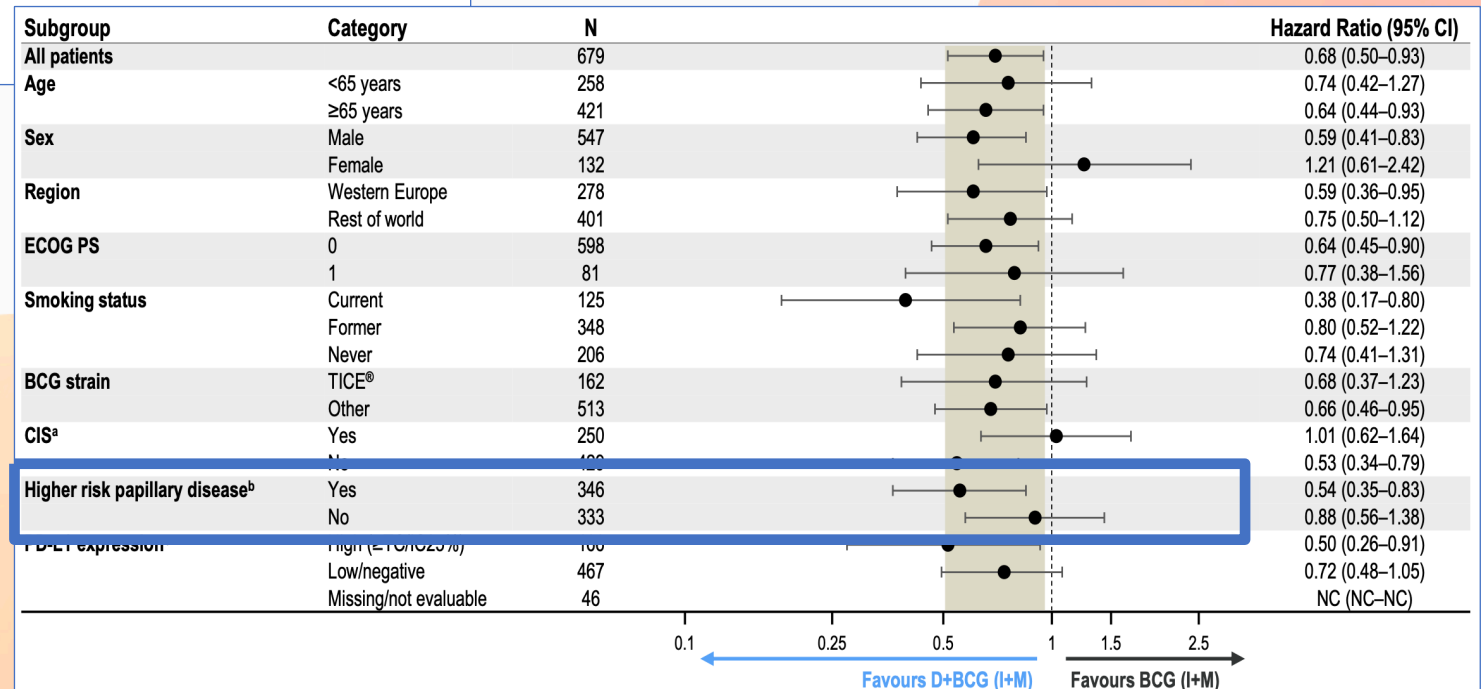
The risk of experiencing an EFS event was 66% lower with sasanlimab + BCG-I+M vs BCG-I+M



	Sasanlimab + BCG-I+M (n=28)	BCG-I+M (n=29)
Patients with EFS event, n (%)	4 (14.3)	10 (34.5)

VHR was defined as high-grade Ta and CIS with all 3 risk factors, high-grade T1 without CIS with all 3 risk factors, or high-grade T1 and CIS with ≥ 1 risk factor. Risk factors were age >70 years, multiple papillary tumors, and tumor diameter ≥ 3 cm.

Higher risk papillary disease was defined as T1G3/T1HG, or multiple AND recurrent AND tumor diameter ≥ 3 cm.



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Pivotal studies for IO in BCG naïve

ALBAN

Atezolizumab + BCG (i+m)
vs
BCG (i+m) 12mo

No benefit in EFS

CREST

Sasanlimab + BCG (i+m)
vs
Sasanlimab + BCG (i)
vs
BCG (i+m) 24mo

Arm A: EFS benefit 7.3%

Arm B: No benefit in EFS

POTOMAC

Durvalumab + BCG (i+m)
vs
Durvalumab + BCG (i)
vs
BCG (i+m) 24mo

Arm A: DFS benefit 4.4%

Arm B: No benefit in DFS

ALBAN (Atezolizumab + BCG)

Table 2. Safety summary (safety population)

Events, <i>n</i> (%)	BCG (<i>N</i> = 250)	BCG + atezolizumab (<i>N</i> = 255)
Any AEs	235 (94.0)	252 (98.8)
Grade ≥ 3 AEs	59 (23.6)	102 (40.0)
Serious AEs	53 (21.2)	97 (38.0)
Any TRAEs	189 (75.6)	240 (94.1)
Grade ≥ 3 TRAEs	22 (8.8)	58 (22.7)
Serious TRAEs	21 (8.4)	60 (23.5)
TRAEs leading to dose interruption	19 (7.6)	47 (18.4)
TRAEs leading to withdrawal	22 (8.8)	73 (28.6)
BCG withdrawal only	22 (8.8)	32 (12.5)
Atezolizumab withdrawal only	0 (0.0)	41 (16.1)
BCG + atezolizumab	0 (0.0)	8 (3.1)

CREST (Sasanlimab + BCG)

Table 2 | TRAEs by preferred term and maximum CTCAE grade during the on-treatment period in the safety analysis set

	Sasanlimab + BCG-I+M (N=350)		Sasanlimab + BCG-I (N=348)		BCG-I+M (N=349)	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Patients with any event, n (%)	305 (87.1)	102 (29.1)	275 (79.0)	76 (21.8)	245 (70.2)	22 (6.3)
Dysuria	103 (29.4)	0	46 (13.2)	0	112 (32.1)	0
Pollakiuria	80 (22.9)	0	27 (7.8)	0	66 (18.9)	0
Hematuria	73 (20.9)	14 (4.0)	31 (8.9)	5 (1.4)	70 (20.1)	11 (3.2)
Urinary tract infection	67 (19.1)	7 (2.0)	28 (8.0)	2 (0.6)	70 (20.1)	2 (0.6)
Lipase increased	61 (17.4)	21 (6.0)	42 (12.1)	5 (1.4)	0	0
Pyrexia	54 (15.4)	1 (0.3)	35 (10.1)	0	41 (11.7)	0
Hypothyroidism	50 (14.3)	2 (0.6)	44 (12.6)	0	0	0
Amylase increased	41 (11.7)	8 (2.3)	33 (9.5)	3 (0.9)	0	0
Alanine aminotransferase increased	38 (10.9)	8 (2.3)	24 (6.9)	2 (0.6)	6 (1.7)	1 (0.3)
Cystitis	38 (10.9)	1 (0.3)	10 (2.9)	0	30 (8.6)	0
Aspartate aminotransferase increased	37 (10.6)	7 (2.0)	21 (6.0)	4 (1.1)	5 (1.4)	0
Micturition urgency	36 (10.3)	0	11 (3.2)	0	37 (10.6)	0
Fatigue	35 (10.0)	1 (0.3)	26 (7.5)	1 (0.3)	11 (3.2)	0
Pruritus	34 (9.7)	0	37 (10.6)	1 (0.3)	1 (0.3)	0
Asthenia	27 (7.7)	1 (0.3)	19 (5.5)	0	9 (2.6)	0
Hyperthyroidism	27 (7.7)	0	26 (7.5)	0	0	0

POTOMAC (Durvalumab + BCG)

	Durvalumab plus BCG induction and maintenance group (n=336)	Durvalumab plus BCG induction group (n=337)	Comparison group (n=339)
Adverse events of any cause			
Any grade	325 (97%)	322 (96%)	307 (91%)
Maximum grade 3 or 4*	113 (34%)	90 (27%)	56 (17%)
Serious adverse event	108 (32%)	82 (24%)	63 (19%)
Leading to death	6 (2%)	4 (1%)	4 (1%)
Discontinuation of study treatment	105 (31%)	65 (19%)	68 (20%)
Discontinuation of durvalumab	60 (18%)	54 (16%)	..
Discontinuation of BCG	70 (21%)	22 (7%)	68 (20%)
Treatment-related adverse events†			
Any grade	298 (89%)	269 (80%)	245 (72%)
Maximum grade 3 or 4*	71 (21%)	52 (15%)	13 (4%)
Serious adverse event	45 (13%)	38 (11%)	13 (4%)
Leading to death	0	0	0
Discontinuation of study treatment	92 (27%)	54 (16%)	56 (17%)

Pivotal studies for IO in BCG naïve

ALBAN

Atezolizumab + BCG (i+m)
vs
BCG (i+m) 12mo

No benefit in EFS

Arm A: G ≥ 3 TRAEs 23%

Arm B: G ≥ 3 TRAEs 9%

5-7% EFS/DFS benefit

Vs

20-30% Grade ≥ 3 TRAEs

NNT $\approx 14-20$

&

NNH $\approx 3-5$

POTOMAC

Durvalumab + BCG (i+m)
vs
Durvalumab + BCG (i)

Arm A: DFS benefit 4.4%

Arm A: G ≥ 3 TRAEs 21%

Arm C: G ≥ 3 TRAEs 4%

Regulatory conflict

How did BCG do in this studies?

75% EFS at 36 months

15% high risk recurrences at 36 months

6% progression to MIBC at 36 months

85 % complete response rate for CIS

6.3 % Grade ≥ 3 TRAE rate

No deterioration of quality of life

Recurrence after BCG

It no longer equates to an immediate cystectomy

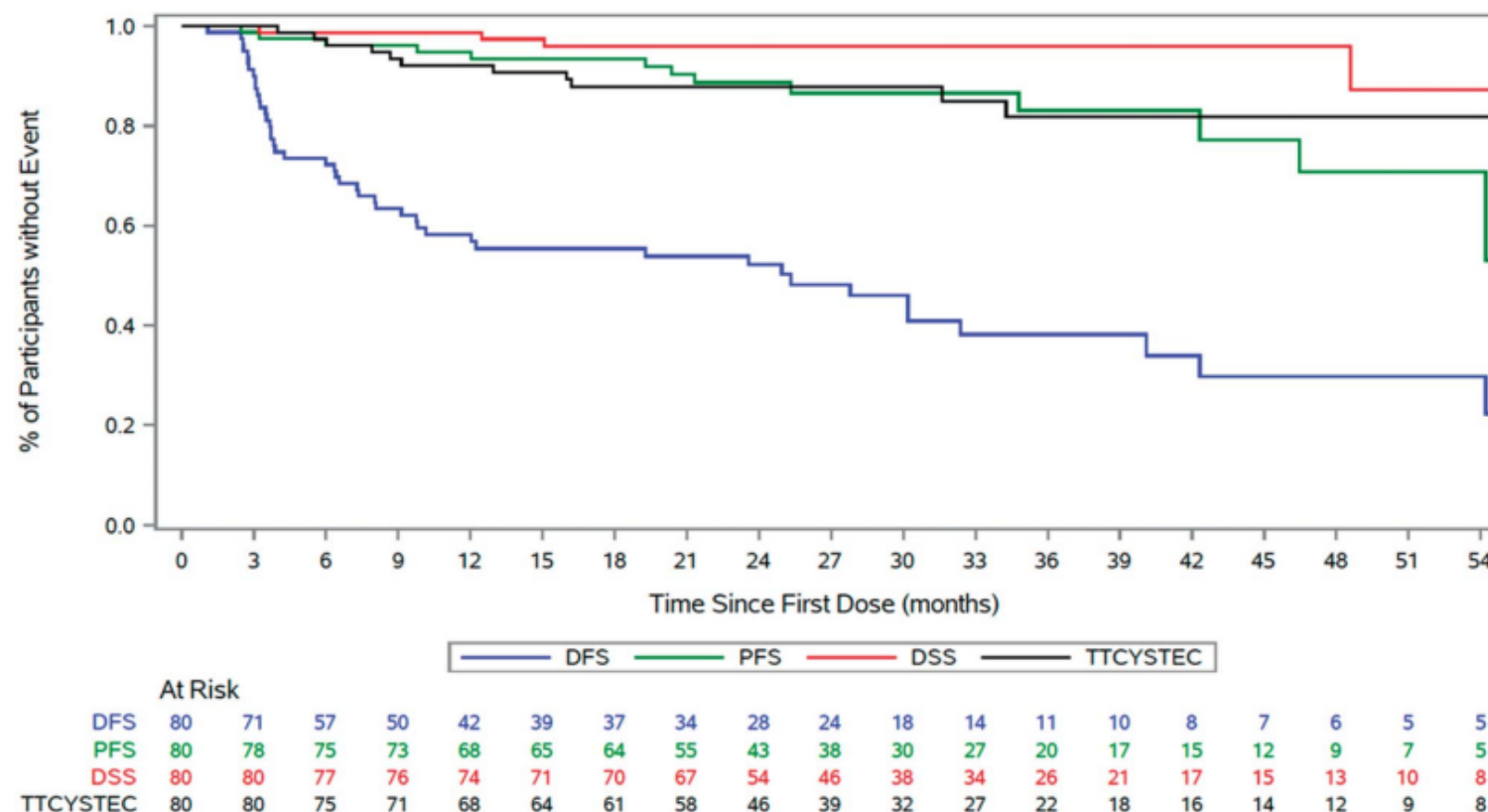


Figure 2. Kaplan-Meier plot for cohort B efficacy population (N = 80). Blue line indicates disease-free survival (DFS); green line, progression-free survival (PFS); red line, disease-specific survival (DSS); black line, time to cystectomy (TTCYSTE).

FDA approvals for **CIS** BCG unresponsive

2021

FDA approves pembrolizumab for BCG-unresponsive, high-risk non-muscle invasive bladder cancer

CRR 41%
DoR 12mo 46%

Cystectomy 49%
MIBC 12%

2022

FDA D.I.S.C.O. Burst Edition: FDA approval of Adstiladrin (nadofaragene firadenovec-vncg) for patients with high-risk Bacillus Calmette-Guérin unresponsive non-muscle invasive bladder cancer with carcinoma in situ with or without papillary tumors

CRR 53.4%
DoR 12mo 24.3%

Cystectomy 26%
MIBC 12.5%

2024

FDA approves nogapendekin alfa inbakicept-pmln for BCG-unresponsive non-muscle invasive bladder cancer

CRR 71%
DoR 12mo 61.6%

Cystectomy 15.6%
MIBC N/R

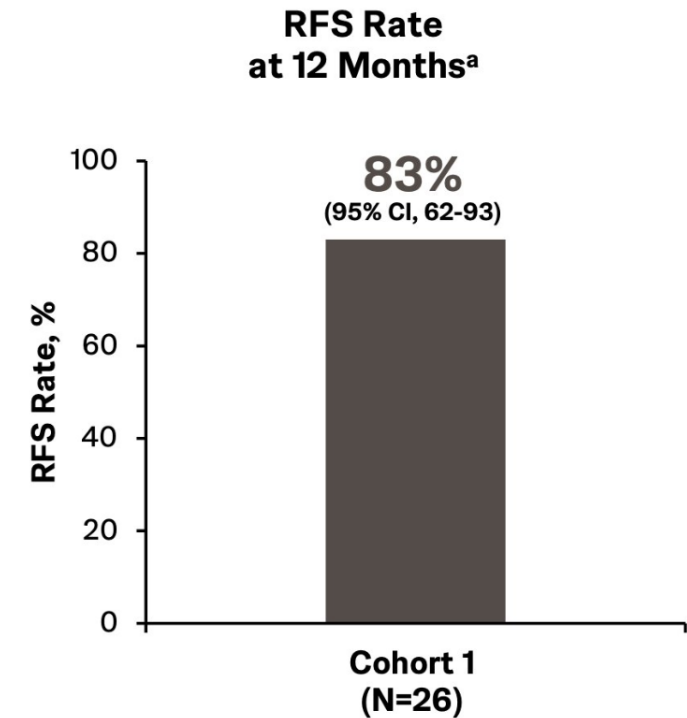
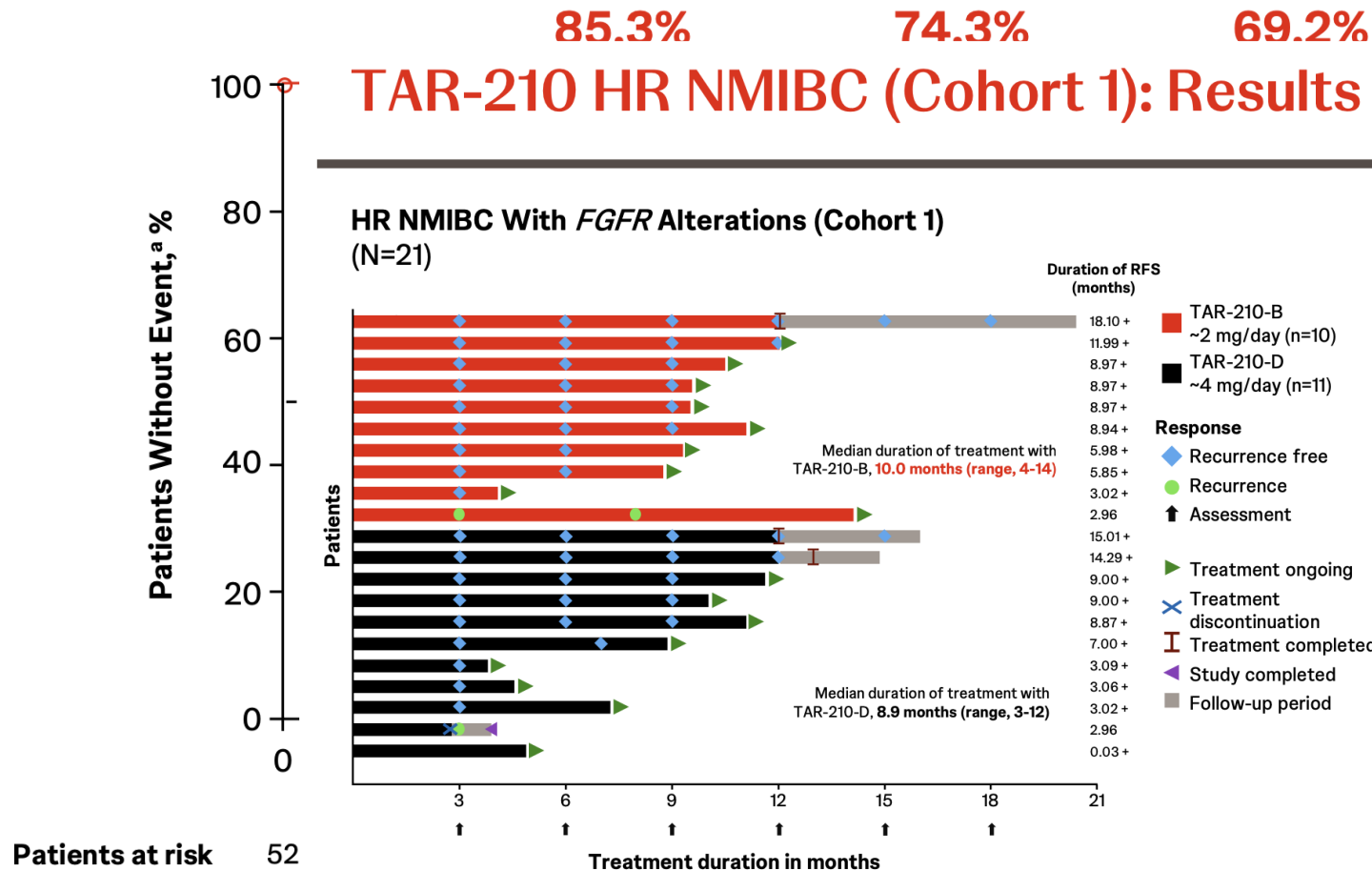
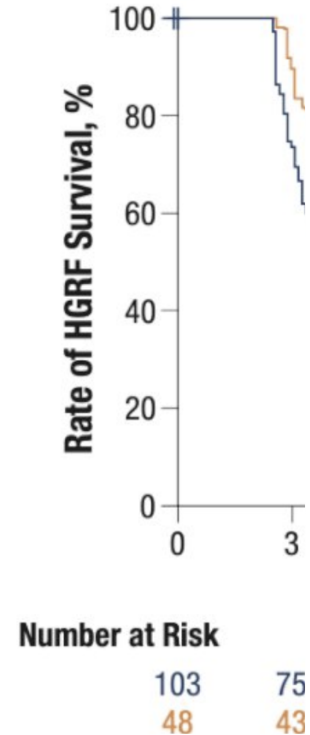
2025

FDA approves gemcitabine intravesical system for non-muscle invasive bladder cancer

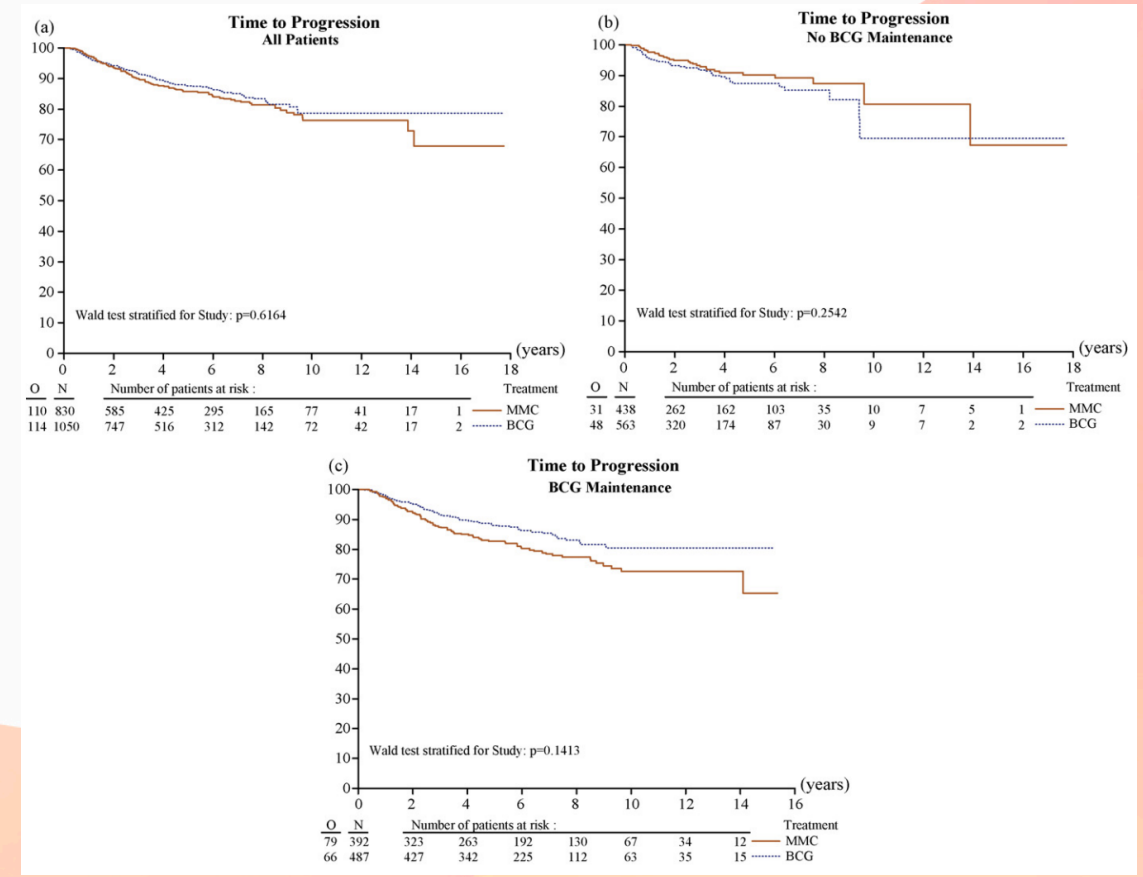
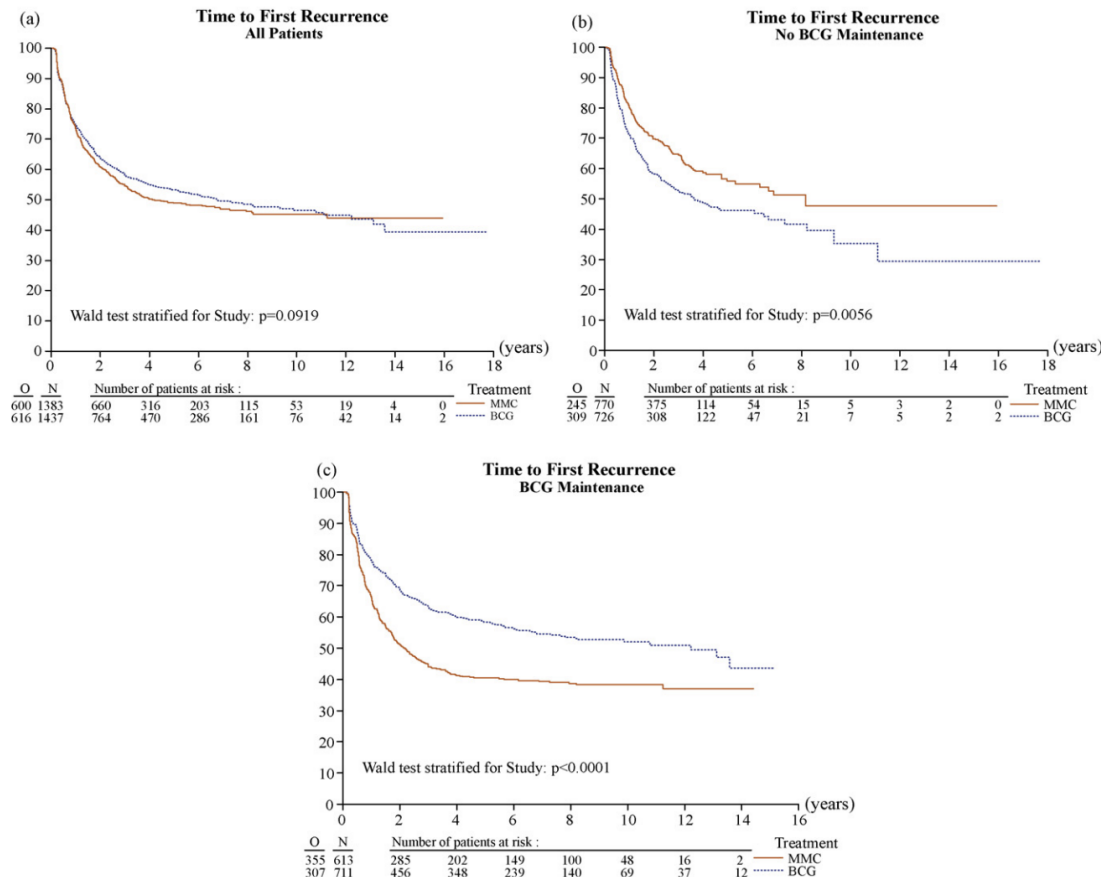
CR 82.4%
DoR 12mo 56.2%

Cystectomy 21.2%
MIBC 8.2%

Papillary only disease



Maintenance, key to success



Cost

Durvalumab: 13.200\$ each dose

Sasanlimab: 24.225\$ each dose

Astiladrin: 60.000\$ each dose

Anktiva: 35.800\$ each dose

HOWEVER... a low number of patients will need the intravesical new treatments given the low rates of BCG unresponsive disease

Why keeping it intravesical?

- BCG keep proving itself worthy (Be meticulous with **maintenance**)
- Adding ICIs just gives a **modest benefit** at the expense of a **relevant toxicity**
- The range of intravesical therapies keep growing (**Sequencing**)
- Intravesical administration is **logistically** convenient
- BCG is extraordinarily **cheap**
- It keeps us urologists **independent** in NMIBC (Manageable toxicity)



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¡Gracias!



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