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In high-risk NMIBC, intravesical or systemic treatment?

Félix Guerrero-Ramos, MD PhD FEBU
Hospital Universitario 12 de Octubre
Madrid, Spain

CONFLICTS OF INTEREST

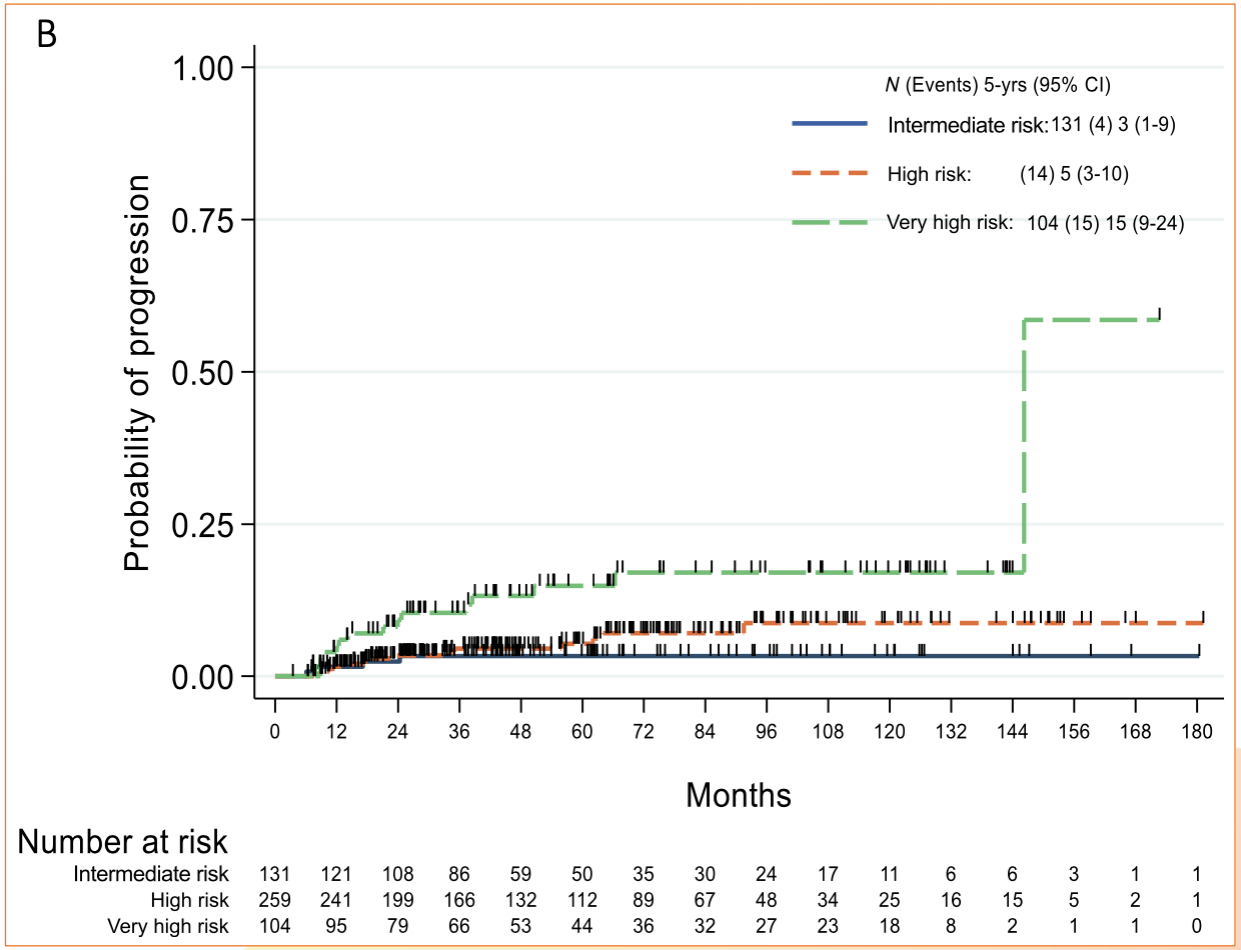
Research support/PI	Johnson & Johnson, Pfizer, Taris, BMS, Roche, Seagen, AstraZeneca, Combat Medical, Cepheid, Fidia, Astellas, UroGen, MSD, enGene
Employee	SERMAS (Servicio Madrileño de Salud)
Consultant	Johnson & Johnson, Pfizer, Merck, Roche, Taris, Combat Medical, AstraZeneca, MSD, BMS, enGene, Nanobots Therapeutics
Stockholder	CG Oncology, Johnson & Johnson, Pfizer
Speaker bureau	Janssen, Nucleix, MSD, Pfizer, Merck, BMS, AstraZeneca, Palex, Combat Medical, Johnson & Johnson, Recordati
Travel	Pfizer, Recordati, Ipsen, Combat Medical, Alter, Salvat, Nucleix, AstraZeneca, Fidia, Johnson & Johnson
Scientific advisory board	AstraZeneca, BMS, Combat Medical, Johnson & Johnson, Nucleix, Pfizer, Taris, Roche, MSD, enGene
Manuscript support	Pfizer, Janssen, Combat Medical, AstraZeneca, Johnson & Johnson, BMS

How does BCG perform?

Table 2. *Survival analysis based on Kaplan-Meier estimates at 1, 3 and 5-year time points*

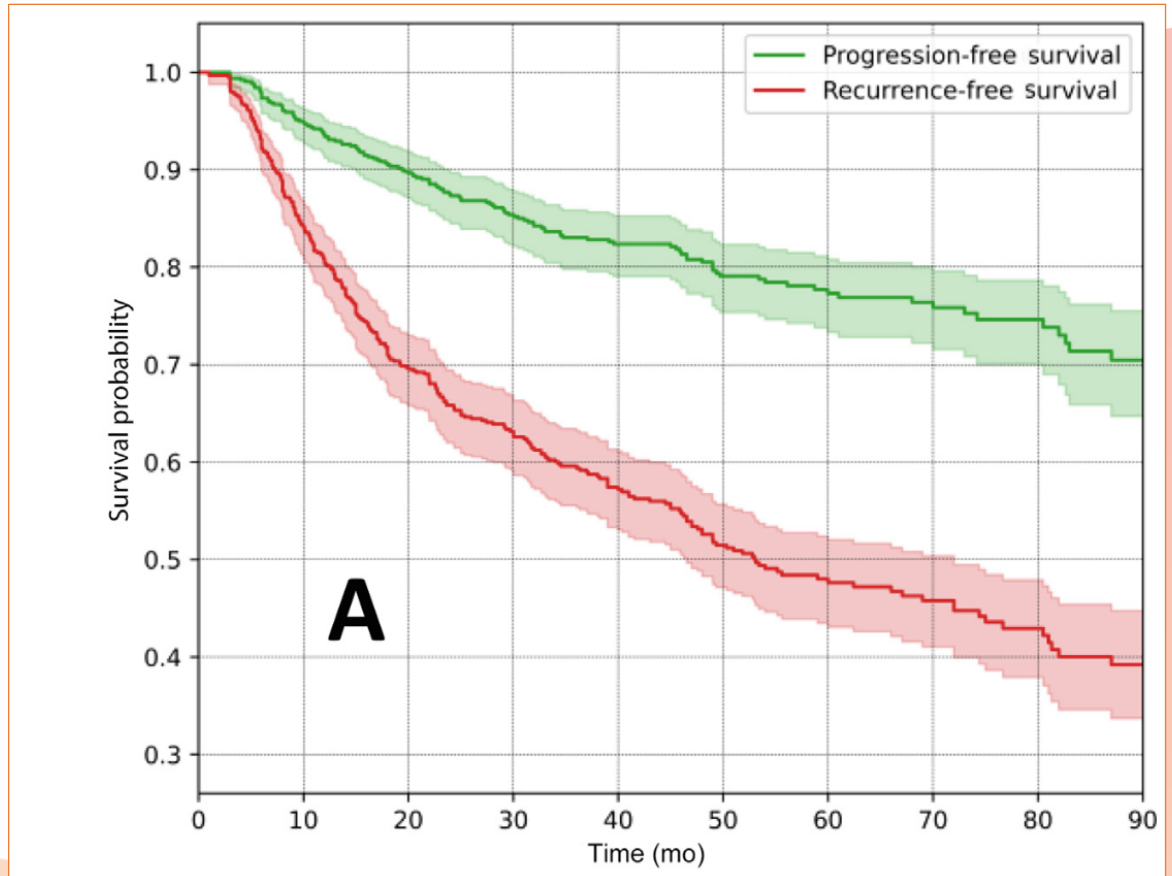
	RFS-HG			PFS			CFS			OS			
	1 Yr	3 Yrs	5 Yrs	1 Yr	3 Yrs	5 Yrs	1 Yr	3 Yrs	5 Yrs	1 Yr	3 Yrs	5 Yrs	Median Mos Followup
% Overall	81	76	74	97	93	92	95	89	86	99	93	86	47.8
% EAU risk group:													
Intermediate	95	92	86	100	100	100	98	96	90	98	94	79	43.1
High	80	74	72	96	92	91	95	88	86	99	93	87	49.4
% AUA NMIBC risk group:													
Intermediate	89	85	82	98	98	98	93	91	88	99	96	86	46.9
High	79	73	71	96	94	93	96	89	86	99	92	86	48.2
% Presence of CIS:													
LG Ta/T1 only	94	90	85	100	100	100	98	96	92	98	94	82	43.0
HG Ta/T1 only	81	77	75	97	93	92	96	91	89	99	94	88	44.8
CIS only	77	70	66	91	91	91	81	74	74	97	90	80	42.3
Ta/T1+CIS	77	68	67	96	92	89	94	85	81	99	91	86	65.3

How does BCG perform? Very high-risk



Number at risk

Intermediate risk	131	121	108	86	59	50	35	30	24	17	11	6	6	3	1	1
High risk	259	241	199	166	132	112	89	67	48	34	25	16	15	5	2	1
Very high risk	104	95	79	66	53	44	36	32	27	23	18	8	2	1	1	0



Progression									
At risk	640	602	544	456	361	270	190	139	95	69
Censored	0	5	31	93	174	253	328	376	418	439
Events	0	33	65	91	105	117	122	125	127	132
Recurrence										
At risk	640	534	420	331	247	182	119	91	59	45
Censored	0	5	28	77	135	178	229	253	280	289
Events	0	101	192	232	258	280	292	296	301	306

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Lobo N, Eur Urol Oncol 2022; Subiela JD, Guerrero-Ramos F, Eur Urol Oncol 2024

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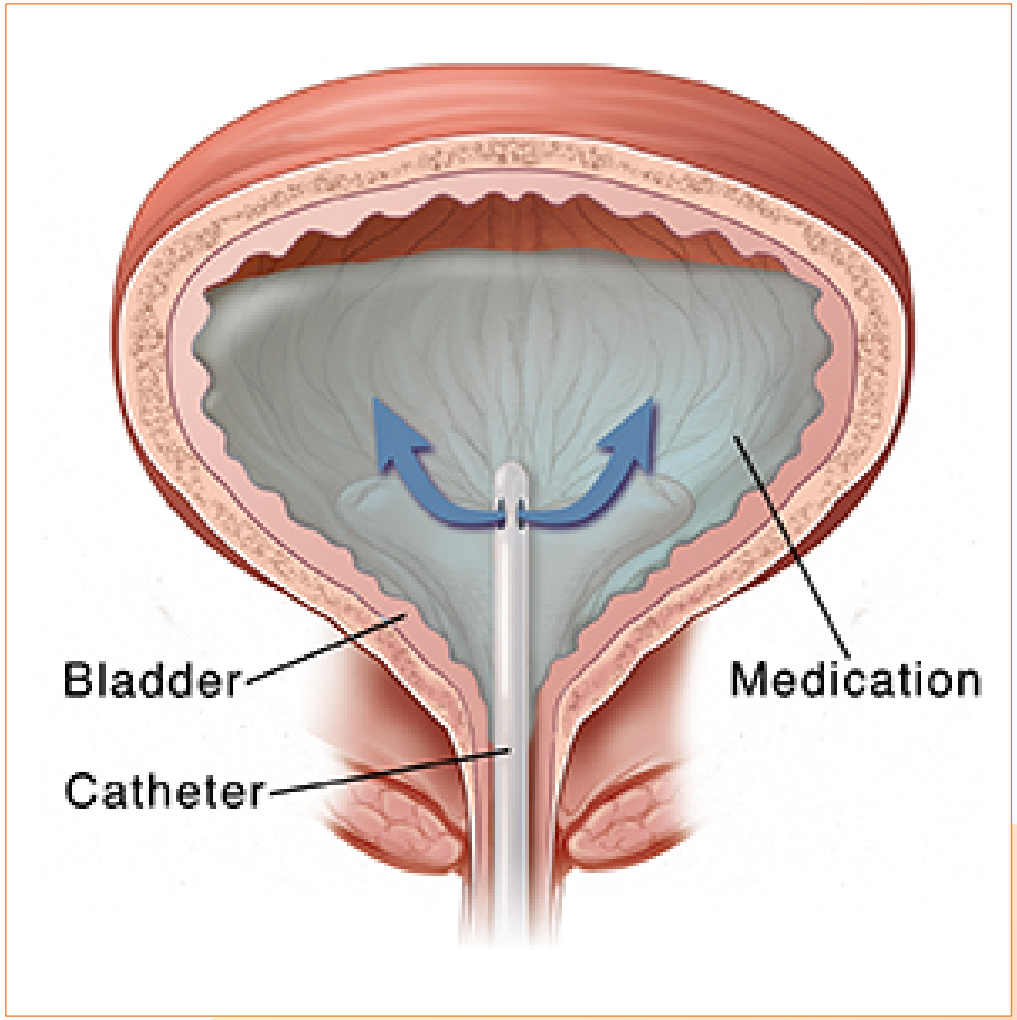
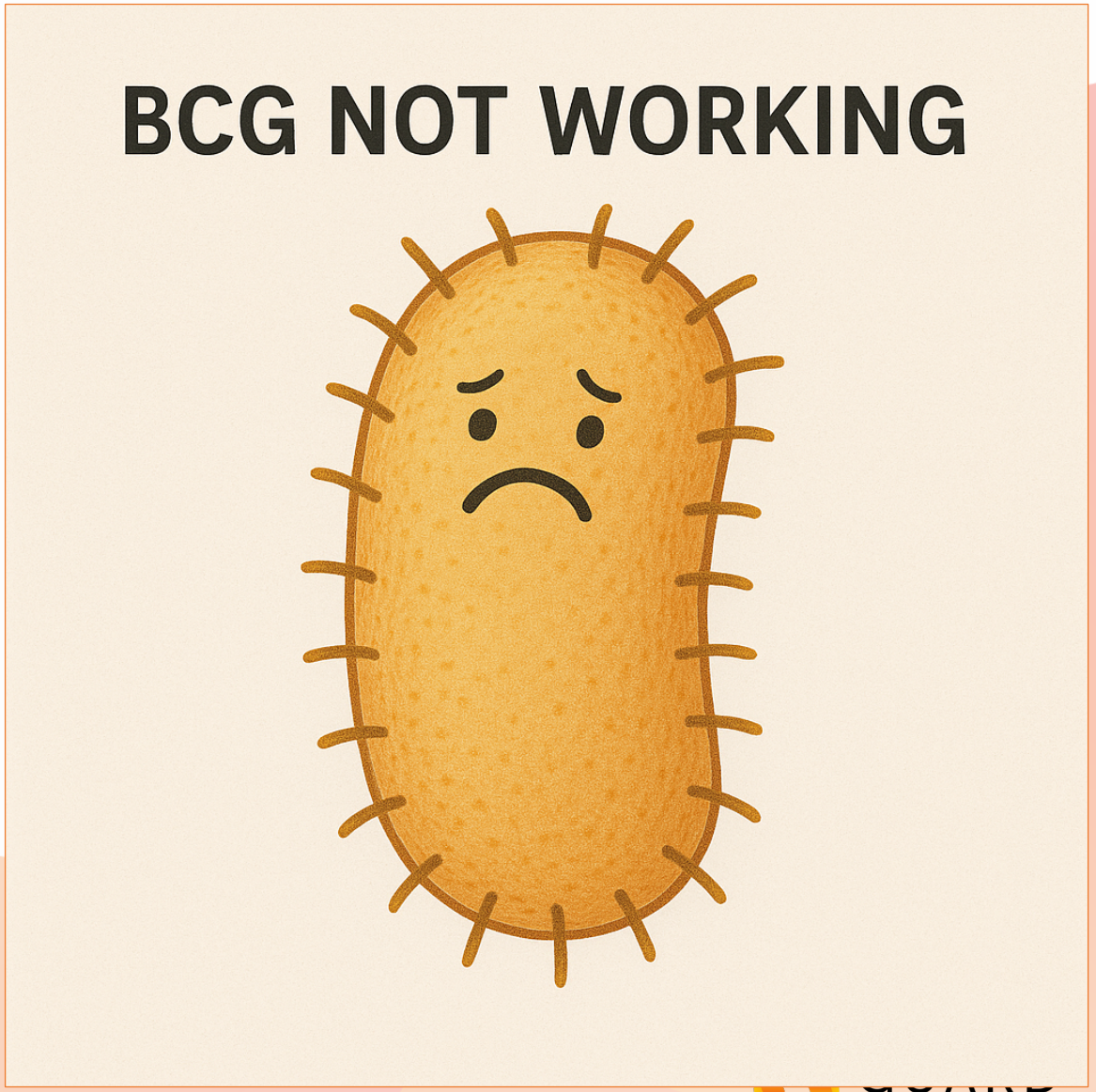
Two scenarios





BCG naïve

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Let me show you this new intravesical treatment

At 3 years, 75% of the patients are **event-free**

BCG

have a HG recurrence

ression

rate is 1.4%

No deterioration of the **quality of life**

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Pivotal trials for BCG naïve HR-NMIBC

Table 1 – Compa ... **sive bladder cancer**

Study title	BRIDGE
Study ID	NCT05538663
Intervention	Sequential Gem/Doc vs BCG (I + M)
Administration route	Gem/Doc: IVS BCG: IVS
BCG M	36 mo
Participants (*n*)	870
Primary EP	EFS
Key secondary EPs	QoL, safety, toxicity, PFS, CFR
BCG strain	OncoTICE
Current status	Recruiting
eSCD	October 2030

BCG = bacillus Ca... e-free survival; DOR: duration of response; DSS... study completion date; Gem/Doc = gemcitabin... urvival; NRC = not recruiting; OS = overall surv... survival; SC = subcutaneous; TTC = time to cys...

AstraZeneca

Imfinzi regimen demonstrated statistically significant and clinically meaningful improvement in disease-free survival for high-risk non-muscle-invasive bladder cancer in POTOMAC Phase III trial

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CREST trial

Patient Population:

- BCG-naive, high-risk NMIBC: T1, high-grade Ta, and/or CIS
- No prior PD-(L)1, PD-L2, or CTLA-4 inhibitors or immunostimulatory agents

N=1055

Randomization 1:1:1

Stratified by CIS (Y/N) and geographic region

Arm A
Sasanlimab + BCG-Induction + Maintenance (I+M)

Arm B
Sasanlimab + BCG-Induction (I)

Arm C
BCG-Induction + Maintenance (I+M)

Primary endpoint
EFS: A vs C
(recurrence of high-grade disease, progressive disease, persistence of CIS, death from any cause)

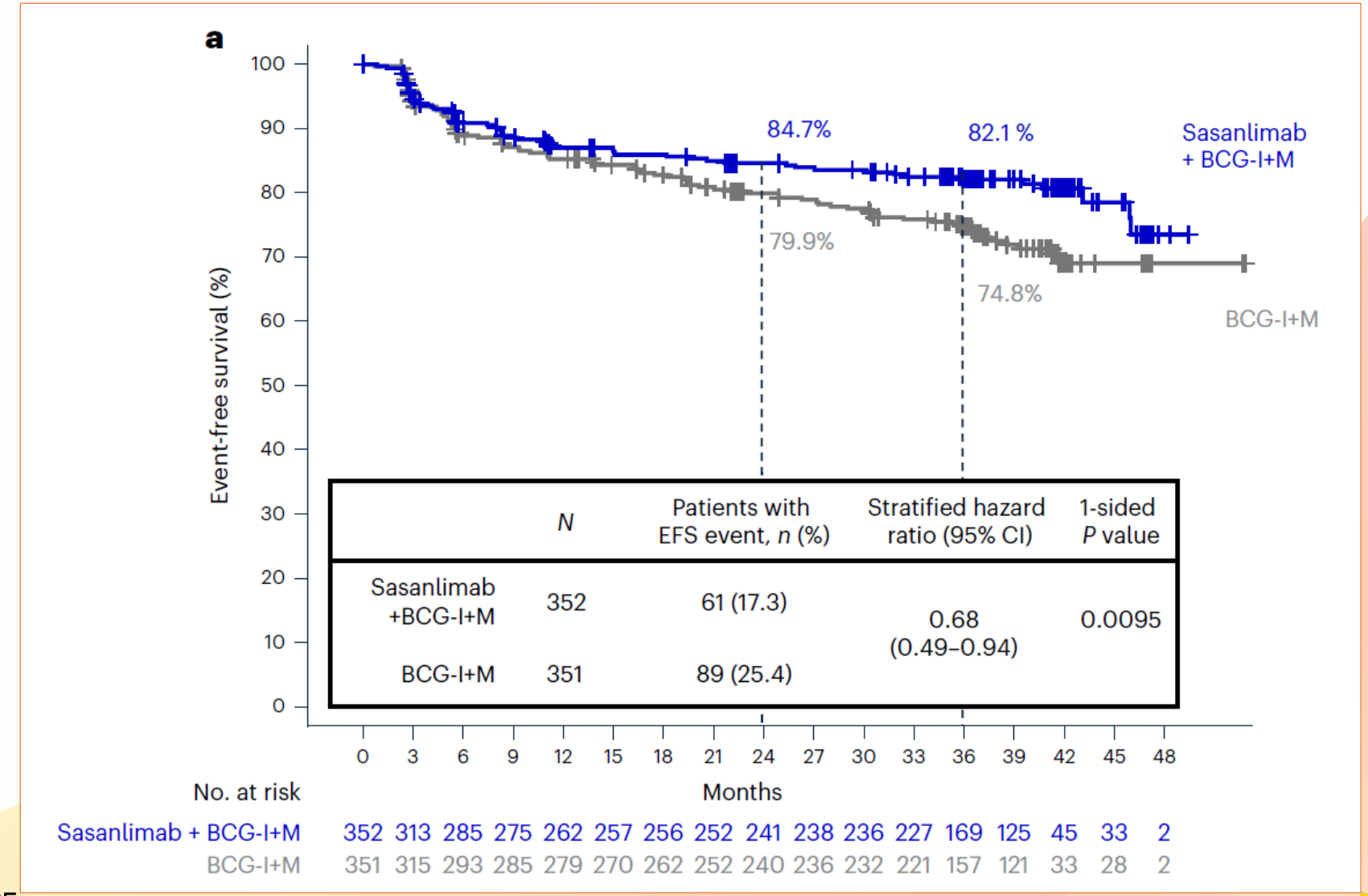
Key secondary endpoints
EFS: B vs C
OS

Select secondary endpoints
CR (patients with CIS)
Duration of CR (patients with CIS)
Safety
QoL

Final EFS analysis data cut-off date: Dec 2, 2024
Median follow-up for EFS: 36.3 mo

BCG-I+M: BCG induction (6 doses)[a] and maintenance (up to 2 years) therapy
BCG-I: BCG induction (6 doses)[a] only
Sasanlimab: Administered SC for up to 25 four-week cycles

CREST trial



	N	Patients with EFS event, *n* (%)	Stratified hazard ratio (95% CI)	1-sided *P* value
Sasanlimab +BCG-I+M	352	61 (17.3)	0.68 (0.49–0.94)	0.0095
BCG-I+M	351	89 (25.4)		

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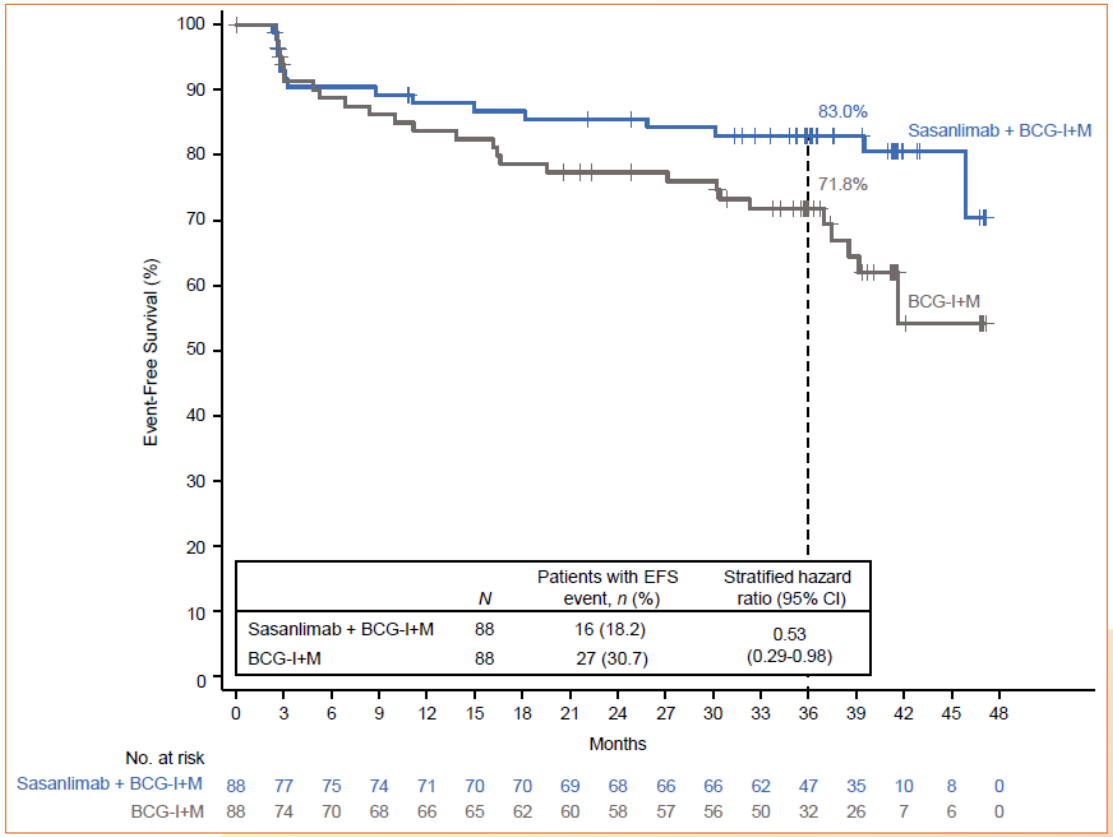
CREST trial

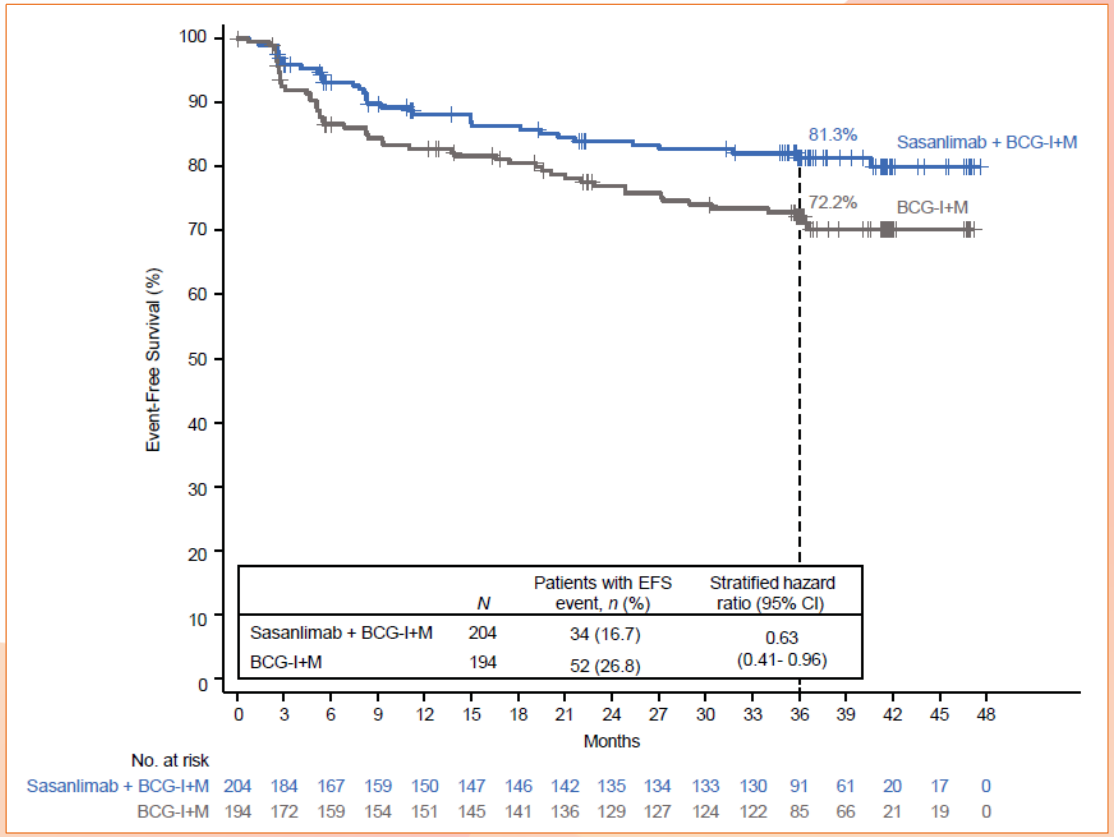
	Sasanlimab + BCG-I+M (N=352)	BCG-I+M (N=351)
Patients with EFS event, n (%)	61 (17.3)	89 (25.4)
Recurrence of high-grade disease	**26 (7.4)**	**53 (15.1)**
Persistence of CIS	1 (0.3)	1 (0.3)
Progressive disease	18 (5.1)	22 (6.3)
Progression to N+/M+, n	3	7
Progression to MIBC (≥T2), n	7	7
Stage Progression (high-grade Ta, T1), n	7	7
Unknown, n	1	1
Death	16 (4.5)	13 (3.7)

CREST trial

Población CIS (± Ta/T1)



Población T1 (± CIS)



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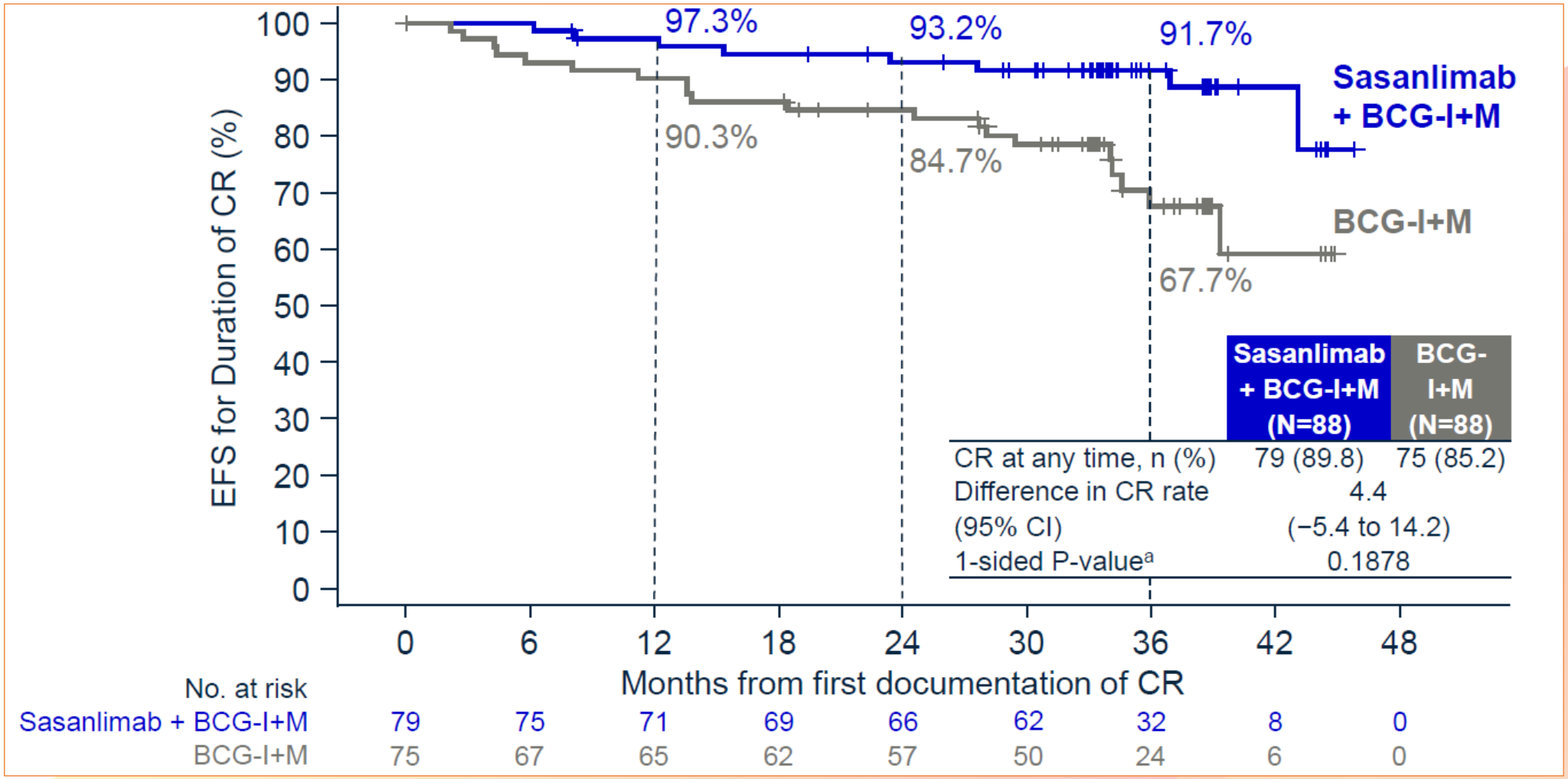
CREST trial



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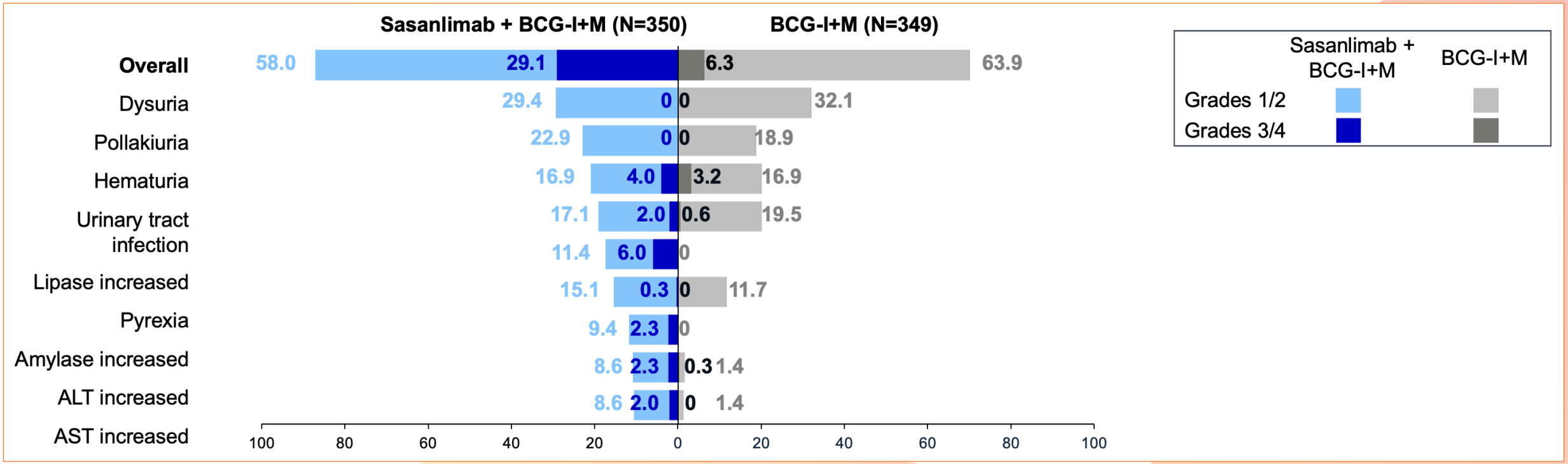
CREST trial



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BCG unresponsive

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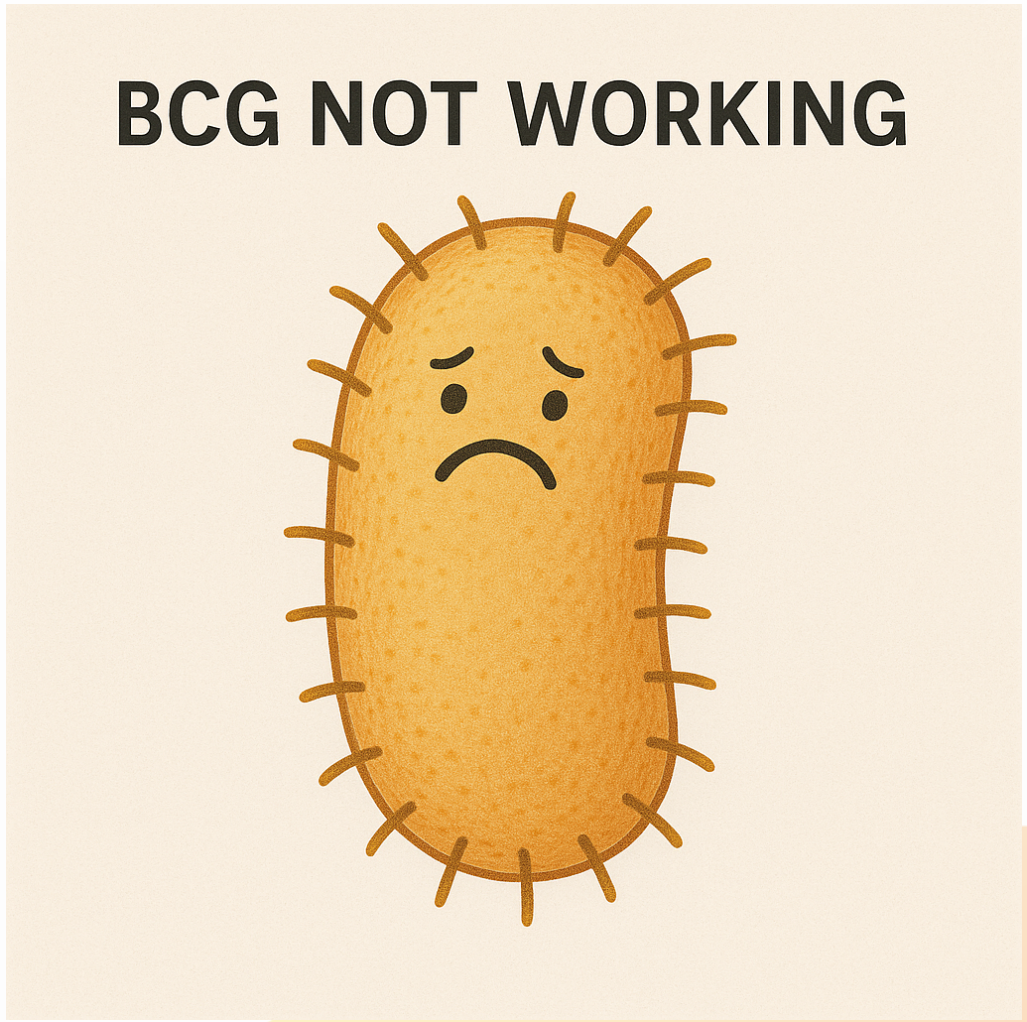
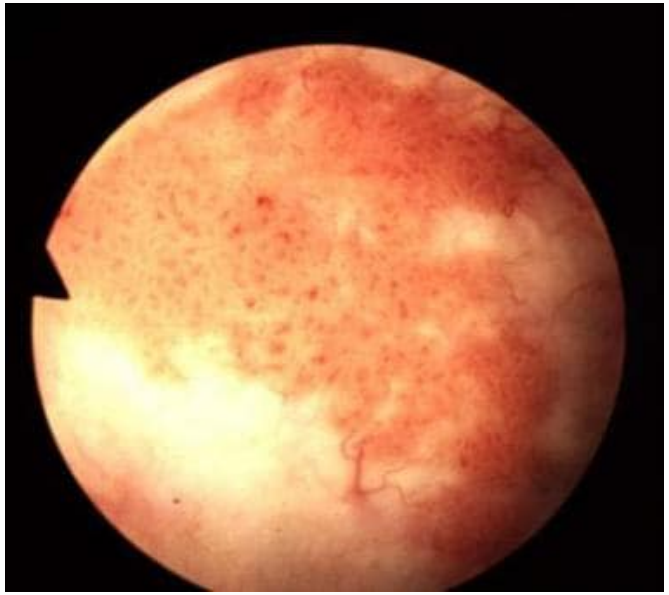
CREST trial





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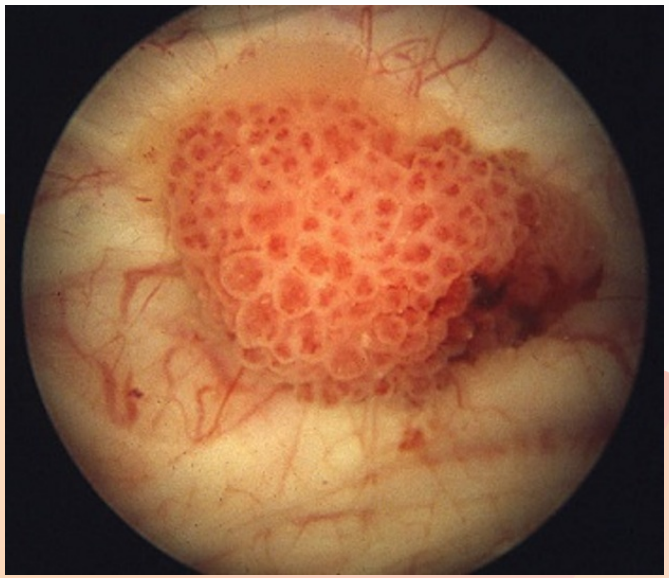
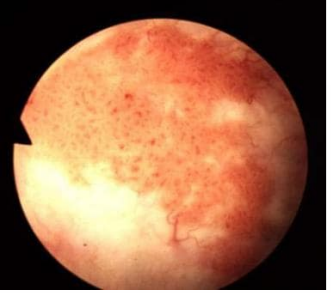


90%



	FDA approves pembrolizumab for BCG-unresponsive, high-risk non-muscle invasive bladder
2022	patients with high-risk Bacillus Calmette-Guérin unresponsive non-muscle invasive bladder
2024	pmln for BCG-unresponsive non-muscle invasive bladder cancer

TAR-200
82.4% AAT

CG0070 + pembrolizumab
82.9% 3m

CG0070
75.5% 3m

Detalimogene voraplasmid
67.0% 3m

CRR 41% 3m

CRR 53.4% 3m

CRR 71% AAT

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www.fda.gov. Balar AV, Lancet Oncol 2021. Boorjian SA, Lancet Oncol 2021. Chamie K, NEJM Evid 2022. Jacob J, AUA 2025. Tyson MD, AUA 2025. Li R, Nat Med 2024. Taylor JA, ASCOGU 2025. Guerrero-Ramos F, Eur Urol Oncol 2024

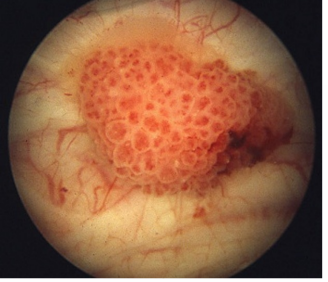
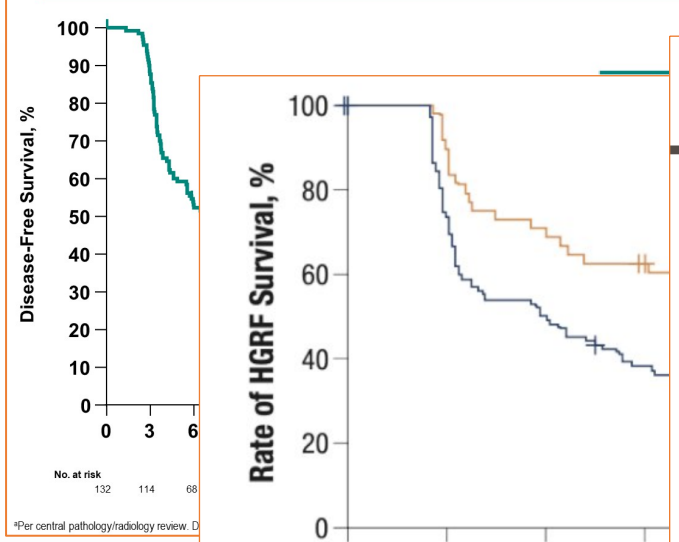


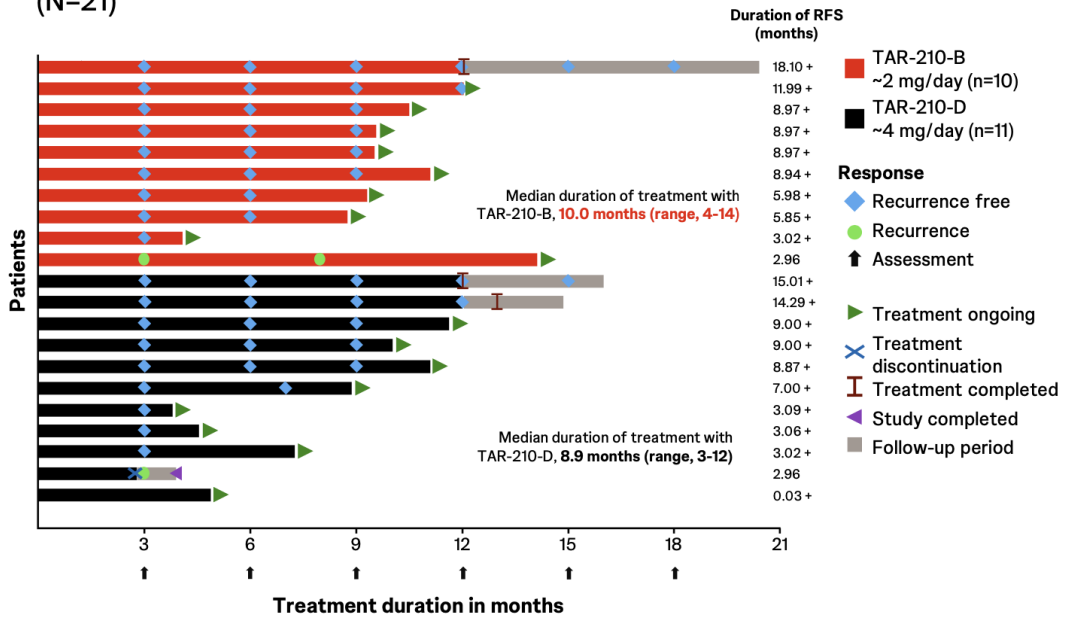
Table 2. Summary of Efficacy in Cohort B.*	
Response	**Value**
Median duration of follow-up — mo	20.7
Range of follow-up of all patients — mo	2.9–37.1
Disease-free survival (n=72)	
Median disease-free survival — mo (95% CI)†	19.3 (7.4 to upper bound not reached)
Disease-free survival rate — % (95% CI)†	
12 mo	55.4 (42.0–66.8)

Disease-Free Survival for HR NMIBC[a]



TAR-210 HR NMIBC (Cohort 1): Results

HR NMIBC With *FGFR* Alterations (Cohort 1)
(N=21)



- **90% estimated 12-month RFS rate[a]** (n=21)
  - Median RFS was not estimable
  - 2 of 21 patients have recurred
  - Median duration of follow-up 8.9 months
- No difference observed in RFS between the TAR-210 dose levels

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Necchi A, ASCOGU 2023; Chamie K, NEJM Evidence 2022; Dinney CP, EAU 2024, Vilaseca A, AUA 2024

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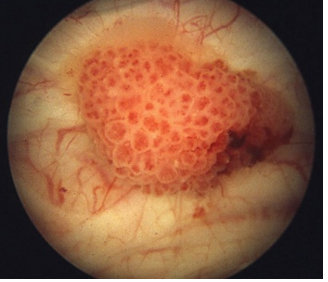


NCT04640623

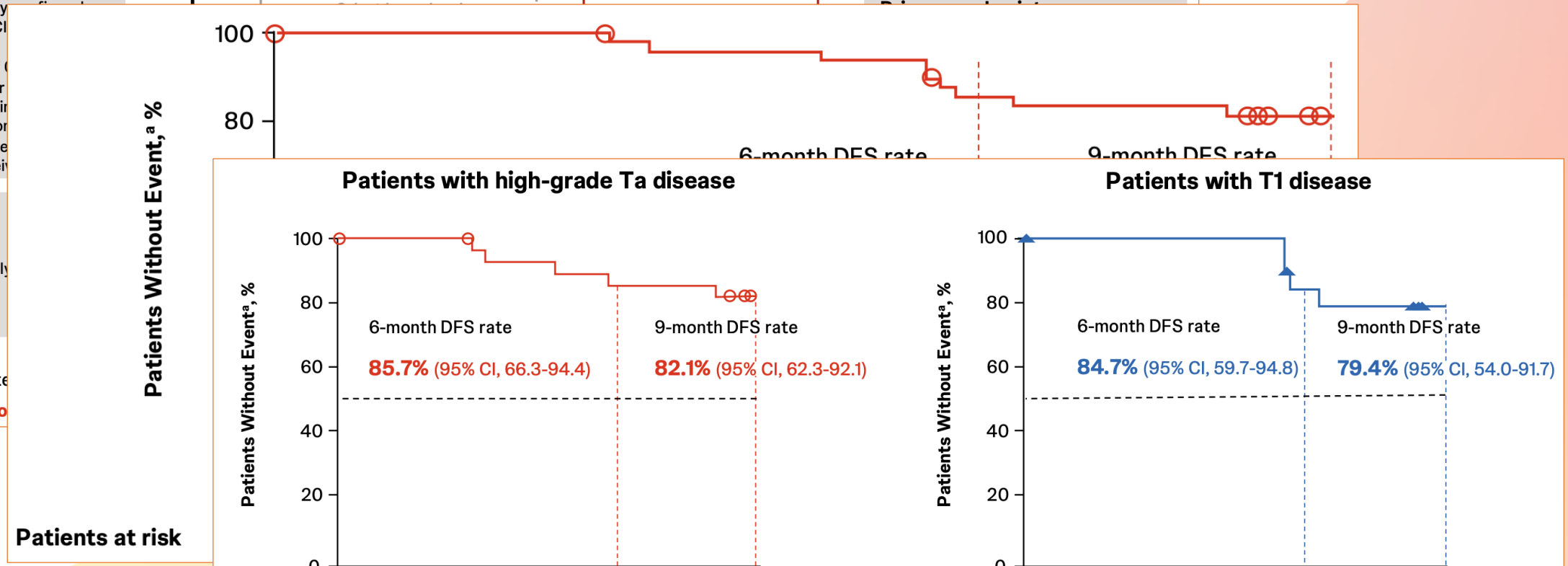
Population:
- Aged ≥18 years
- Histologically
- HR NMIBC CI
- disease)
- ECOG PS of
- Persistent or
- disease within
- of completion
- Unresponsive
- and not recei

TAR-200 + Cetrelimab[b]
Cohort 1 (N=53)[c]

Cohorts 1-3:

Population:
- Papillary-only
- (no CIS)[a]

- Response is dete
- The **study proto**



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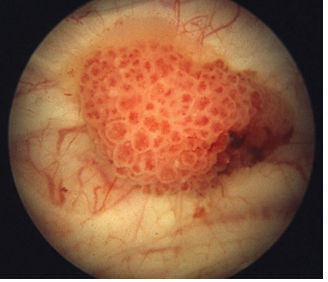

SunRISe-5 (NCT06211764) Is an Open-Label, Multicenter Phase 3 Study

Key eligibility criteria

- Histologically confirmed, papillary-only HR NMIBC (high grade Ta or any T1), recurrent within the first year of last dose of BCG
- No CIS at time of papillary

1:1 (N≈250)

Group A (n≈125)
TAR-200 monotherapy

Q3W during an induction phase
Q12W during a maintenance phase

Crossover
Patients in Group B may receive TAR-

Primary end point
Disease-free survival

Secondary end points

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 NMBIC:**
  - High-grade Ta
    -or-
    Any T1 (no CIS)
  - Recurrent after BCG
    -or-
    Intolerant of BCG
- ECOG performance status ≤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)
Treatment cycles 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
Key secondary end points
• Recurrence-free survival
• Time to next intervention
• Time to disease worsening
• Time to progression
• Overall survival
• Safety and tolerability

NCT06919965

CONCLUSIONS

- BCG works → BCG will be with us for a long time
  - Both alone and in combination with other therapies
- When BCG fails…
  - FDA approvals for CIS (one-arm trials)
  - 90% are papillary-only: no approvals (controlled trials)
- Intravesical approach clearly preferred (safety and efficacy)
- Upcoming challenges:
  - Approvals
  - Cost
  - Logistics
  - Sequencing/combining

¡Gracias!

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