

Treatment Intensification in high-risk NMIBC

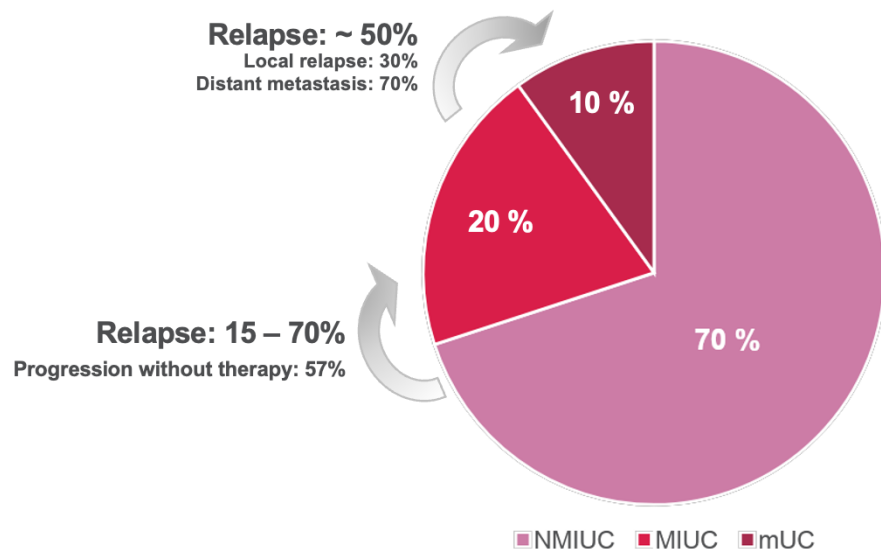
Van Damme Julien MD,PhD
julien.vandamme@saintluc.uclouvain.be
Cliniques universitaires Saint-Luc
Université catholique de Louvain
Brussels, Belgium

Credentials and conflicts of interest

- Honoria as consultant/speaker : Astellas, Bayer, Bristol Myers-Squibb, Janssen, Sanofi, Ipsen, MSD.
- Honoria for scientific advisory Board: Janssen, Ipsen, MSD
- I have no potential conflict of interest related to this topic

Urothelial Carcinoma

Incidence at diagnosis



5 Year - Survival



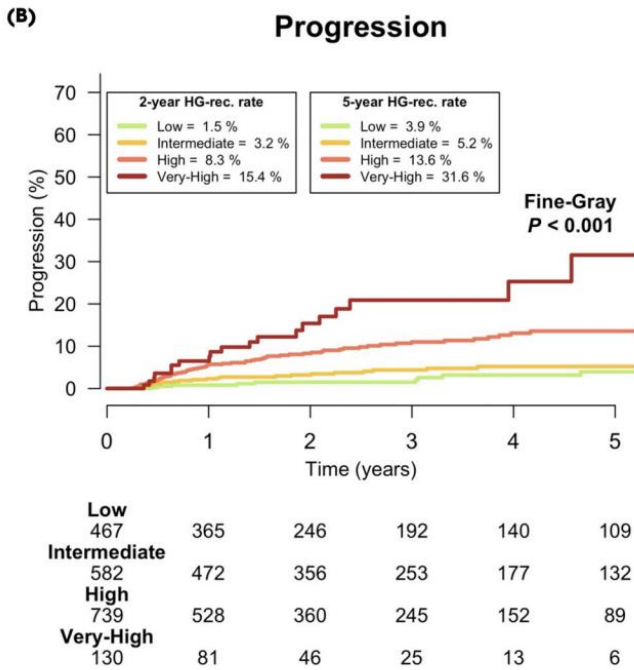
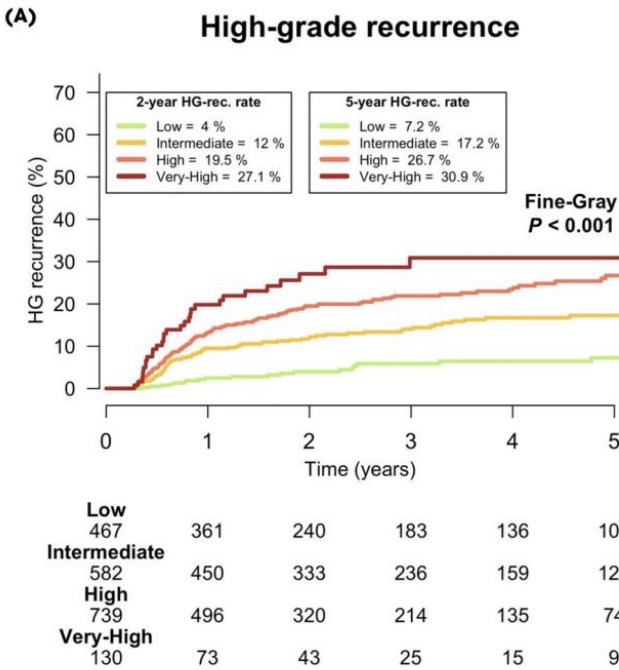
Risk groups stratification

Clinical risk factors:

- age > 70
- multiple papillary tumours
- tumour diameter > 3 cm.

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 T1G1, no CIS with all 3 risk factors • Ta HG/G3 or T1 LG, no CIS with at least 2 risk factors • T1G2 no CIS with at least 1 risk factor
Very High Risk	Stage, grade with additional clinical risk factors: • Ta HG/G3 and CIS with all 3 risk factors • T1G2 and CIS with at least 2 risk factors • T1 HG/G3 and CIS with at least 1 risk factor • T1 HG/G3 no CIS with all 3 risk factors

Cumulative incidence curves depicting HG recurrence (A) and progression (B) according to the EAU 2021 risk categories of the 1918 patients with NMIBC from six European tertiary referral centres treated with TURBT between 2015 and 2022.



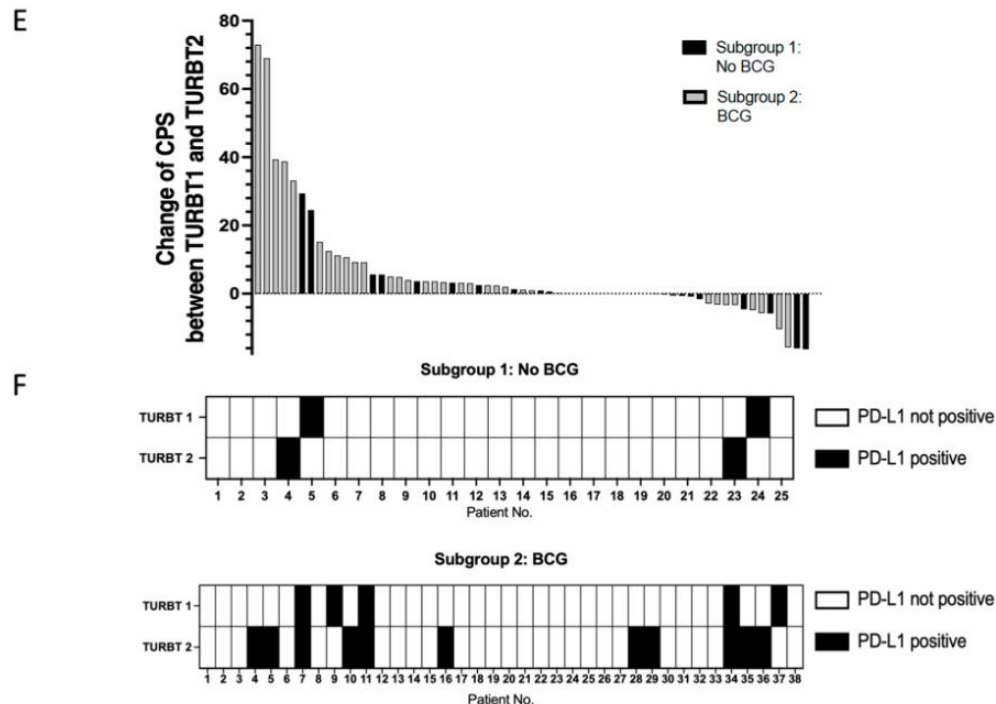
EORTC Nomograms and Risk Groups for Predicting Recurrence, Progression, and Disease-specific and Overall Survival in Non-Muscle-invasive Stage Ta-T1 Urothelial Bladder Cancer Patients Treated with 1-3 Years of Maintenance Bacillus Calmette-Guérin

✓ T1G3

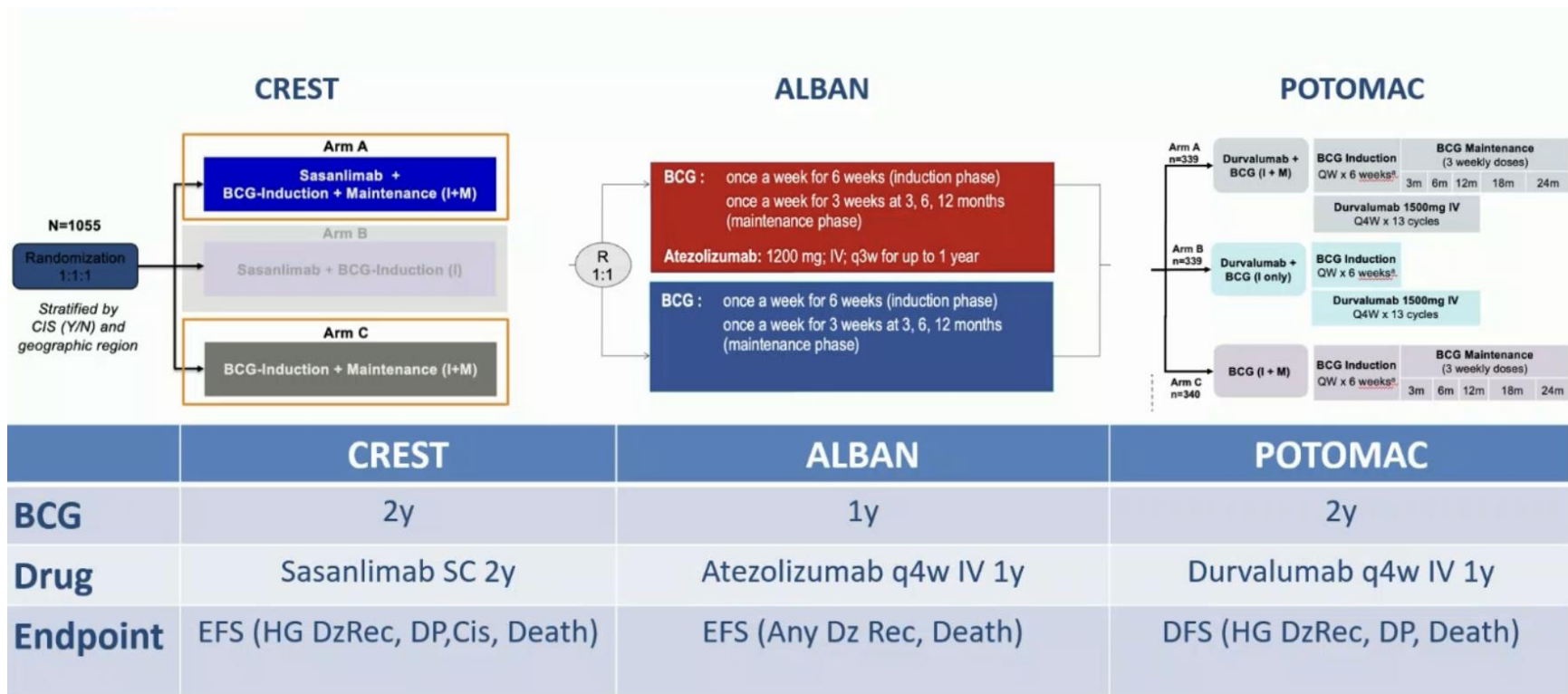
- 1 Yr disease progression rate of 11,4%
- 5 Yrs disease progression rate of 19,8%
- 1 Yr disease specific death rate of 4,8 %
- 5 Yrs disease specific death rate of 11,3%

Rationale for adding IO to BCG

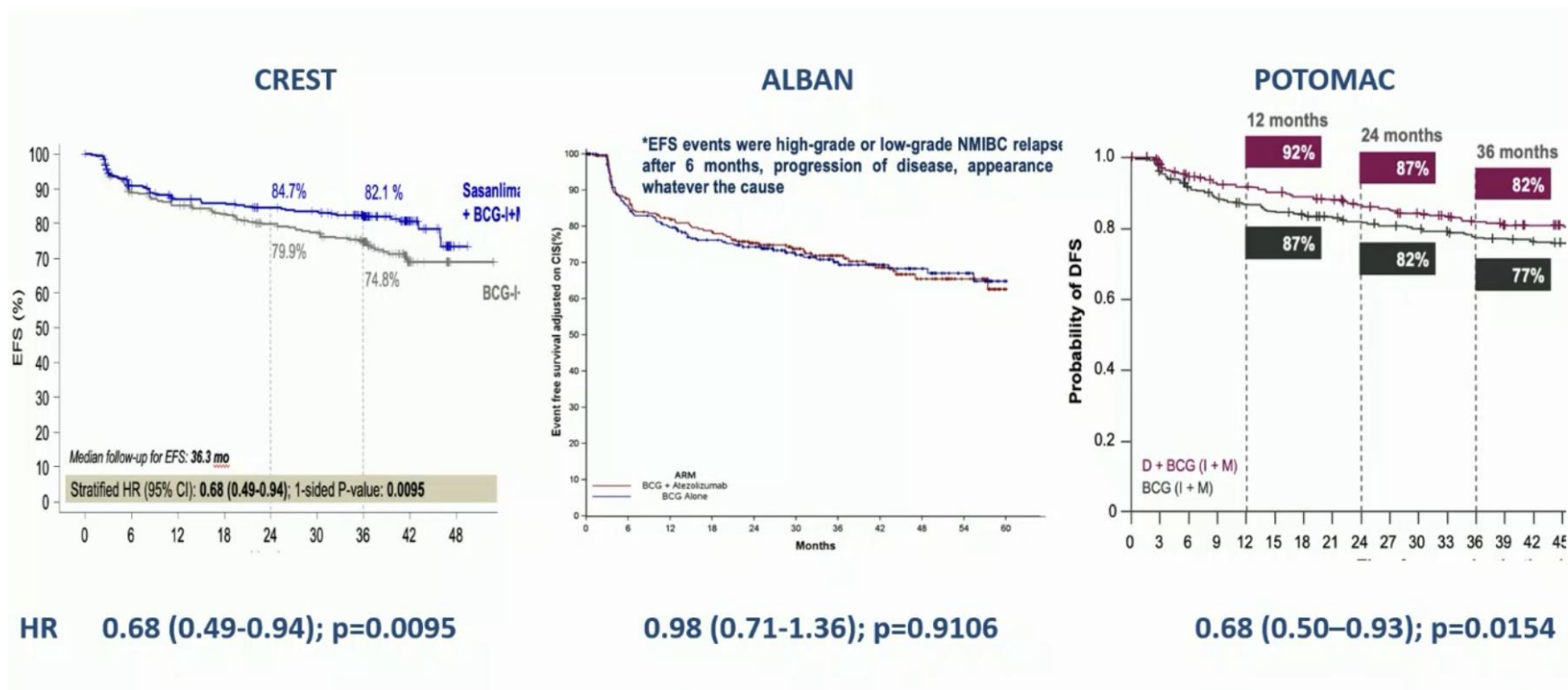
PD-L1 Expression in High-Risk Non-Muscle-Invasive Bladder Cancer Is Influenced by Intravesical Bacillus Calmette–Guérin (BCG) Therapy



Available Intensification Trials in HR NMIBC



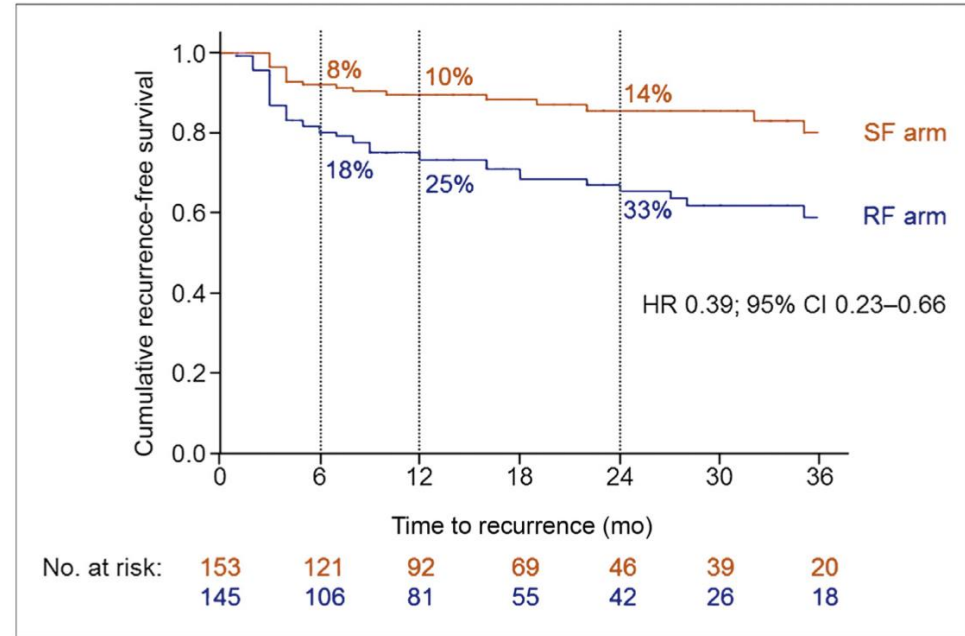
Available Intensification trials in HR NMIBC



1. Validity of the control arm

Treatment of High-grade Non-muscle-invasive Bladder Carcinoma by Standard Number and Dose of BCG Instillations Versus Reduced Number and Standard Dose of BCG Instillations

Time to recurrence in all patients (ITT analysis)



2. Events Contributing to EFS/DFS benefit : Clinically valid ?

CREST

	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)

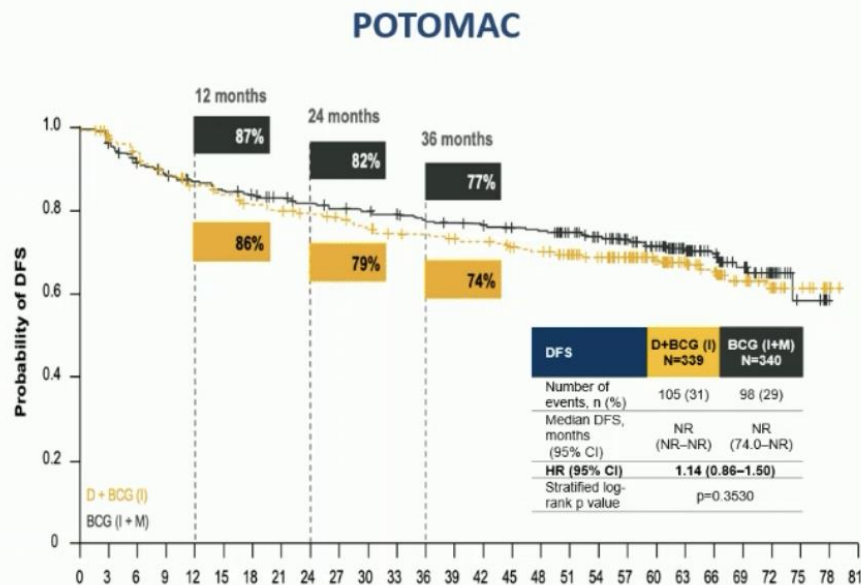
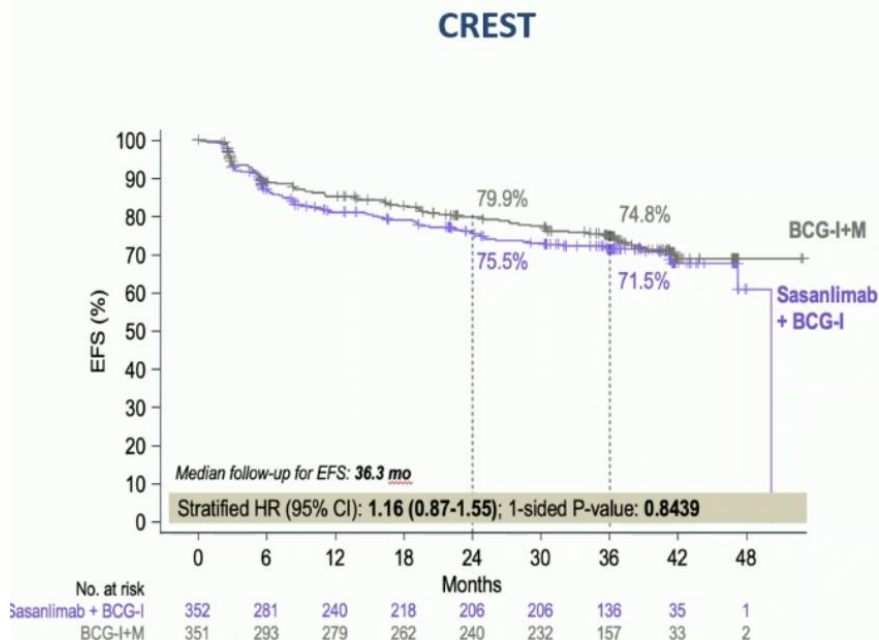
POTOMAC

	Durvalumab + BCG-I+M	BCG-I+M
DFS event		
HG recurrence	36 (10.6%)	71 (20.9%)
Persistence of Cis	1 (0.3%)	3 (0.9%)
MIBC/M+	16 (4.7%)	13 (3.8%)
Death	14 (4.1%)	18 (5.3%)

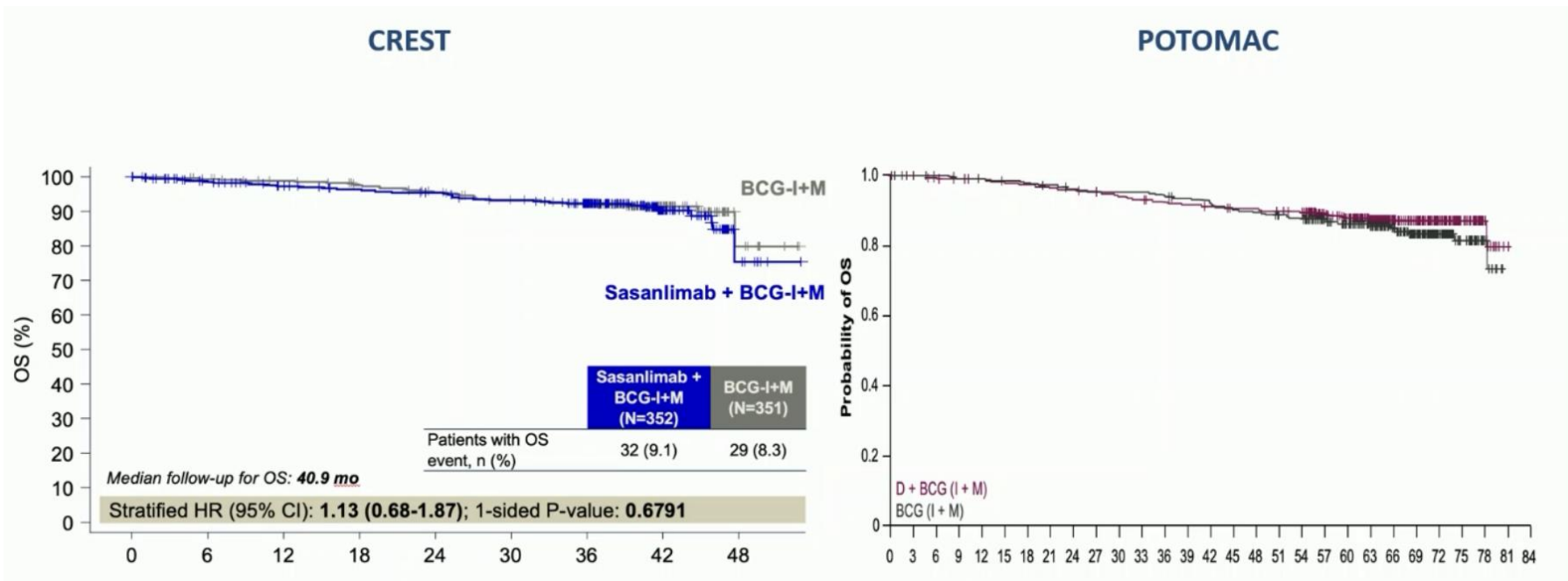
Impact of Recurrence Events in HR NMIBC

- Acces to BCG-Unresponsive Treatments
 - ✓ Gem/Doce
 - ✓ Nadofaragene Firadenovec (Adstiladrin)
 - ✓ NAI + BCG (Anktiva)
 - ✓ TAR-200
 - ✓ Pembrolizumab
- More Procedures
 - ✓ TURBT
 - ✓ Cystectomy
 - ✓ Q3monthly cystoscopy
- Urinary Symptoms
- Cost

3. Importance of BCG maintenance



4. Intensification by IO does not impact negatively OS

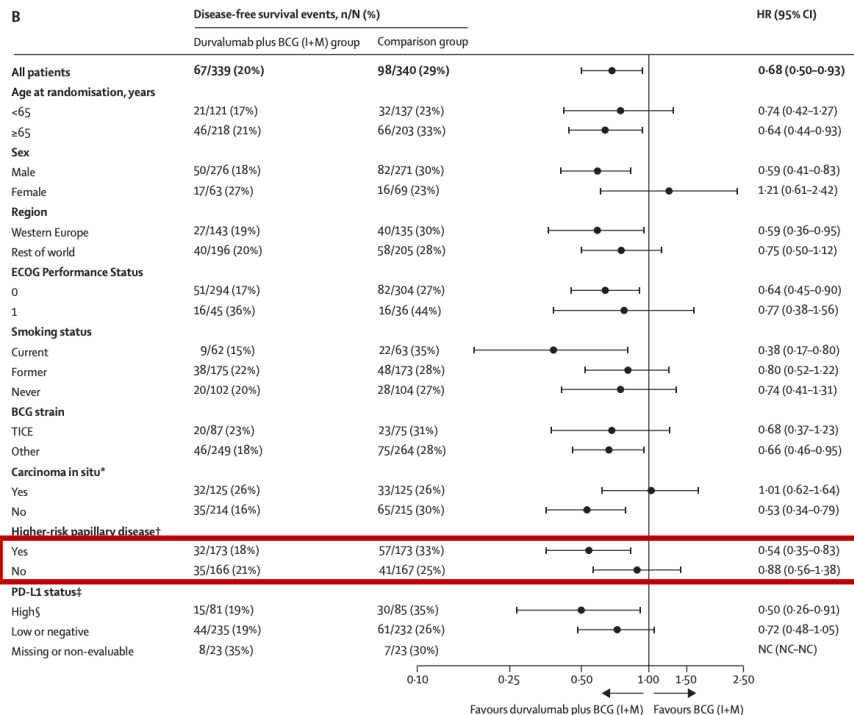


5. Impact of Advers Events

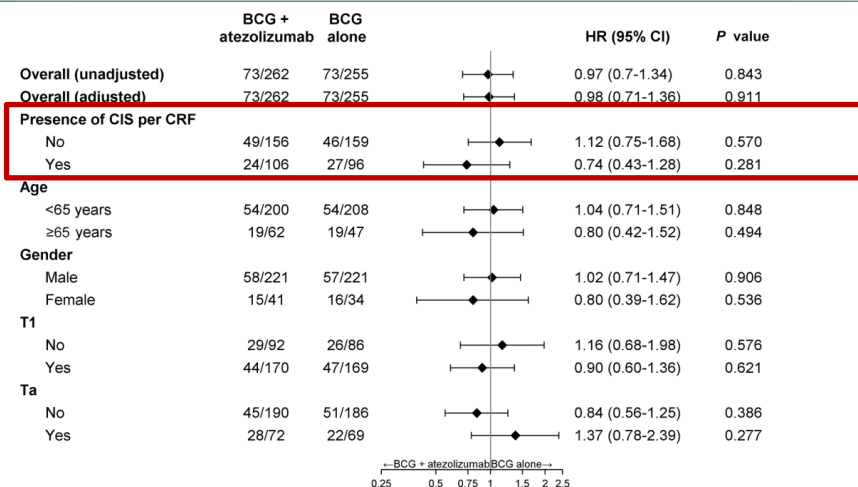
	CREST		POTOMAC		ALBAN	
Treatment Arm	S + BCG (I+M)	BCG (I+M)	D + BCG (I+M)	BCG (I+M)	A + BCG (I+M)	BCG (I+M)
Any Grade 3-4	49%	26%	34%	17%	40%	24%
Treatment Related Adverse Events (TRAEs) Gr 3-4	29%	6%	21%	4%	23%	9%
Immune Related Adverse Events (irAEs) Gr 3-4	16%	0%	8%	<1%	6%	1%
Corticosteroid Use	20%	<1%	16%	<1%	NR	NR
Discontinuation of Study Treatment Due to TRAE	26%	9%	27%	17%	29%	9%
TRAE Death	0%^	0%	0%	0%	0%	0%

6. Selection of Best Candidates

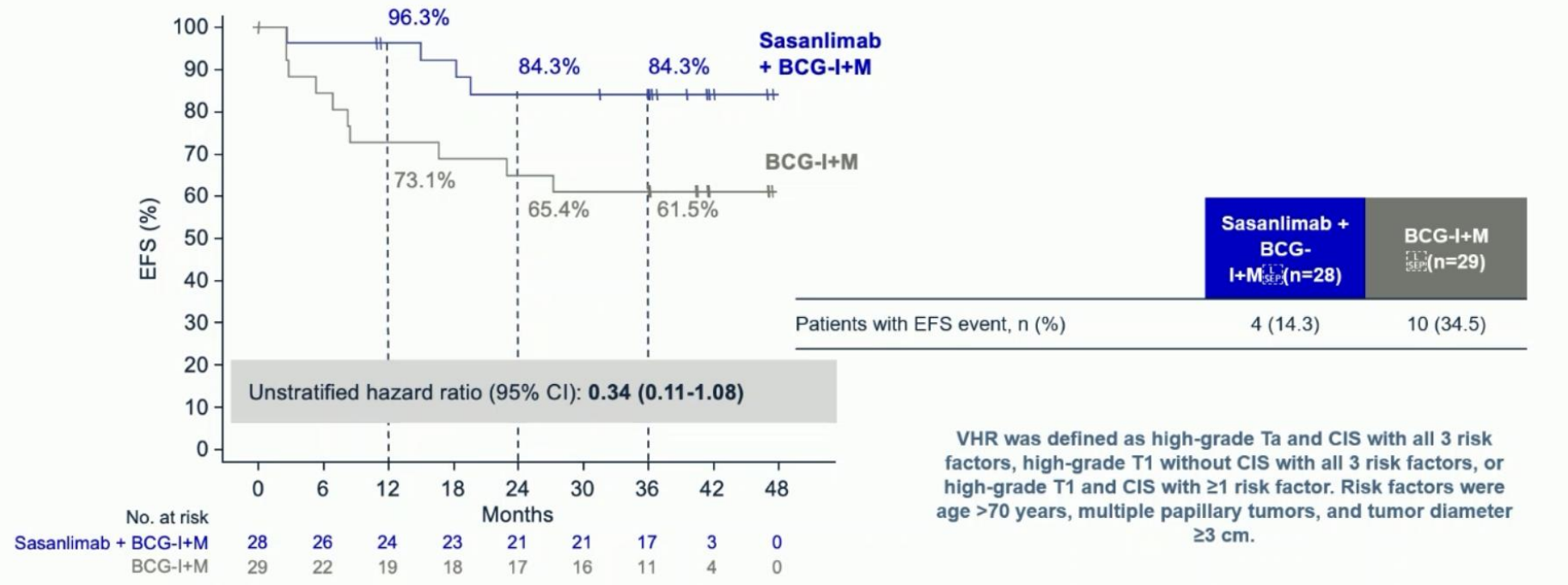
POTOMAC



ALBAN



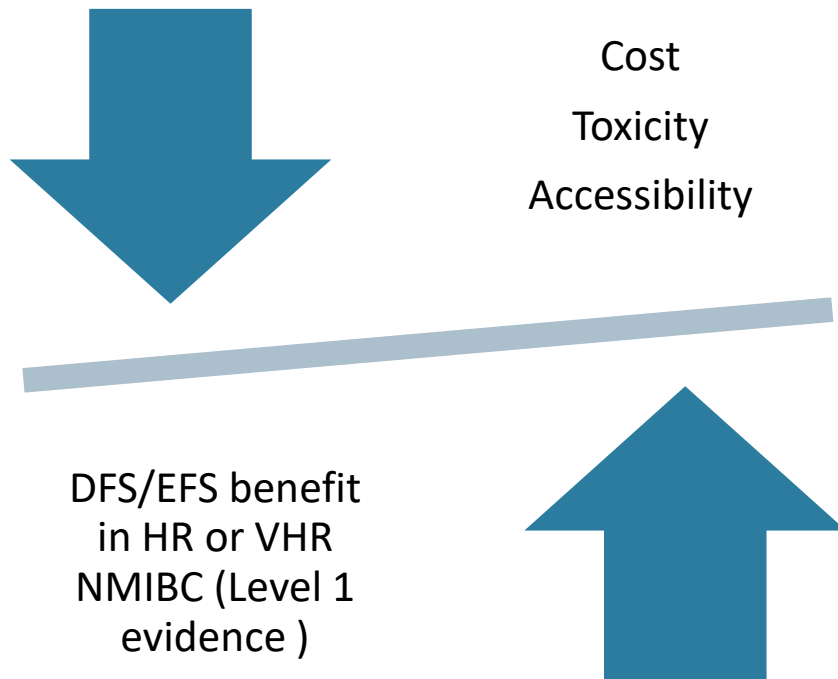
Exploratory Analysis of Very High-Risk population – CREST Study



Conclusions

- 3 phase III RCT well designed, fully accrued, correct follow-up
- CREST and POTOMOC are two positive trials
 - ✓ EFS/DFS benefit
 - ✓ « Higher risk » population – 58% T1
 - ✓ Relevant BCG control arm duration of 2y maintenance
- ALBAN is negative trial
 - ✓ No EFS benefit
 - ✓ « Lower Risk » population – 39 % T1
 - ✓ Truncated BCG control arm duration of only 1y maintenance
 - ✓ EFS included low grade recurrence

Share Decision Making for adding IO to BCG in HR NMIBC



Thank You

Van Damme Julien MD,PhD
julien.vandamme@saintluc.uclouvain.be
Cliniques universitaires Saint-Luc
Université catholique de Louvain
Brussels, Belgium