

Characteristics, treatment patterns and clinical outcomes for patients with non-muscle invasive bladder cancer in Belgium: the BLABEL study

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Background

- Bladder cancer ranks 13th globally in terms of incidence, 7th in Europe, and even 6th in Belgium ¹.
- Numerous clinical trials are currently investigating innovative therapeutic strategies for treating non-muscle invasive bladder cancer (NMIBC).
- Despite the high incidence of bladder cancer in Belgium, there is limited country-specific data on disease characteristics and treatment patterns.
- Additionally, the impact of the chronic BCG shortage, an important first-line treatment option for NMIBC, on the therapeutic algorithm remains unclear.

Objective

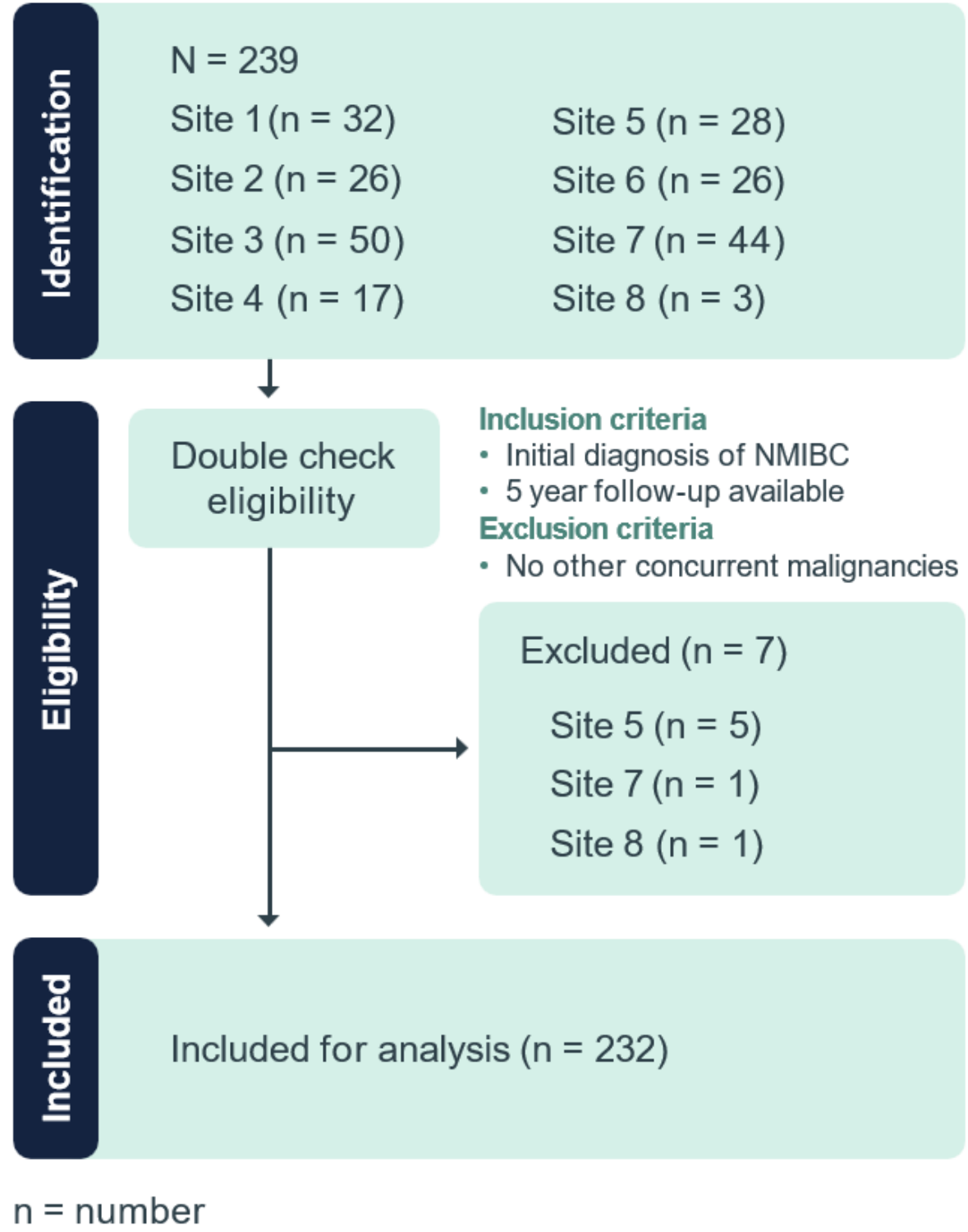
- To investigate first-line treatment patterns for NMIBC in Belgium, including analyzing how baseline patient and tumor characteristics impact initial treatment decisions and their evolution during the first 5 years after the initial diagnosis.

Methods

Study population

- 239 patients were included in the study.
- The inclusion criteria included:
 - Patients diagnosed for the first time with NMIBC in 2016-2017 (01-JAN-2016 to 31-DEC-2017).
 - 5-year follow-up data available, or follow-up until death in case subject died during the 5-year follow-up period.
- Patients who had other concurrent malignancies were excluded from the study.

Figure 1. Study population



Study setting and statistical analyses

- Patients from 8 different sites in Belgium from both academic and non-academic hospitals were included in the study.
- Study timeline: Start – 02-DEC-2022; First site ready – 16-JAN-2023; End – 17-NOV-2023.
- Endpoints and variables were summarized using descriptive statistics and visualized where appropriate.
- Continuous variables included mean, SD, median, Q1–Q3, 95% CI, min, and max.
- Categorical variables were reported as absolute and relative frequencies.
- Continuous variables were compared using t-test/ANOVA or Wilcoxon/Kruskal-Wallis, based on data distribution.
- Categorical variables were compared using chi-squared or Fisher's Exact test, depending on cell counts.
- Test choice for continuous data was based on histogram and Q-Q plot inspection; Satterthwaite was used if variances were unequal.
- Fisher's Exact test was used when $\geq 20\%$ of cells had expected counts < 5 or any cell < 1 .
- CI estimation methods were specified in output footnotes.
- All outputs were generated using SAS® 9.4.
- No formal hypothesis or sample size calculation was used due to the study's descriptive nature.

Results

Patient and tumor characteristics

Table 1. Patient characteristics at initial diagnosis of NMIBC

Characteristics	Total (N = 232)	Characteristics	Total (N = 232)
Age at initial diagnosis, years		NLR, n (%) [95% CI]	
n	232	n	191
Mean (SD)	69.5 (10.20)	Normal - [1; 2]	76 (39.8) [33.1; 46.9]
Sex, n (%) [95% CI]		Abnormal - < 1 or > 2	115 (60.2) [53.1; 66.9]
n	232	ECOG performance status, [n]	
Female	18 (20.7) [15.7; 26.5]	0	<Ref> [83]
Male	184 (79.3) [73.6; 84.0]	1	[67]
Smoking status, n (%) [95% CI]		2	[14]
n	214	3	[6]
Never smoked	64 (29.9) [24.2; 36.4]	Not available	[62]
Former smoker	91 (42.5) [36.1; 49.2]		
Current smoker	59 (27.6) [22.0; 33.9]		
BMI kg/m ²			
n	230		
Mean (SD)	26.76 (4.902)		
BMI status kg/m ² , n (%) [95% CI]			
n	230		
Underweight (< 18.5)	5 (2.2) [0.7; 5.0]		
Healthy ([18.5; 24.9])	82 (35.7) [29.7; 42.0]		
Overweight ([25.0; 29.9])	89 (38.7) [32.6; 45.1]		
Obese (≥ 30)	54 (23.5) [18.5; 29.4]		

BMI: Body mass index; CI: Confidence interval; CRF: Case report form; ECOG: Eastern Cooperative Oncology Group; n: Number of patients in the category; N: Number of patients in the population; NLR: Neutrophil-to-lymphocyte ratio; SD: Standard deviation.

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Table 2. Tumor characteristics at initial diagnosis of NMIBC

Characteristics	Total (N = 232)	Characteristics	Total (N = 232)
TURB/Cystectomy results		TURB/Cystectomy results	
Number of polyps, n (%) [95% CI] ^[1]		Risk classification (EAU 2016, NICE and EAU 2021), n (%) [95% CI] ^[1]	
n	229	n	207
Flat tumor	8 (3.5) [1.5; 6.8]	Low	71 (34.3) [28.2; 41.0]
1	144 (62.9) [56.5; 68.9]	Intermediate	35 (16.9) [12.1; 22.7]
[2, 7]	73 (31.9) [26.2; 38.2]	High	97 (46.9) [40.2; 53.7]
≥ 8	4 (1.7) [0.5; 4.4]	Very high	4 (1.9) [0.5; 4.9]
Prostatic urethra affected, n (%) [95% CI] ^{[1][2]}		Risk reclassification (EAU 2016)	
n	183	n	232
Yes	3 (1.6) [0.3; 4.7]	Low	43 (18.53)
No	109 (59.6) [52.3; 66.4]	Intermediate	49 (21.1)
Not analyzed	71 (38.8) [32.0; 46.0]	High	140 (60.3)
T classification, n (%) [95% CI] ^{[1][2]}		Risk reclassification (NICE 2015)	
n	222	n	232
T0	0 [0.0; 1.6]	Low	64 (27.59)
Ta	125 (56.3) [49.7; 62.7]	Intermediate	43 (18.53)
T1	97 (43.7) [37.3; 50.3]	High	125 (53.88)
New T group, n (%) [95% CI] ^{[1][3]}		EORTC - Recurrence	
CIS with or without Ta/T1	31 (13.4) [9.3; 18.4]	n	182
Ta/T1 without CIS	201 (86.6) [81.7; 90.4]	Median	3.0
Tis, n (%) [95% CI] ^{[1][2]}		Q1, Q3	1.0; 6.0
n	232	EORTC - Progression	
Tis	21 (9.1) [5.7; 13.5]	n	182
No Tis	201 (86.6) [81.7; 90.4]	Median	5.0
100% Tis	10 (4.3) [2.1; 7.8]	Q1, Q3	0.0; 12.0
Histological subtype, n (%) [95% CI] ^[1]		Urine cytology	
n	231	Urine cytology performed	119
Pure urothelial	219 (94.8) [91.1; 97.0]	Urine cytology results	
Variant	12 (5.2) [2.7; 8.9]	n	117
Lymphovascular invasion, n (%) [95% CI] ^[1]		Not sufficient material	3 (2.6) [0.5; 7.3]
n	232	Negative for high-grade	34 (29.1) [21.0; 38.2]
Yes	1 (0.4) [0.0; 2.4]	Atypical	35 (29.9) [22.4; 38.7]
No	146 (62.9) [56.6; 68.9]	Suspicious for high-grade	26 (22.2) [15.1; 30.8]
Not analyzed	85 (36.6) [30.7; 43.0]	High-grade	9 (7.7) [3.6; 14.1]
Histological tumor grade, n (%) [95% CI] ^[1]		Low-grade	1 (0.9) [0.0; 4.7]
n	205	Other	9 (7.7) [3.6; 14.1]
Grade 1	61 (29.8) [23.9; 36.3]		
Grade 2	51 (24.9) [19.5; 31.2]		
Grade 3	93 (45.4) [38.7; 52.2]		

CI: Confidence interval; EORTC: European Organization for Research and Treatment of Cancer; n: Number of patients in the category; N: Number of patients in the population; NMIBC: Non-muscle invasive bladder cancer; Q1: 25th percentile; Q3: 75th percentile; Tis: Carcinoma in situ; TURB: Transurethral resection of bladder tumor.

^[1]Percentages and 95% CI calculated using the number of patients/recurrences with TURB performed at Imipont. ^[2]In cases of cystectomy performed, the results from cystectomy pathology report are used in case they are not consistent or missing in the TURB pathology report.

^[3]Risk classification defined as any patient with a different risk classification assigned by the central medical monitor (sponsor) when compared to the risk classification recorded by the site.

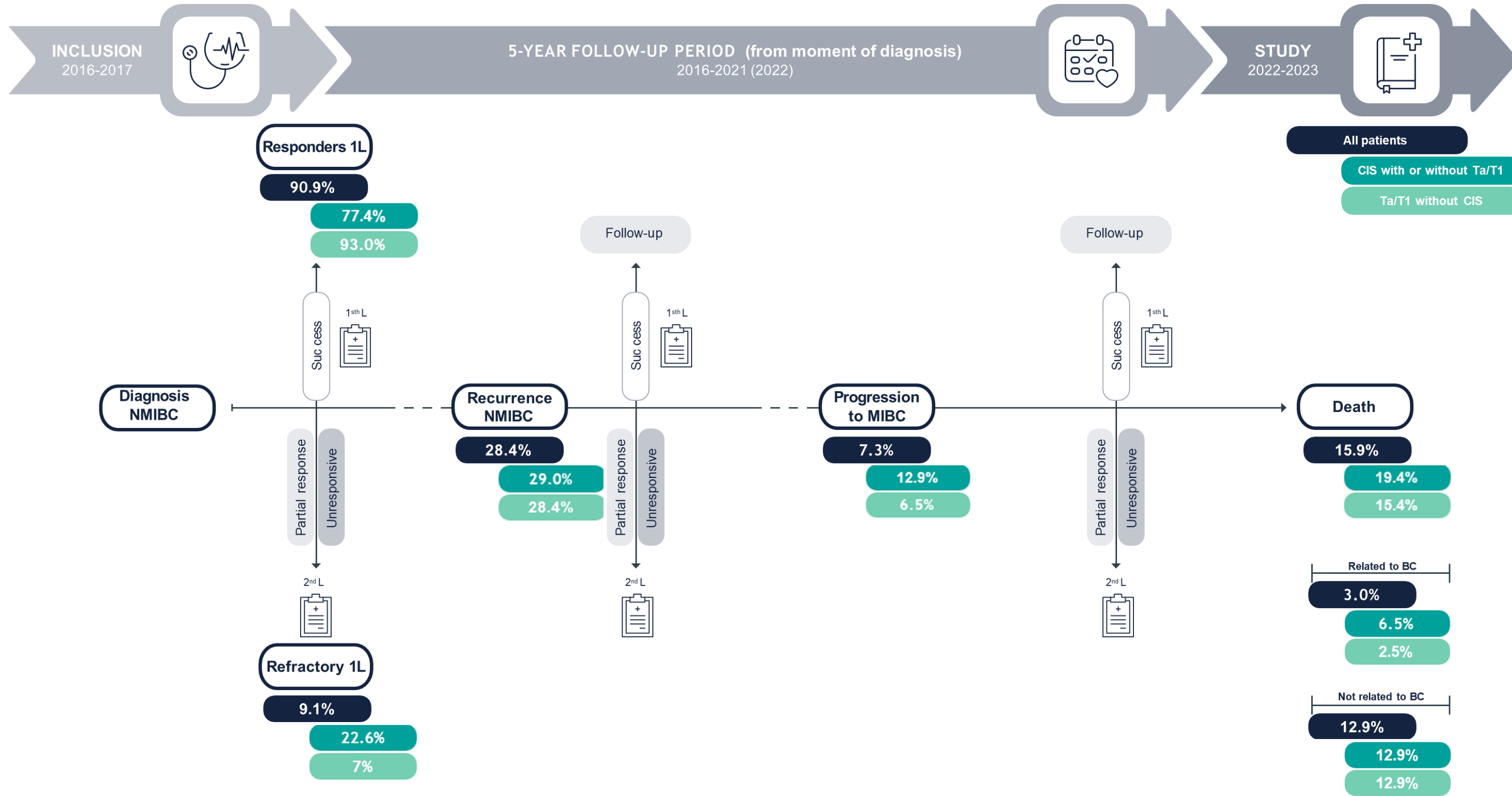
Main Results

- In total, 232 patients with a median age at initial diagnosis of 70 years were enrolled.
- At diagnosis, respectively, 27.6%, 18.5% and 53.9% of patients had low-, intermediate- or high-risk disease (NICE 2015).
- Overall, 86.6% of patients had Ta/T1 disease without carcinoma in situ (CIS), while the remaining 13.4% had CIS with or without T1/Ta disease.
- All patients underwent a transurethral resection of the bladder tumour (TURBT).
- A single, immediate, post-operative intravesical instillation of chemotherapy was given to 42.8% of patients and 20.7% underwent a re-TURBT.
- Overall, 42.2% of patients were monitored through observation. Observation rates were 89.1% for low-risk patients, 46.5% for intermediate-risk, and 16.8% for high-risk patients.
- BCG installations were the first line treatment in 44.4% of patients, with rates of 1.6%, 30.2% and 72% in low-, intermediate- and high-risk patients.
- Overall, 10.8% of patients received intravesical chemotherapy in first line.*
- 90.9% of patients had initially a complete response to their first line treatment, and 28.4% presented with a recurrence during the 5-year follow-up. Of the patients with recurrence almost half were classified as high risk at diagnosis, one third as low risk and nearly one fifth as intermediate risk.†
- During 5 years follow-up, 7.3% of patients progressed to muscle-invasive bladder cancer (MIBC) and 3% developed metastatic bladder cancer.
- Overall, 3% of patients died due to bladder cancer during the 5-year follow-up.
- At 5 years of follow-up, 65.5% of patients remained disease-free without recurrence or progression of disease.
- The presence of carcinoma in situ (CIS) adversely affected patient outcomes, resulting in a first-line complete response rate of only 77.4%.
- Additionally, 29% of patients with CIS experienced a recurrence, and 12.9% progressed to MIBC or metastatic bladder cancer.

* The remaining 2.6% of patients received alternative treatments: 1.7% cystectomy, 0.4% BCG + cystectomy and 0.4% other.

† based on the 2016 EAU criteria.

Figure 2. Disease evolution



Conclusions

- Real-world treatment patterns for patients with NMIBC in Belgium are largely in accordance to the contemporary guidelines.
- The majority of patients had a complete response to the initial treatment, with more than half remaining disease free after five years.
- Compared to low- and intermediate-risk patients, high-risk NMIBC patients, particularly those with CIS, have worse clinical outcomes and prognosis, demonstrating higher unmet need.

References

- GLOBOCAN. Cancer today: data visualization tools for exploring the global cancer burden in 2020: GLOBOCAN; 2020 [cited 2022 Feb 10th]. Available from: <https://gco.iarc.fr/today/home>.

Disclosures

H. Maes is an employee of Merck Sharp & Dohme (MSD).
L. De Smedt is an employee of Merck Sharp & Dohme (MSD).
B. Tombal is an advisor and/or consultant for Accord, Astellas, Amgen, Bayer, Curium, Ferring, MSD, Myovant, Janssen, and Novartis.

