

SUPPLEMENTARY APPENDIX

On the Horizon: A Global Multidisciplinary Perspective on Delivering Emerging Therapies for Patients With BCG-Naïve High-Risk NMIBC

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Figure S1. Treatment of NMIBC: Current responsibilities and additional responsibilities in case of approval of PD-(L)1 inhibitors for BCG-naïve NMIBC by country: **(a)** Canada, **(b)** Germany, **(c)** Spain, **(d)** UK, and **(e)** US.

AE, adverse event; BC, bladder cancer; BCG, Bacillus Calmette-Guérin; ICI, immune checkpoint inhibitor; irAE, immune-related adverse event; IV, intravenous; MIBC, muscle invasive bladder cancer; MDT, multidisciplinary team; NMIBC, non-muscle invasive bladder cancer; PD-(L)1, PD-1/PD-L1; SC, subcutaneous; TURBT, transurethral resection of bladder tumor.

(a) CANADA

Treatment of NMIBC: Current responsibilities

Urologist

- Cystoscopy, TURBT, biopsy
- Diagnosis
- Initial treatment decision
- Intravesical BCG or chemotherapy
- Cystectomy
- Follow-up and monitoring disease progression
- Referral to medical oncology for IV ICI for very high-risk NMIBC, ICI clinical trials

Medical oncologist

Up to now: Administration of systemic chemotherapy and IV ICIs, and AE monitoring and management, for advanced BC and clinical trials in NMIBC

Nurses

(registered nurses, specialized oncology nurses)

Urology registered nurses:

- Administration of intravesical treatment
- Setting up surveillance cystoscopies
- Catheter care

Oncology nurses:

Up to now: Involved in IV administration of chemotherapy and ICIs, AE monitoring, and patient education on chemotherapy and ICIs for advanced BC and clinical trials in NMIBC

- There is currently little multidisciplinary collaboration in the NMIBC setting outside of clinical trials; however, patients with very high-risk NMIBC may be discussed across urology and medical oncology
- For clinical trials, urology teams administer BCG and may administer SC ICIs with medical oncology support; medical oncology is responsible for IV ICIs

Treatment of NMIBC: Additional responsibilities in case of approval of PD-(L)1 inhibitors for BCG-naïve NMIBC

Urologist

- Referral of eligible patients to medical oncology
- Administration of SC ICIs (potentially)
- Some irAE management, in conjunction with medical oncology
- Need for education on ICI therapy and irAE monitoring

Medical oncologist

Increased capacity required for NMIBC:

- Administration of ICIs (IV and SC)
- irAE monitoring and management for ICIs
- Support with irAE management for SC ICIs administered by urology
- Patient education on ICIs
- Need for education on NMIBC

Nurses

(registered nurses, specialized oncology nurses)

- Coordinating appointments across disciplines

Urology nurses:

- SC injection of ICIs (potentially)

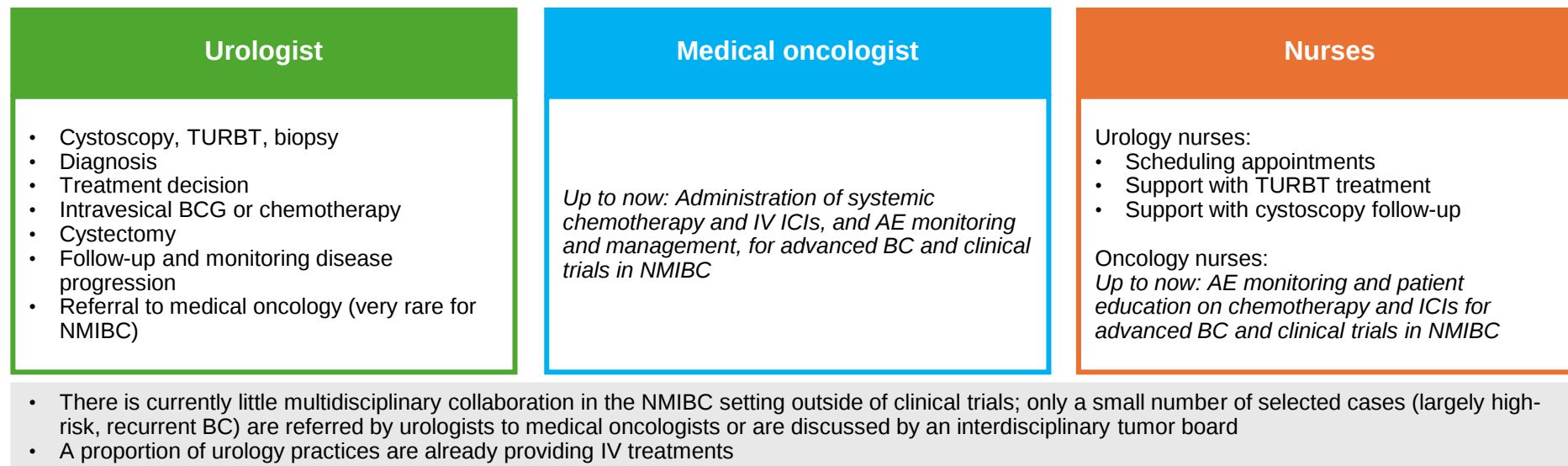
Oncology nurses – increased capacity required for NMIBC:

- IV administration of ICIs
- irAE monitoring
- Patient education on ICIs

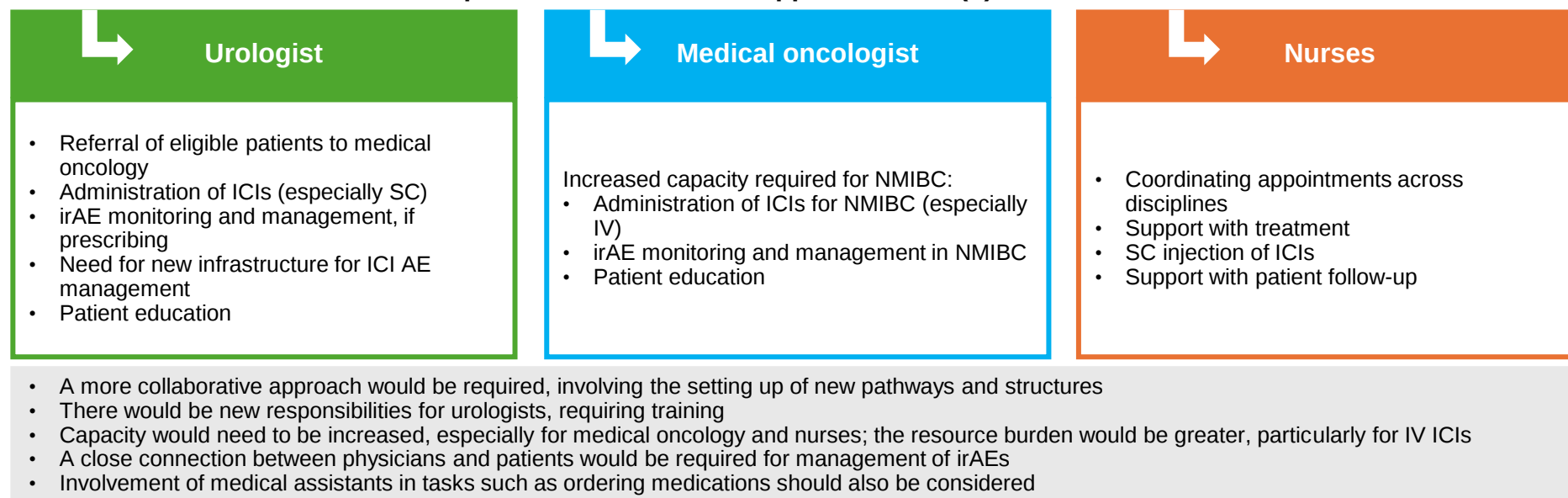
- A more multidisciplinary approach would be required, with increased collaboration between urologists and medical oncologists
- An increase in responsibilities would be expected for all team members involved, in particular for urology teams
- Capacity would need to be increased, especially for medical oncology and nurses, to accommodate the increase in the number of eligible patients
- Increasing support from registered nurses could help urologists and reduce the additional burden for medical oncologists
- Involvement of other advanced practice providers in tasks such as scheduling tests, treatment administration, and AE monitoring should also be considered

(b) GERMANY

Treatment of NMIBC: Current responsibilities



Treatment of NMIBC: Additional responsibilities in case of approval of PD-(L)1 inhibitors for BCG-naïve NMIBC



(c) SPAIN

Treatment of NMIBC: Current responsibilities

Urologist	Medical oncologist	Nurses
• Cystoscopy, TURBT, biopsy • Diagnosis • Treatment decision (initial and post-BCG) • Intravesical BCG or chemotherapy • Cystectomy • Follow-up and monitoring disease progression	<i>Up to now: Administration of systemic chemotherapy and IV ICIs, and AE monitoring and management, for advanced BC and clinical trials in NMIBC</i>	Urology nurses: • Assist with cystoscopies • Scheduling treatment • Administering intravesical treatment • Catheter care • Patient follow-up Oncology nurses: <i>Up to now: Involved in IV administration of chemotherapy and ICIs, AE monitoring and patient education on chemotherapy and ICIs for advanced BC and clinical trials in NMIBC</i>
• Treatment is largely by urology outside of clinical trials; some centers may have a dedicated bladder cancer unit for all disease stages; at some centers, selected complex or borderline NMIBC cases (mostly very high-risk or recurrence) and candidates for clinical trials are discussed by an MDT • For clinical trials, IV ICIs are the responsibility of medical oncology; for SC ICIs, administration may be done by urology nurses, with follow-up shared between urology and medical oncology		

Treatment of NMIBC: Additional responsibilities in case of approval of PD-(L)1 inhibitors for BCG-naïve NMIBC

Urologist	Medical oncologist	Nurses
• Potentially administration of ICIs (SC, potentially also IV) • irAE monitoring and management, in conjunction with medical oncology • Need for education on ICI therapy and irAE monitoring	Increased capacity required for NMIBC: • Administration of ICIs (IV, also SC) for NMIBC • irAE monitoring and management, potentially in conjunction with urology	Urology nurses: • Administration of ICIs, especially SC • AE monitoring Oncology nurses – increased capacity required for NMIBC: • Administration of ICIs, especially IV • irAE monitoring • Patient education on ICIs
• A culture focused more on teamwork would need to be developed, with urologists and medical oncologists largely drawing on their existing expertise but collaborating during discussion and follow-up of patients, as done for clinical trials; training on multidisciplinary management would be needed • Collaboration and excellent communication between urologists and medical oncologists would be crucial, regardless of who administers the treatment • Not all candidates for PD-(L)1 inhibitors would need to be discussed by an MDT; there is insufficient capacity for MTD discussion of all high-risk NMIBC cases, but for non-borderline cases, efficient ways to refer and communicate between disciplines are sufficient • An increase in workload, including for nurses, is expected		

(d) UK

Treatment of NMIBC: Current responsibilities

Urologist	Medical oncologist	Nurses (clinical nurse specialists)
• Cystoscopy, TURBT, biopsy • Diagnosis • Involved in MDT discussions for NMIBC • Intravesical BCG or chemotherapy • Review of patient and potentially referral to medical oncologist • Cystectomy • Assessing response to therapy • Follow-up and monitoring disease progression	• Involved in MDT discussions for NMIBC <i>Also: Administration of systemic chemotherapy and IV ICIs, and AE monitoring and management, for advanced BC and clinical trials in NMIBC</i>	Potentially involved in all steps: • Triaging referrals from general practitioner or emergency care • Delivering hematuria clinic (clinical assessment, flexible cystoscopy, biopsy, imaging) • Scheduling treatments • Administration of intravesical treatment • Performing follow-up cystoscopies • Patient education and training <i>Also: IV administration of chemotherapy and ICIs, irAE monitoring and management, patient education on chemotherapy and ICIs for advanced BC and clinical trials in NMIBC</i>

- All patients who had TURBT or bladder biopsy are discussed by local MDTs, and all high-risk NMIBC cases at regional MDTs (in the same way as MIBC); these are centrally mandated pathways; however, there is a national drive towards streamlining
- MDTs include urologists, oncologists, and nurses, as well as radiologists, radiation oncologists, pathologists, and MDT coordinators
- Clinical nurse specialists often play integral roles across all elements of the NMIBC pathway; the extent of their involvement at individual centers is dependent on availability, but they are capable of delivering the great majority of patient care in NMIBC
- Close collaboration between urology and oncology is already in place for clinical trials, with treatment pathways mapped out

Treatment of NMIBC: Additional responsibilities in case of approval of PD-(L)1 inhibitors for BCG-naïve NMIBC

Urologist	Medical oncologist	Nurses (clinical nurse specialists)
• Administration of ICIs (potentially) • Need for education on ICI therapy and irAE monitoring (early and late toxicities)	Increased capacity required for NMIBC: • Assessing patient's fitness for ICI therapy • Administration of ICIs (IV or SC) • irAE monitoring and management	Increased capacity required for NMIBC: • Administration of ICIs (IV or SC) • irAE monitoring • Patient education on ICIs

- Use of ICIs in the NMIBC setting would increase substantially; the medical oncology workforce and resource allocation would need to be increased to deliver these treatments
- There would be a substantial need for additional clinical nurse specialists, especially in smaller hospitals
- It would be very important for urologists and medical oncologists to work together closely in NMIBC

(e) US

Treatment of NMIBC: Current responsibilities

Urologist

- Cystoscopy, TURBT, biopsy
- Diagnosis
- Treatment decision
- Intravesical BCG or chemotherapy
- Cystectomy
- AE monitoring
- Follow-up and monitoring disease progression
- Referral to medical oncology for IV therapy is common; some practices can administer IV therapy

Medical oncologist

- Use of IV pembrolizumab for some patients with BCG-unresponsive NMIBC

Also: Administration of systemic chemotherapy and IV ICIs, and AE monitoring and management, for advanced BC and clinical trials in NMIBC

Nurses

- Scheduling of treatments and clinic visits, assisting in referral process
- Administration of intravesical treatment
- Preparation and administration of ICIs
- AE monitoring
- Patient education on ICIs
- Liaising between clinicians and patients

- High-risk NMIBC is typically managed by urology, but medical and radiation oncology may be involved, e.g., for BCG-unresponsive cases; a multidisciplinary approach, or close collaboration and referrals, is used for such patients, with complicated cases discussed at tumor board meetings
- In NMIBC, ICIs are largely used in clinical trials; the level of use (of pembrolizumab) in the indicated setting is low
- Most urology clinics do not administer IV treatments, but some uro-oncology practices offer the full range of available therapies
- Urology/uro-oncology teams, clinic and research nurses, and pathologists communicate closely throughout all stages of a patient's treatment journey

Treatment of NMIBC: Additional responsibilities in case of approval of PD-(L)1 inhibitors for BCG-naïve NMIBC

Urologist

- Administration of SC ICIs
- Adaptation for administration of IV ICIs or referral to medical oncology
- irAE monitoring and management
- Need for education on ICI therapy and irAE monitoring

Medical oncologist

Increased capacity required for NMIBC:

- Administration of ICIs, especially IV
- irAE monitoring and management
- Patient education on ICIs

Nurses

Increased capacity required for NMIBC:

- Administration of ICIs (IV or SC)
- irAE monitoring
- Patient education on ICIs

- A well-structured dedicated MDT team with relevant expertise and sufficient resources would be essential, with medical oncology as the cornerstone for collaboration with other team members for diagnosis, toxicity assessment, and optimal management of AEs, follow-up, etc
- MDT-based working would need to be expanded substantially for community urology practices
- Pathways should be adapted to individual clinics to take existing structures into account
- Medical assistants, for tasks such as administration of treatment, and nurse navigators, for patient support and education, should also be included