Treatment of Non-Metastatic Muscle-Invasive Bladder Cancer: AUA/ASCO/ASTRO/SUO Guideline

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PLENARY SESSION
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DISCLOSURES

Consultant/Meeting participant: Janssen

PURPOSE

This guideline provides a risk-stratified, clinical framework for the management of muscle-invasive urothelial bladder cancer and is the product of a multidisciplinary collaboration between the American Urological Association (AUA), the American Society of Clinical Oncology (ASCO), the American Society for Radiation Oncology (ASTRO) and the Society of Urologic Oncology (SUO).

SYSTEMATIC REVIEW

AHRQ SYSTEMATIC REVIEW
January 1990- October 2014

REPORT SUPPLEMENTATION
AHRQ Report Publication- February 2016

A
- **Well conducted RCT's**
- **Exceptional observational studies**

B
- **RCT's and/or observational studies with some weaknesses**

C
- **Observational studies that are inconsistent -difficult to interpret**

EPIDEMIOLOGY

There are 79,030 new cases of bladder cancer and 16,870 bladder cancer deaths predicted for 2017 in the U.S. Approximately 25% of newly diagnosed patients have muscle-invasive disease,[7] a rate that has not changed over the last 10 years.

Estimated New Cases

	Males	
Prostate	161,360	19%
Lung & bronchus	116,990	14%
Colon & rectum	71,420	9%
Urinary bladder	60,490	7%
Melanoma of the skin	52,170	6%
Kidney & renal pelvis	40,610	5%
Non-Hodgkin lymphoma	40,080	5%
Leukemia	36,290	4%
Oral cavity & pharynx	35,720	4%
Liver & intrahepatic bile duct	29,200	3%
All Sites	**836,150**	**100%**

Siegel 2017, Smith 2014, Burger 2013, Charlton 2014

PROGNOSIS

The overall prognosis of patients with MIBC has not changed in the last 30 years. In patients who undergo cystectomy, systemic recurrence rates vary by stage.

Most recurrences occur within the first two to three years after cystectomy, and at this time, most patients with recurrence after cystectomy are not cured with current systemic therapies.

Pathologic Stage	Approx. Systemic Recurrence Rate Following Cystectomy (%)
pT2	20-30
pT3	40
pT4	>50
Node-positive	70

Karakiewicz 2006, International Bladder Cancer Nomogram Consortium 2006, Seisen 2016

PROGNOSIS

The dominant pathologic predictors for recurrence and survival are tumor stage and nodal status. Other prognostic factors include gender, presence of hydronephrosis, lymphovascular invasion, soft tissue margin status, and molecular subtyping characteristics.

There is also a significant impact of treatment choices on outcome with the type and timing of therapy playing an important role.

Survival Rates for Bladder Preserving Combined-Modality Therapy (%)	
Overall	
5-year	57
10-year	36
Disease-Specific	
5-year	71
10-year	65

Mak 2014, Dobruch 2016, Lotan 2005, Choi 2014, Zylinas 2013, Cancer Genome Atlas Research Network 2014, Sjodahl 2012, Choi 2014, Damrauer 2014

GUIDELINE STATEMENTS

INITIAL EVALUATION AND COUNSELING

1. History and physical examination
2. Staging evaluation
   - Imaging
   - Laboratory evaluation
3. Review of suspected variant histology by an experienced GU pathologist
4. Discussion of curative treatment options
5. Discussion of treatment implications for QOL

Multi-disciplinary discussion → Surgery, Chemotherapy, Radiotherapy

GUIDELINE STATEMENTS

TREATMENT: CHEMOTHERAPY (NAC/AC)

6. Cisplatin-based NAC to eligible radical cystectomy patients prior to cystectomy
7. Carboplatin-based NAC; cisplatin-ineligible patients
8. Timing of radical cystectomy following NAC
9. Cisplatin-based AC

- *There are no validated predictive factors or clinical characteristics associated with an increased or decreased probability of response and benefit using cisplatin-based NAC*
- *The best regimen and duration for cisplatin-based NAC remains undefined*
- *The decision regarding eligibility for cisplatin-based NAC should be based on comorbidities and performance status*

GUIDELINE STATEMENTS

TREATMENT: RADICAL CYSTECTOMY

10. Radical cystectomy with bilateral pelvic lymphadenectomy for surgically eligible patients
11. Standard radical cystectomy
    - Males: bladder, prostate, and seminal vesicles
    - Females: bladder, uterus, fallopian tubes, ovaries, and anterior vaginal wall
12. Consideration of sexual function preserving procedures for patients with organ-confined disease

GUIDELINE STATEMENTS

TREATMENT: URINARY DIVERSION

13. Ileal conduit, continent cutaneous, and orthotopic neobladder urinary diversions
14. Verification of a negative urethral margin for orthotopic diversions

The choice of urinary diversion has a significant impact on long-term QOL for patients who undergo radical cystectomy, and each type of diversion is associated with its own unique potential complications.

GUIDELINE STATEMENTS

TREATMENT: PERIOPERATIVE MANAGEMENT

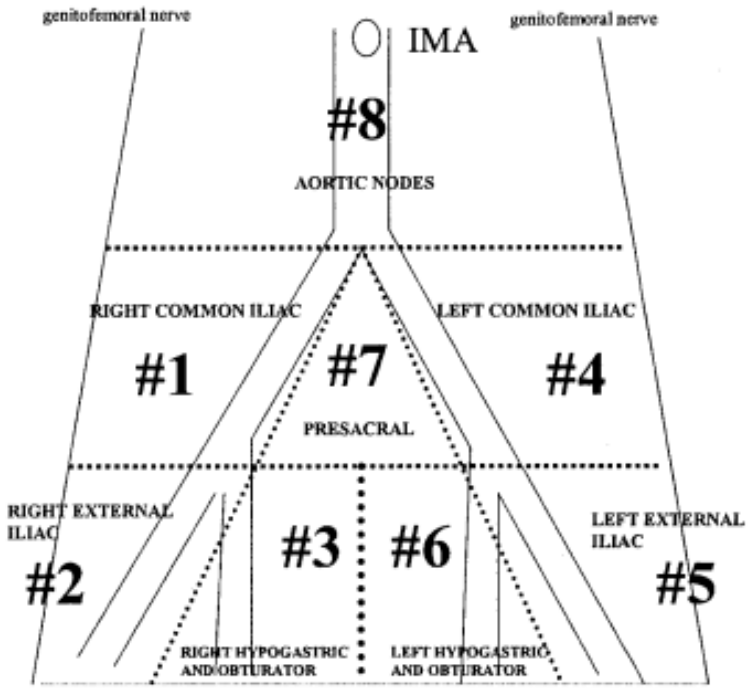
15. Optimization of patient performance status
    - Optimization in accordance with enhanced recovery pathway principles
    - Nutritional counseling
    - Smoking cessation
    - Bowel preparation
16. Pharmacologic thromboembolic prophylaxis
    - AUA Best Practice Statement on the Prevention of Deep Vein Thrombosis
17. μ -opioid antagonist therapy
18. Care of urinary diversion

GUIDELINE STATEMENTS

TREATMENT: PELVIC LYMPHADENECTOMY

19. Bilateral pelvic lymphadenectomy at the time of any surgery with curative intent

20. Standard lymphadenectomy



Bochner 2004

GUIDELINE STATEMENTS

BLADDER PRESERVATION: PATIENT SELECTION

21. Patients who desire to retain the bladder; patients unfit for radical cystectomy
22. Maximal debulking transurethral resection of bladder tumor and assessment of multifocal disease/carcinoma in situ

Panel preferred approach → TURBT, systemic chemotherapy, radiation therapy, and ongoing cystoscopy to evaluate response

GUIDELINE STATEMENTS

MAXIMAL TURBT & PARTIAL CYSTECTOMY

23. Patients who are fit and consent to radical cystectomy should not undergo maximal TURBT/partial cystectomy as primary curative therapy

PRIMARY RADIATION THERAPY

24. Primary radiation therapy should not be offered as a curative treatment

GUIDELINE STATEMENTS

MULTIMODAL BLADDER PRESERVING THERAPY

25. Maximal transurethral resection of bladder tumor, chemotherapy combined with external beam radiation therapy, and planned cystoscopic re-evaluation
26. Radiation sensitizing chemotherapy regimens with cisplatin or 5- fluorouracil and mitomycin C
27. Surveillance of patients who elect bladder preservation

Those who are biopsy-proven complete responders to bladder preserving protocols remain at risk for both invasive and non-invasive recurrences as well as new tumors in the upper tracts. Recurrences may be successfully managed by prompt salvage therapy.

GUIDELINE STATEMENTS

BLADDER PRESERVING TREATMENT FAILURE

28. Surgical treatment of patients with recurrent or residual disease
29. Non-muscle invasive recurrences after bladder preserving therapy

PATIENT SURVEILLANCE & FOLLOW UP

30. Patient imaging
31. Laboratory assessment
32. Urethral remnant as a site for potential recurrence

GUIDELINE STATEMENTS

PATIENT SURVEILLANCE & FOLLOW UP

33. Participating in a cancer support group/individual counseling

bcan.org
cancersupportcommunity.org
cancercare.org
bladdercancersupport.org
cancer.org
urologyhealth.org

34. Adoption of healthy lifestyle habits

VARIANT HISTOLOGY

35. Unique clinical characteristics that may require divergence from standard evaluation and management

As variant histologies become recognized, the most appropriate care and evaluation may also become better understood as well as increasingly defined. Importantly, treatment recommendations previously outlined may NOT apply to these patients who represent a small but significant number.

FUTURE RESEARCH

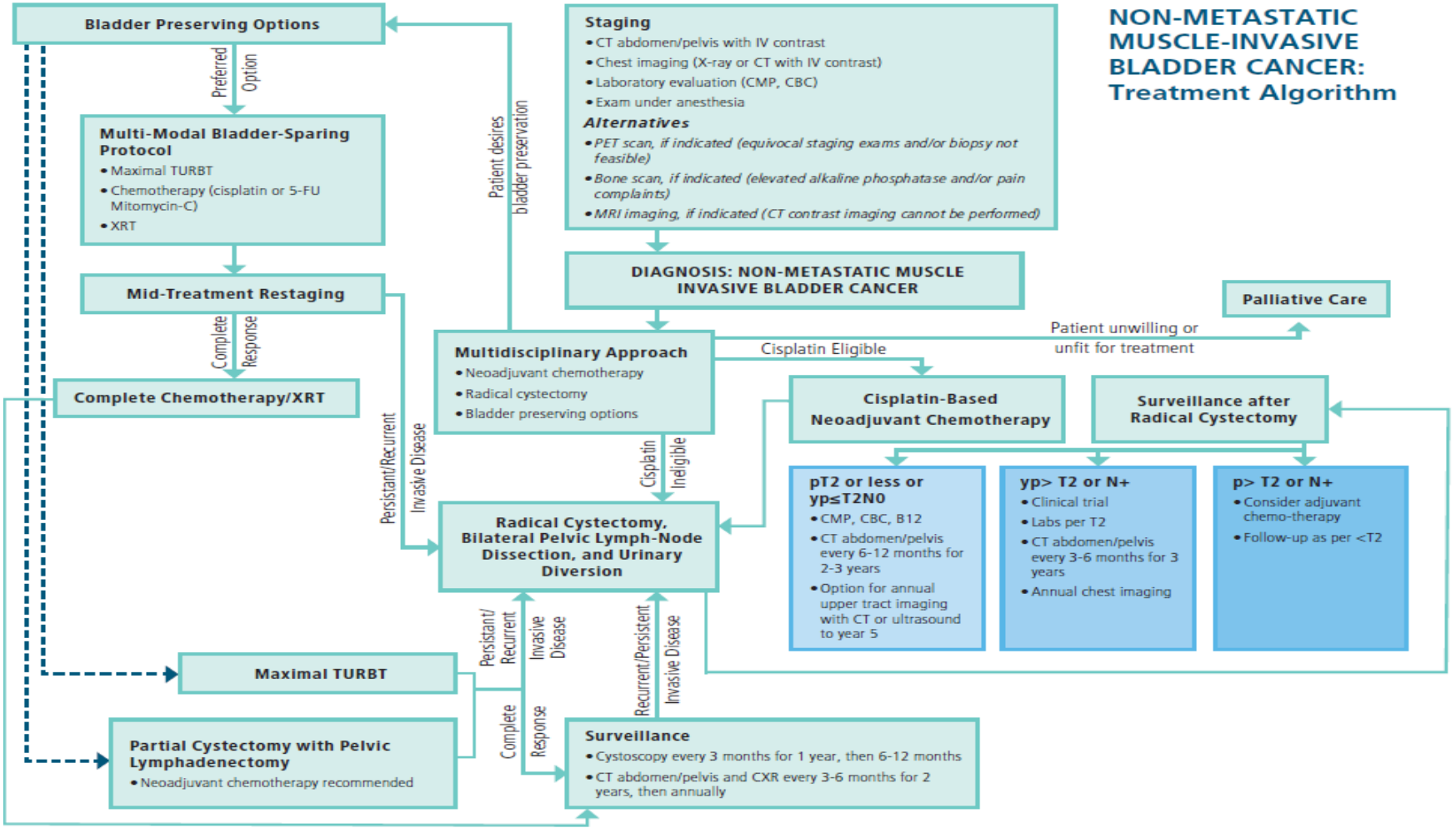
Several key areas of future research need emphasis to improve clinical care and provide a path to better patient outcomes with invasive bladder cancer.

Detection & markers: Enhanced detection of bladder cancer cells via imaging technology or other means is needed to identify patients with high-risk disease and advanced disease.

Therapy: The rapid introduction of novel immunotherapeutic agents into the therapeutic armamentarium for treatment of bladder cancer has begun to show promise.

Surveillance: the role of specific imaging tests and laboratory studies as well as their appropriate interval has yet to be established, and future studies are needed to define a patient specific approach.

NON-METASTATIC MUSCLE-INVASIVE BLADDER CANCER: Treatment Algorithm



CBC= complete blood count; CMP= comprehensive metabolic panel; CXR= chest X-ray; p= pathologic stage; TURBT=trans-urethral resection of bladder tumor; XRT= external beam radiation therapy; yp= pathologic stage after neoadjuvant chemotherapy

ACKNOWLEDGEMENTS

Muscle-Invasive Bladder Cancer Panel

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Muscle-Invasive Bladder Cancer Guideline Course: Monday, May 15, 10am-12pm