AUA 2024 Genitourinary Updates

AUA 2024 San Antonio MAY 3-6

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UCI Urology

Outline

1. Prostate Cancer
2. Bladder Cancer/UTUC
3. Testicular Cancer
4. Kidney Cancer

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Prostate Cancer

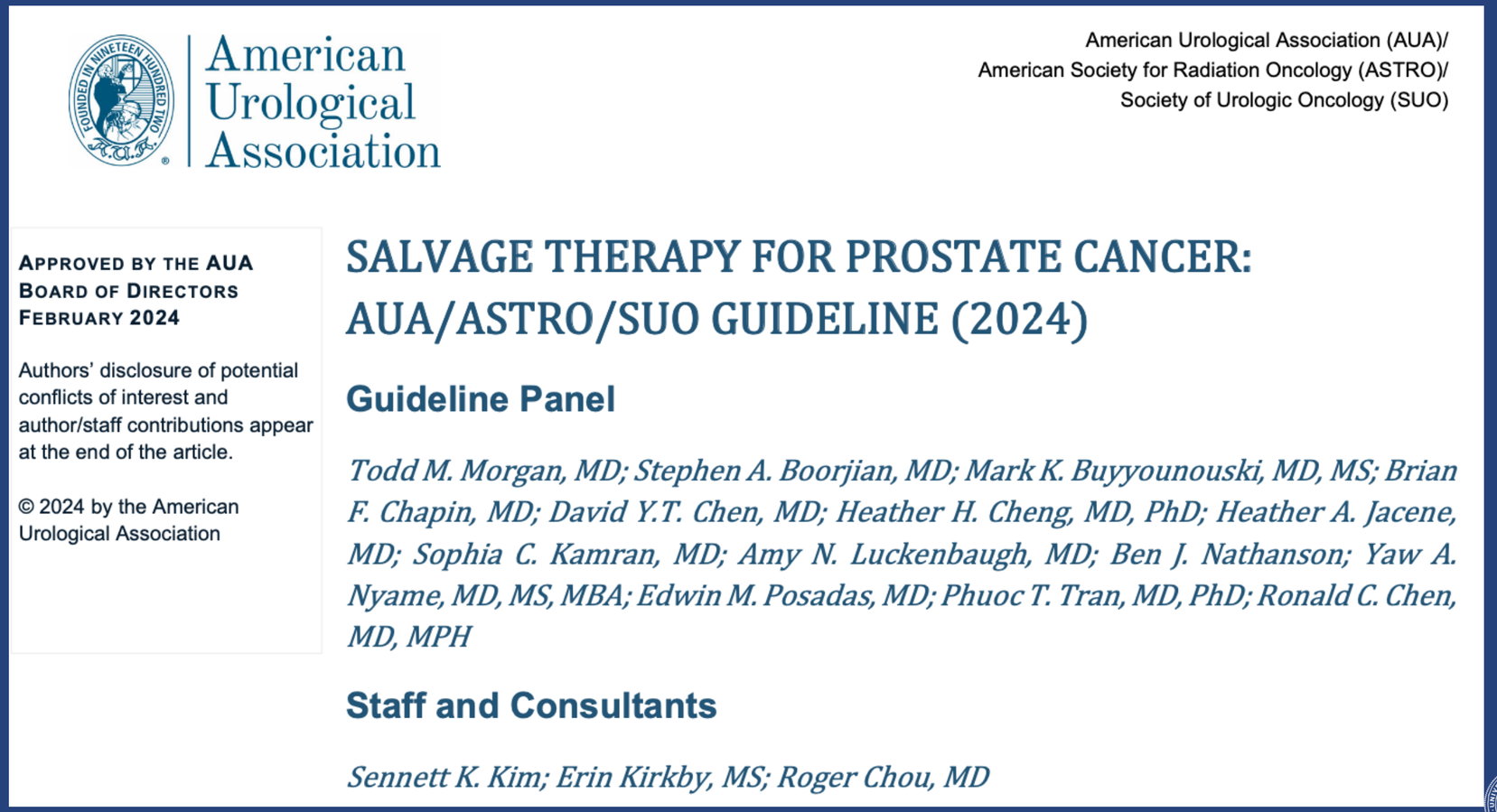
2023: Guidelines for PSA screening

2024: Guidelines: Salvage Therapy for Prostate Cancer

UCI Urology

Prostate Cancer

Guidelines: Salvage Therapy for Prostate Cancer



American Urological Association

American Urological Association (AUA)/
American Society for Radiation Oncology (ASTRO)/
Society of Urologic Oncology (SUO)

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Authors' disclosure of potential conflicts of interest and author/staff contributions appear at the end of the article.

SALVAGE THERAPY FOR PROSTATE CANCER: AUA/ASTRO/SUO GUIDELINE (2024)

Guideline Panel

Todd M. Morgan, MD; Stephen A. Boorjian, MD; Mark K. Buyyounouski, MD, MS; Brian F. Chapin, MD; David Y.T. Chen, MD; Heather H. Cheng, MD, PhD; Heather A. Jacene, MD; Sophia C. Kamran, MD; Amy N. Luckenbaugh, MD; Ben J. Nathanson; Yaw A. Nyame, MD, MS, MBA; Edwin M. Posadas, MD; Phuoc T. Tran, MD, PhD; Ronald C. Chen, MD, MPH

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Prostate Cancer

Guidelines: Salvage Therapy for Prostate Cancer

TREATMENT DECISION-MAKING AT THE TIME OF SUSPECTED BIOCHEMICAL RECURRENCE AFTER PRIMARY RADICAL PROSTATECTOMY (RP)

1. Clinicians should inform patients that salvage radiation for a detectable prostate-specific antigen (PSA) after RP is more effective when given at lower levels of PSA. (*Strong Recommendation; Evidence Level: Grade B*)
2. For patients with a detectable PSA after RP in whom salvage radiation therapy (RT) is being considered, clinicians should provide salvage radiation when the PSA is ≤0.5 ng/mL. (*Moderate Recommendation; Evidence Level: Grade B*)
3. For patients with a detectable PSA after RP who are at high risk for clinical progression, clinicians may offer salvage radiation when PSA values are <0.2 ng/mL. (*Conditional Recommendation; Evidence Level: Grade C*)
4. Clinicians should inform patients that salvage radiation after RP poses inherent risks to urinary control, erectile function, and bowel function. These risks must be considered in the context of the risks posed by recurrent cancer along with patient life expectancy, comorbidities, and preferences to facilitate a shared decision-making (SDM) approach to management. (*Clinical Principle*)
5. Clinicians should use prognostic factors (e.g., PSA doubling time [PSADT], Gleason Grade Group, pathologic stage, surgical margin status, validated post-prostatectomy genomic classifier and/or positron emission tomography (PET) imaging results) to counsel patients with a detectable PSA about their risk of clinical progression. (*Moderate Recommendation; Evidence Level: Grade B*)

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Prostate Cancer

Guidelines: Salvage Therapy for Prostate Cancer

TREATMENT DELIVERY FOR NON-METASTATIC BIOCHEMICAL RECURRENCE AFTER PRIMARY RADICAL PROSTATECTOMY

13. Clinicians should offer androgen deprivation therapy (ADT) in addition to salvage RT for patients with BCR following RP and any high-risk features (e.g., higher post-prostatectomy PSA such as PSA ≥0.7ng/mL, Gleason Grade Group 4 to 5, PSADT ≤6 months, persistently detectable post-operative PSA, seminal vesicle involvement). (*Moderate Recommendation; Evidence Level: Grade B*)
14. For patients with BCR following RP without any high-risk features, clinicians may offer radiation alone. (*Conditional Recommendation; Evidence Level: Grade C*)
15. Clinicians should discuss treatment side effects and the impact of medical comorbidities when patients are being considered for ADT (as well as duration) with salvage RT, utilizing a shared decision-making approach. (*Clinical Principle*)
16. For patients with pN1 disease being treated with post-operative RT, clinicians should include ADT rather than treating with RT alone. (*Clinical Principle*)

Prostate Cancer

Guidelines: Salvage Therapy for Prostate Cancer

EVALUATION AND MANAGEMENT OF SUSPECTED NON-METASTATIC RECURRENCE AFTER RADIATION THERAPY

23. For patients with BCR following primary RT or ablative therapy who have no evidence of metastatic disease and are candidates for local salvage therapy, clinicians should perform a prostate biopsy to evaluate for local recurrence. (*Clinical Principle*)

24. In patients with a biopsy-documented prostate cancer recurrence after primary RT who are candidates for salvage local therapy, clinicians should offer RP, cryoablation, high-intensity focused ultrasound (HIFU), or reirradiation as part of an SDM approach. (*Moderate Recommendation; Evidence Level: Grade C*)

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Guidelines: Salvage Therapy for Prostate Cancer

EVALUATION AND MANAGEMENT OF SUSPECTED NON-METASTATIC RECURRENCE AFTER FOCAL THERAPY

25. In patients for whom salvage local therapy is being considered following focal ablation, clinicians should offer whole gland treatment by RP or RT. (*Expert Opinion*)

EVALUATION AND MANAGEMENT OF REGIONAL RECURRENCE

26. In patients with pelvic nodal recurrence following primary RP, clinicians should offer ADT plus salvage RT to the prostate bed and pelvic lymph nodes. (*Expert Opinion*)

27. In patients with pelvic nodal recurrence following primary RT who did not receive prior pelvic nodal RT, clinicians should offer salvage pelvic nodal RT plus ADT. (*Expert Opinion*)

28. Clinicians may offer salvage pelvic lymphadenectomy for patients with evidence of pelvic lymph node recurrence after RP or RT; however, these patients should be counseled regarding the uncertain oncologic benefit from surgery in this setting. (*Conditional Recommendation; Evidence Level: Grade C*)

Prostate Cancer

PROSTATE CANCER – EDITOR'S CHOICE · Volume 86, Issue 1, P61-68, July 2024 Download Full Issue

Transperineal Versus Transrectal Magnetic Resonance Imaging–targeted and Systematic Prostate Biopsy to Prevent Infectious Complications: The PREVENT Randomized Trial

Jim C. Hu [a] · Melissa Assel [b] · Mohamad E. Allaf [c] · ... · Michael A. Gorin [l] · Anthony J. Schaeffer [i] · Edward M. Schaeffer [i] ... Show more

Randomized trial of transperineal versus transrectal prostate biopsy to prevent infection complications (PREVENT)

- Multicenter, randomized trial
- Primary outcome: Post biopsy infection
- Secondary outcomes: Urinary retention, significant bleeding, cancer detection, pain
- 658 participants, 567 (86%) in the analysis
- 0 TP infections, 4 (1.4%) TR infections
- Detection of clinically significant prostate cancer: 53% TP, 50% TR

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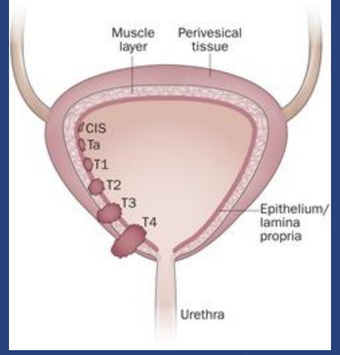
Bladder Cancer



A lot of AUA abstracts are not *breaking news* but continued key takeaways

NMIBC:
3 FDA approved drugs for BCG unresponsive disease (with CIS and papillary disease)

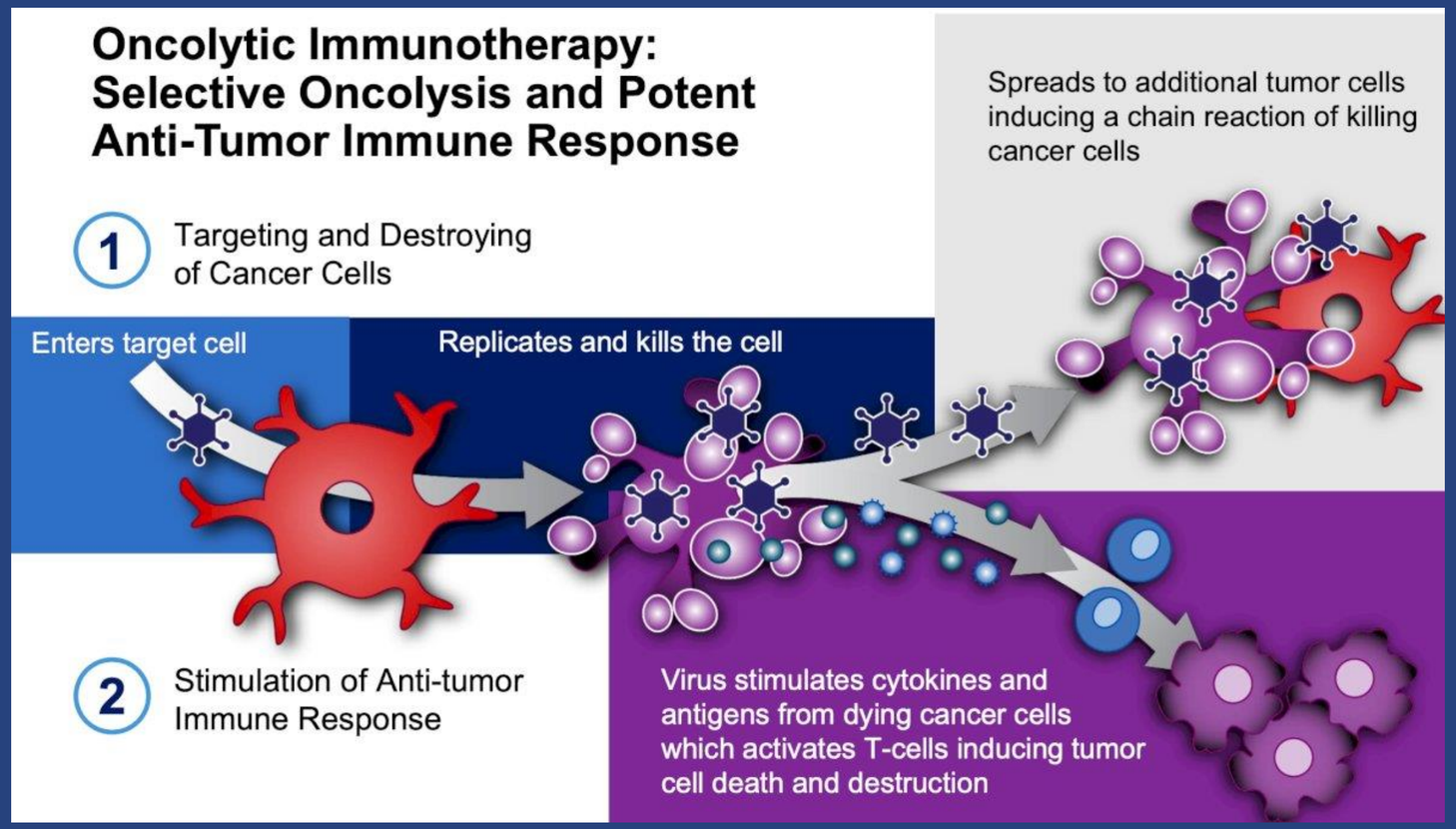
1. Pembrolizumab (Keynote 57)
   - 40% CR at 3-6 mo

2. Nadofaragene firadenovec

3. IL 15 superagonist + BCG

Bladder Cancer: NMIBC

Pivotal Results from BOND-003: A Phase 3, Single-arm Study of Intravesical Cretostimogene Grenadenorepvec for the Treatment of High Risk, BCG-Unresponsive Non-Muscle Invasive Bladder Cancer



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Bladder Cancer: NMIBC

BOND-003:

- Phase 3 trial, Cretostimogene monotherapy for BCG-Unresponsive high risk NMIBC with CIS
- Single arm, open label
- Heavily pretreated cohort

- N=105 patients evaluable (by April 1, 2024)
- 75.2% CR (95% CI 65%-83%)

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Bladder Cancer: NMIBC

BOND-003:

•53.8% of repeat induction patients converted to a complete response

•52 patients have a duration of response >= 6 months
•29 patients have a duration of response >= 12 months
•14 patients have a duration of response >=21 months

•92.4% cystectomy free survival, with none of the patients with a complete response having undergone radical cystectomy, and none having nodal or metastatic progression

•96.7% progression free survival at 12 months

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Bladder Cancer: NMIBC

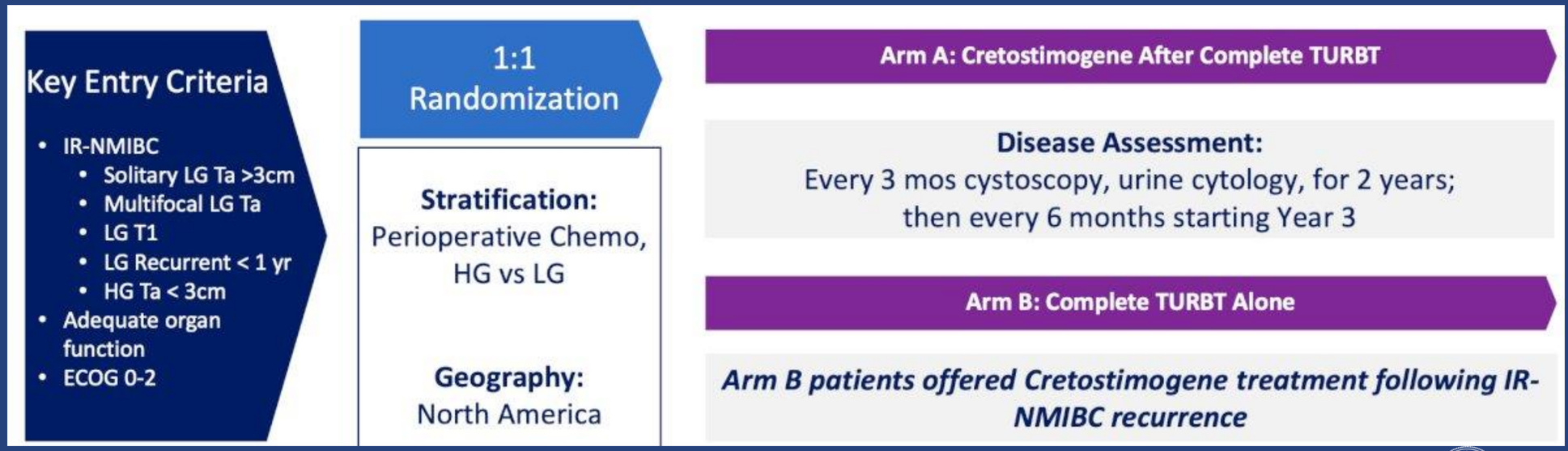
BOND-003:

•Based on these results: FDA has granted fast track designation for Cretostimogene monotherapy in BCG-unresponsive CIS with or without Ta/T1 papillary disease

Bladder Cancer: NMIBC

NMIBC Trials in Progress:

PIVOT-006, Phase 3 randomized study of adjuvant intravesical cretostimogene grenadenorepvec versus surveillance for the treatment of intermediate risk non-muscle invasive bladder cancer



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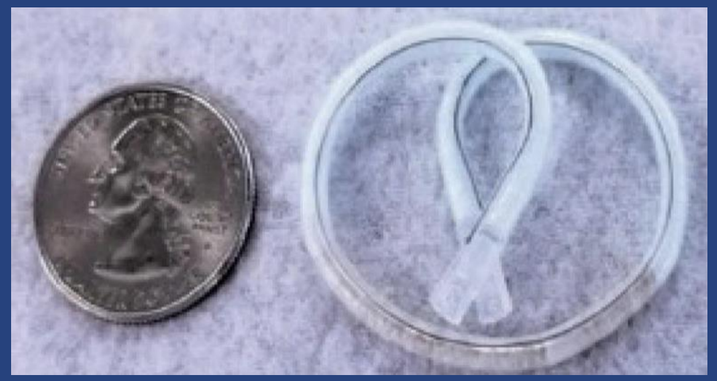
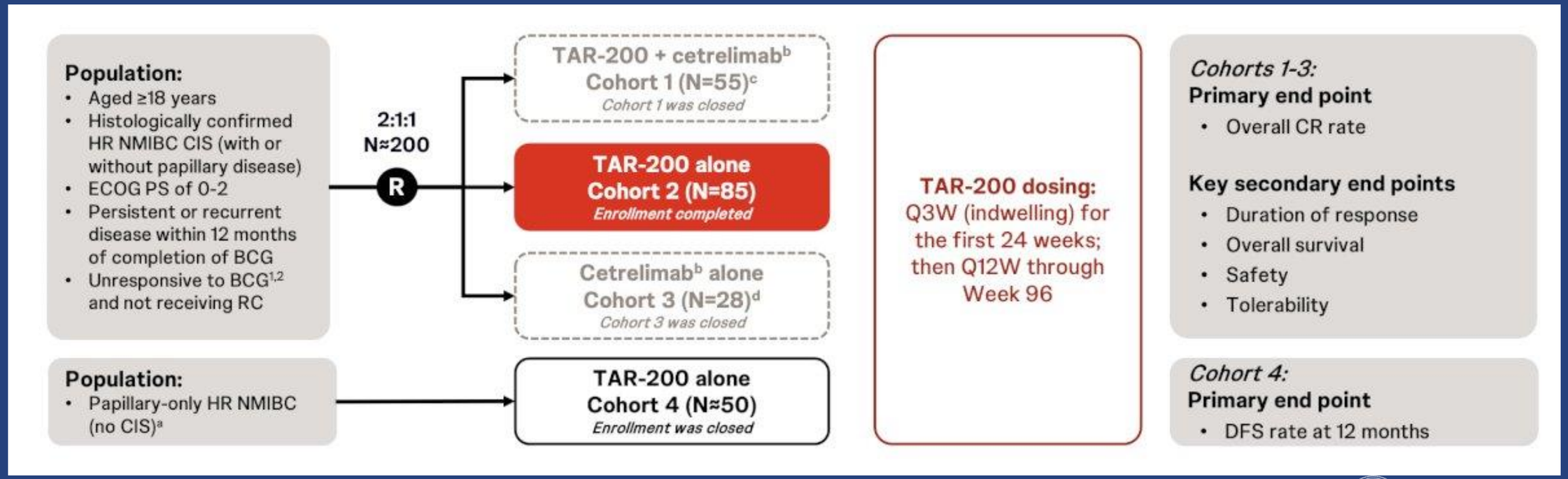
Bladder Cancer: NMIBC



TAR-200 in patients with BCG-Unresponsive High Risk Non-Muscle Invasive Bladder Cancer: Results from SunRISe-1 Study

- Ongoing open-label phase 2b study



Bladder Cancer: NMIBC

TAR-200 in patients with BCG-Unresponsive High Risk Non-Muscle Invasive Bladder Cancer: Results from SunRISe-1 Study

- Complete response rates at 6 & 12 months: 75.7% and 61.9%, respectively
- 5 patients have completed 2 years of treatment, 4 in CR
- None of responders progressed muscle invasive or metastatic disease
- 1 of 48 (2.1%) responders underwent radical cystectomy

TAR-200 has been granted FDA breakthrough therapy designation

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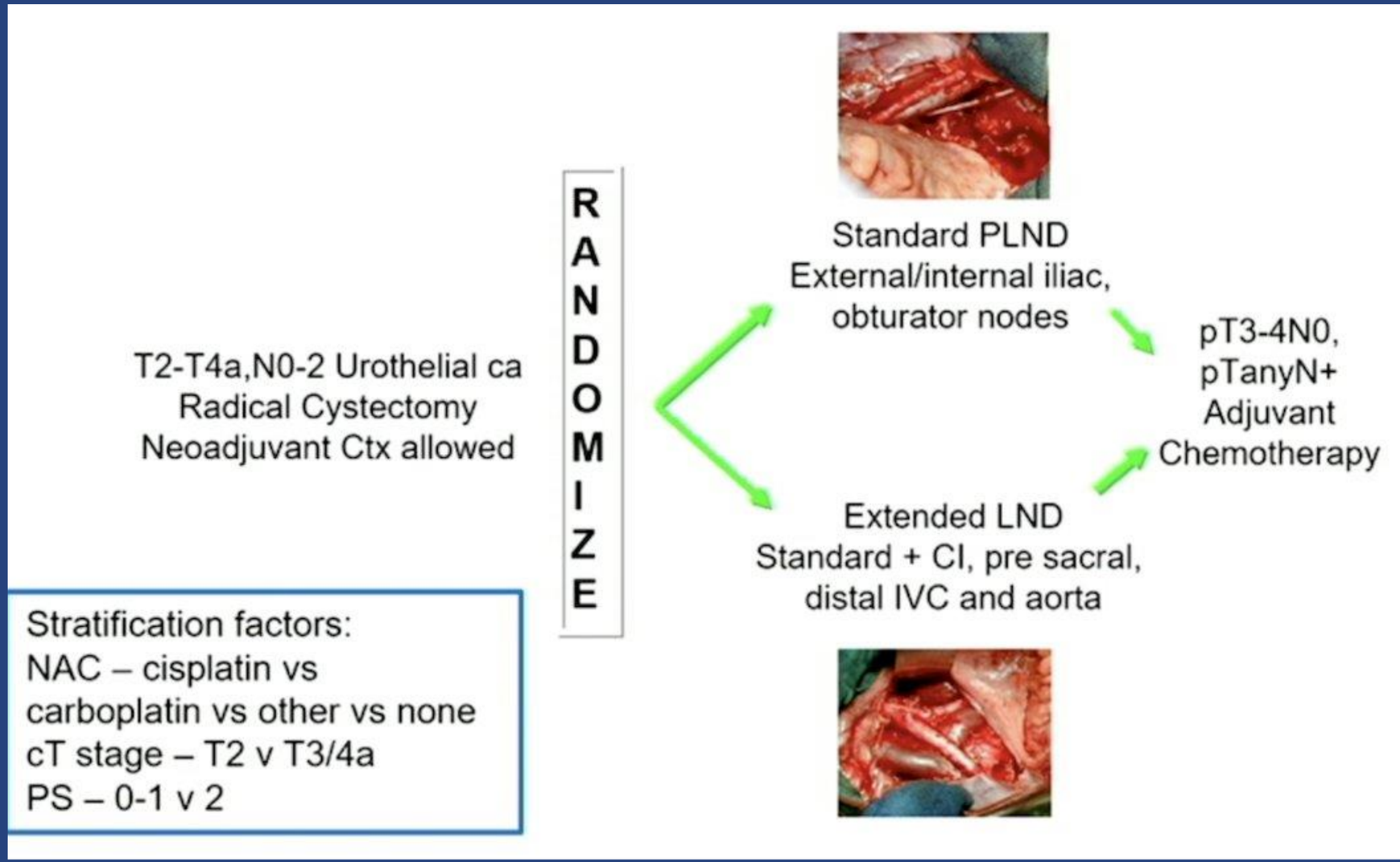
Bladder Cancer

MIBC:

SWOG S1011 Trial assessing the national performance of lymphadenectomy for MIBC to define an optimal lymph node yield



Bladder Cancer

SWOG S1011:

Primary: Comparing disease free survival in patients undergoing cystectomy for MIBC

Secondary: OS, Operative time, post-op morbidity, length of stay, LN yield

592 patients randomized (300 standard, 292 extended)

Standard Nodal Yield: 24 (range 6-61)
Extended Nodal Yield: 39 (range 15-94)

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Bladder Cancer

SWOG S1011:

No difference in DFS (HR 1.10, 95% CI 0.86-1.40)

No difference in OS (HR 1.13, 95% CI 0.88-1.45)

In the extended node arm- Higher rates of:

VTE, perio-op mortality, longer OR time, blood loss, higher number of progression events within 90 days

No survival benefit for extended pelvic lymph node dissection

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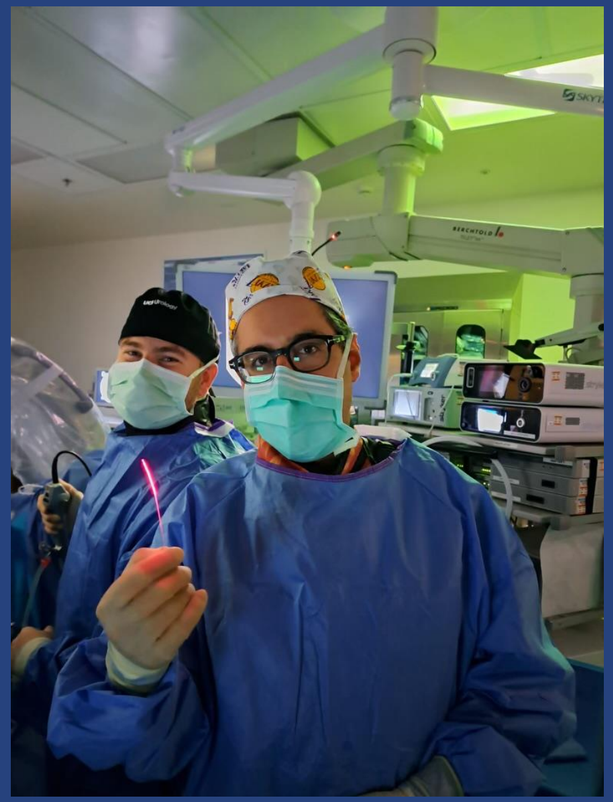
Upper Tract Urothelial Carcinoma

Efficacy and Safety of Padeliporfin Vascular Targeted Photodynamic Therapy (VTP) for Treatment of Low Grade Upper Tract Urothelial Cancer: Phase 3 Preliminary results



ENdoluminal LIGHT activated treatment of upper tract urothelial carcinoma (ENLIGHTED)

Single arm, open label, global pivotal Phase 3 trial, 29 sites: US, France, Spain, Italy, Germany, Austria, Israel

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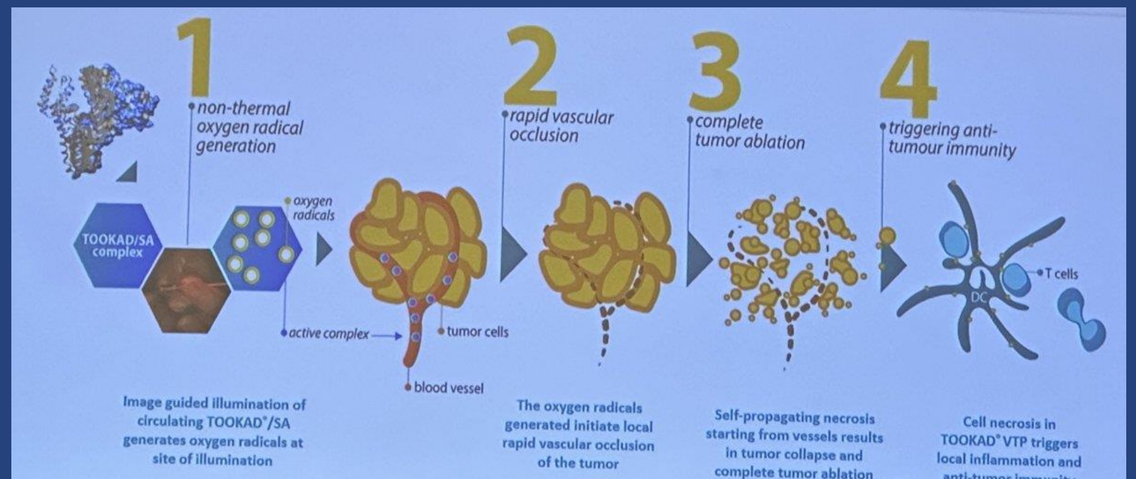
Upper Tract Urothelial Carcinoma

Efficacy and Safety of Padeliporfin Vascular Targeted Photodynamic Therapy (VTP) for Treatment of Low Grade Upper Tract Urothelial Cancer: Phase 3 Preliminary results

Padeliporfin= a photosensitizer, combined with a laser light delivery system

Emits near-infrared light at 753 nm

Upon activation, Padeliporfin triggers a cascade of events that impact tumor vasculature:



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Upper Tract Urothelial Carcinoma

Efficacy and Safety of Padeliporfin Vascular Targeted Photodynamic Therapy (VTP) for Treatment of Low Grade Upper Tract Urothelial Cancer: Phase 3 Preliminary results

- At presentation, 12 patients treated
- 9 with visit 2 completion
  - Of those 6 with CR, 3 with partial response

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Testicular Cancer

Accuracy of FDG-PET Scan in Primary Testicular Seminoma: Analysis from SEMS Trial

Clinical Trial > J Clin Oncol. 2023 Jun 1;41(16):3009-3018. doi: 10.1200/JCO.22.00624. Epub 2023 Mar 13.

Surgery in Early Metastatic Seminoma: A Phase II Trial of Retroperitoneal Lymph Node Dissection for Testicular Seminoma With Limited Retroperitoneal Lymphadenopathy

Siamak Daneshmand [1], Clint Cary [2], Timothy Masterson [2], Lawrence Einhorn [3], Nabil Adra [3], Stephen A Boorjian [4], Christian Kollmannsberger [5], Anne Schuckman [1], Alan So [6], Peter Black [6], Aditya Bagrodia [7], Eila Skinner [8], Mehrdad Alemozaffar [9], Timothy Brand [10], Scott Eggener [11], Phillip Pierorazio [12], Kelly Stratton [13], Lucia Nappi [5], Craig Nichols [14], Chunqiao Luo [14], Ming Li [14], Brian Hu [15]

Phase II, prospective trial

Evaluating efficacy of RPLND in patients with Seminoma

Limited RPLND (diameter 1-3cm)

55 patients: 2 year RFS 81%

22% Recurrence rate

16% pN0 rate

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Testicular Cancer

Accuracy of FDG-PET Scan in Primary Testicular Seminoma: Analysis from SEMS Trial

- F-18 FDG PET scan done as optional study
- 55 total patients
- 26 (47%) had PET scans
- 20 (77%) scans were positive, 18 with pathologically positive lymph nodes
- Mean SUV of positive LN was 7.0 (range 2.6-18.8)

	Pathologic Node Status		
	pN+	pN-	
PET (+)	18	2	PPV 90%
PET (-)	1	5	NPV 83%
	Sensitivity 95%	Specificity 71%	

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Testicular Cancer

Accuracy of FDG-PET Scan in Primary Testicular Seminoma: Analysis from SEMS Trial

- In patients with testicular seminoma and low volume RP adenopathy, PET scan may have a role in improving accuracy of staging
- Need larger studies
- PET scan does not accurately determine number of positive lymph nodes

Kidney Cancer

Stay tuned for AUA 2025 in Las Vegas

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Key Take-away Points

- Prostate: New guidelines for salvage therapy

- Bladder
  - NMIBC: several ongoing trials
    - 3 agents FDA approved
  - MIBC: No longer recommend ELND

- Testis Ca:
  - Based off SEMS trial, can utilize PET imaging in this space

- Kidney Ca: stay tuned!

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Questions?

Thank you!

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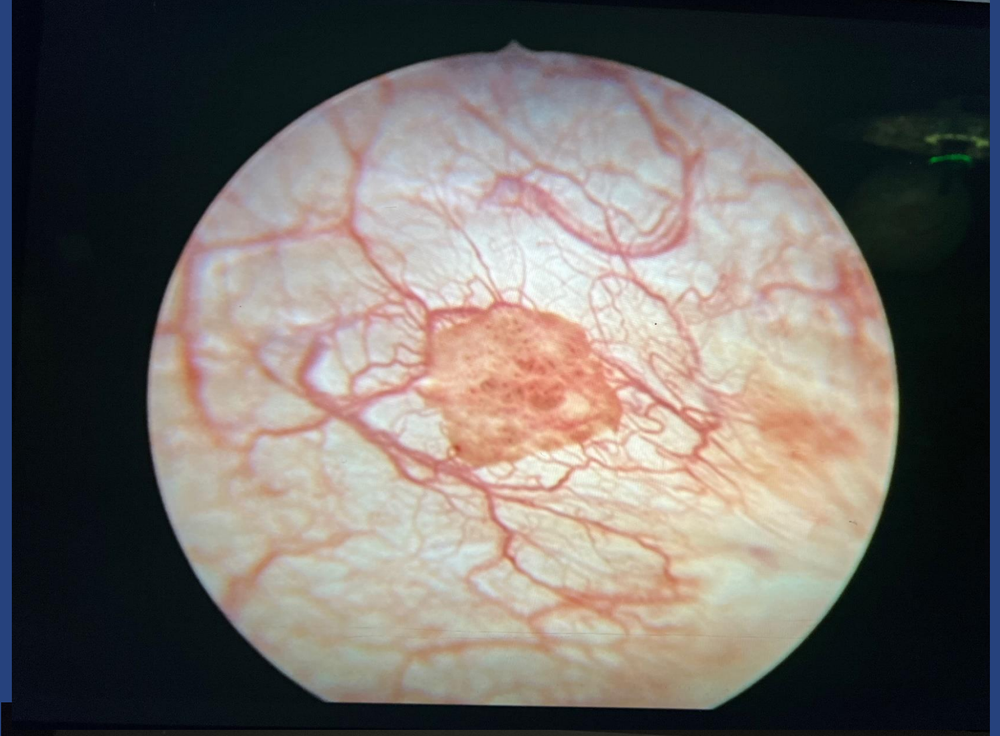

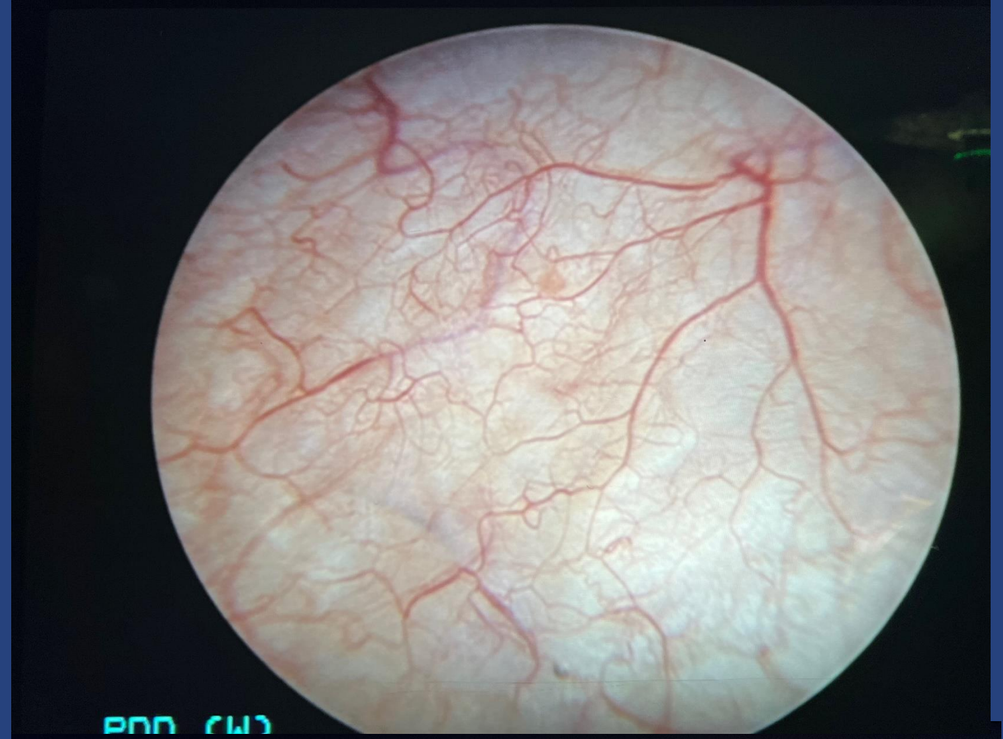

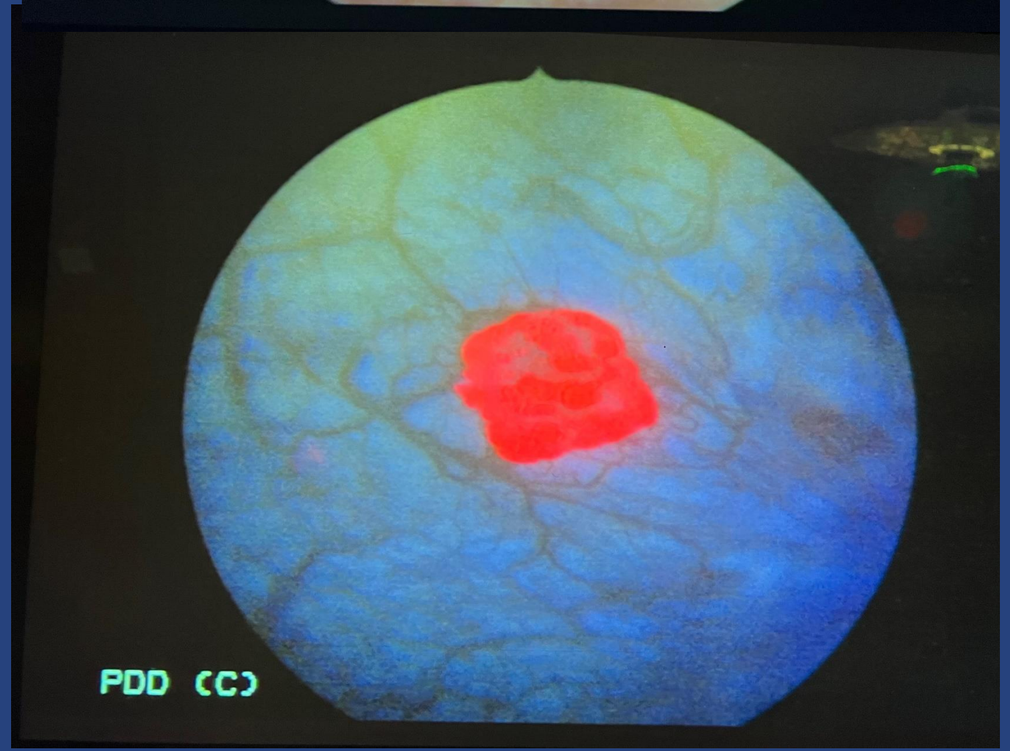

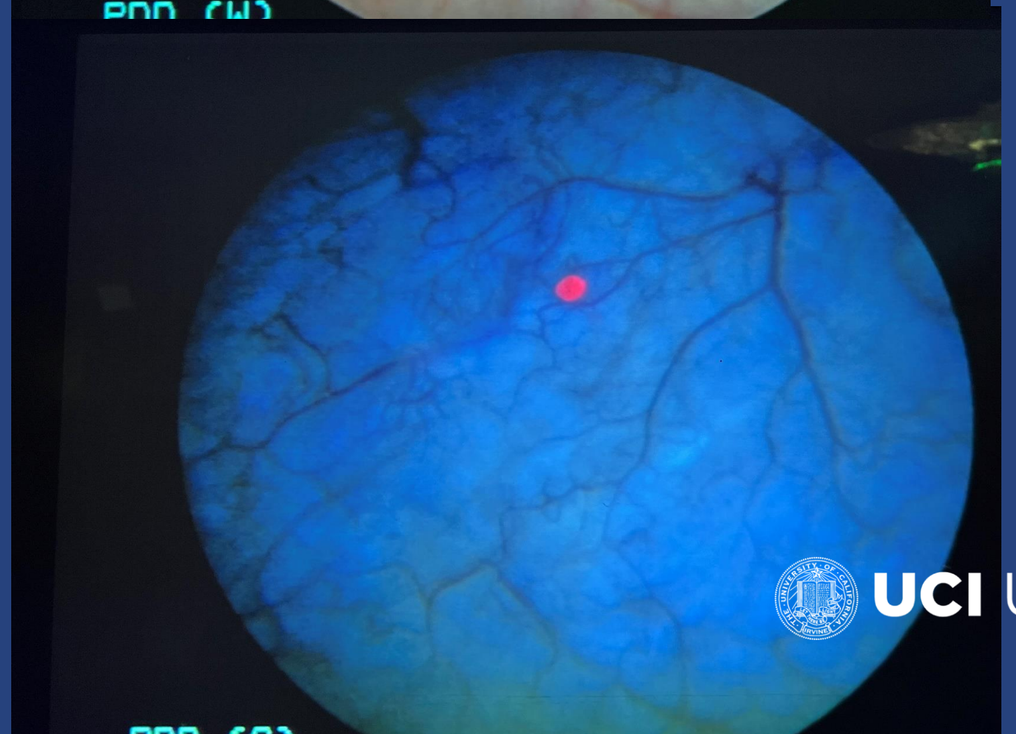

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Non-Muscle invasive Bladder Cancer (NMIBC)

- Intravesical therapy for…
  - Patients with multifocal disease, T1, CIS, those at high risk of progression

  - Induction course followed by maintenance (1-3 years)

Agent	Mechanism of Action
Immunomodulatory Agents	
Bacillus Calmette-Guérin (BCG)	• Inflammatory host response; release of cytokines • May be combined with interferons[90-94]
Interferons	• Lymphocyte activation; cytokine release; phagocyte stimulation • Antiproliferative actions • Antiangiogenic[31,90]
Chemotherapeutic Agents	
Thiotepa	• Alkylating agent; cross-links nucleic acids[95]
Mitomycin C	• Antibiotic; inhibits DNA synthesis[76-78]
Doxorubicin, epirubicin, valrubicin	• Intercalating agents; inhibits DNA synthesis[75,96-98]
Gemcitabine	• Deoxycytidine analog; inhibits DNA synthesis[99-103]

AUA Guidelines

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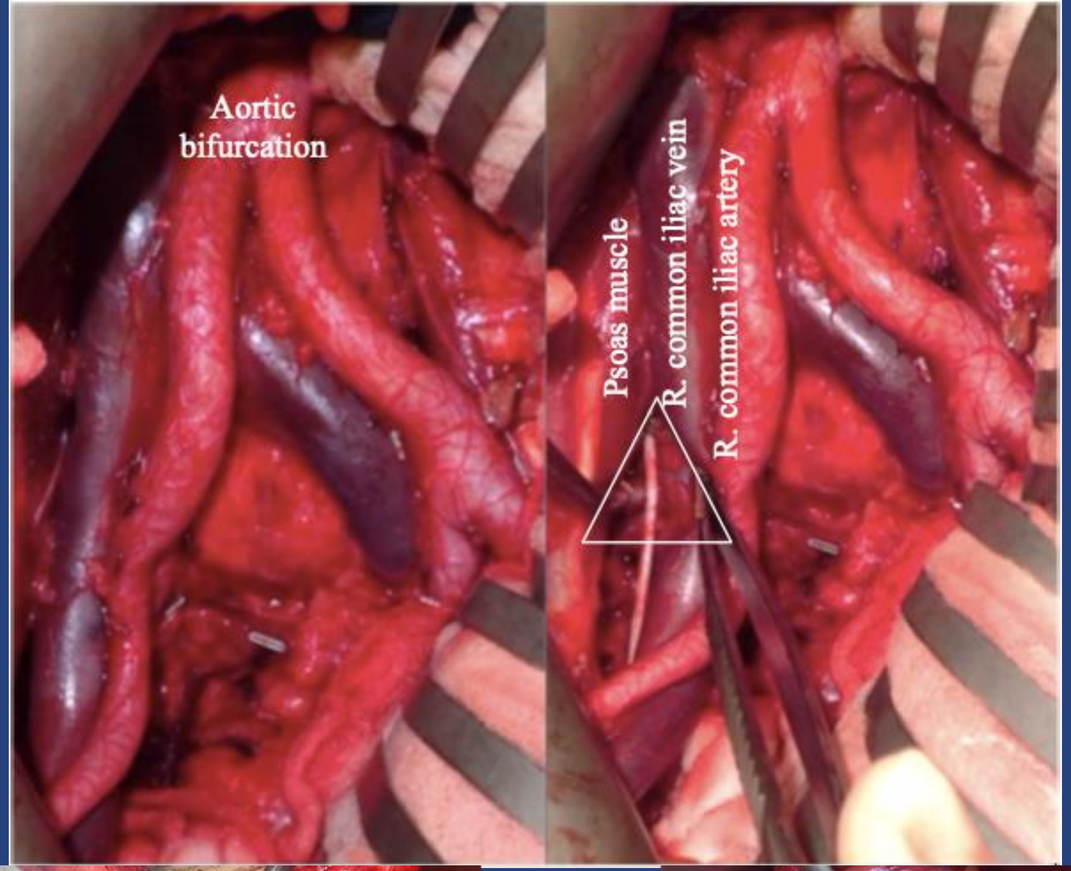
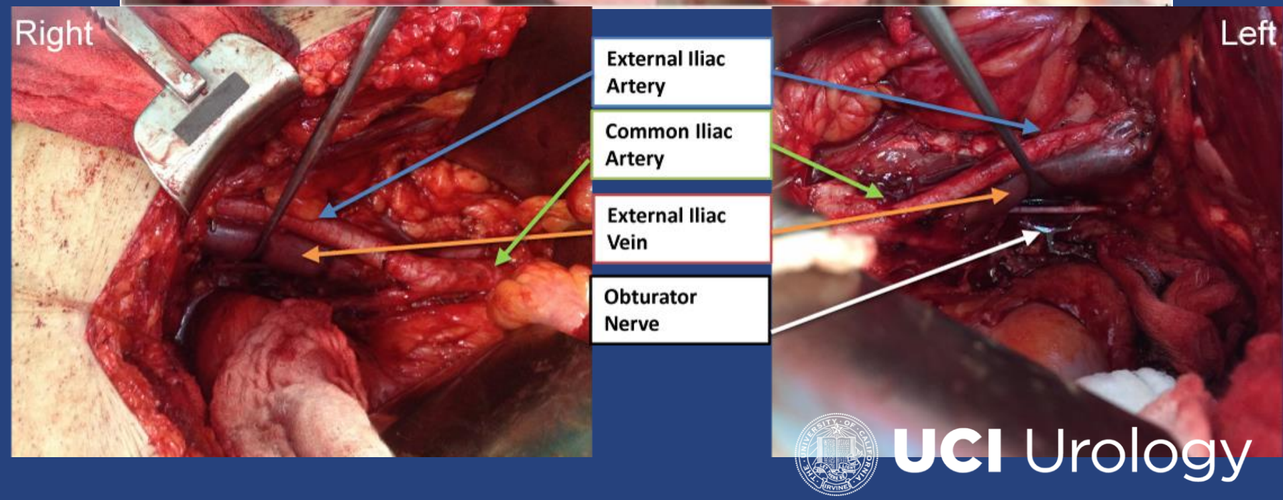
Lymph Node Dissection

- Lymph node dissection is an important part of Radical Cystectomy
  - Extensive low-level evidence notes benefit in 5 year all cause and Cancer specific survival
  - Both in node-negative and node-positive patients
    - Node negative- lymph node yield >16 decreased mortality (May et al 2011)

- Standard vs Extended vs Super Extended?
  - Not so clear





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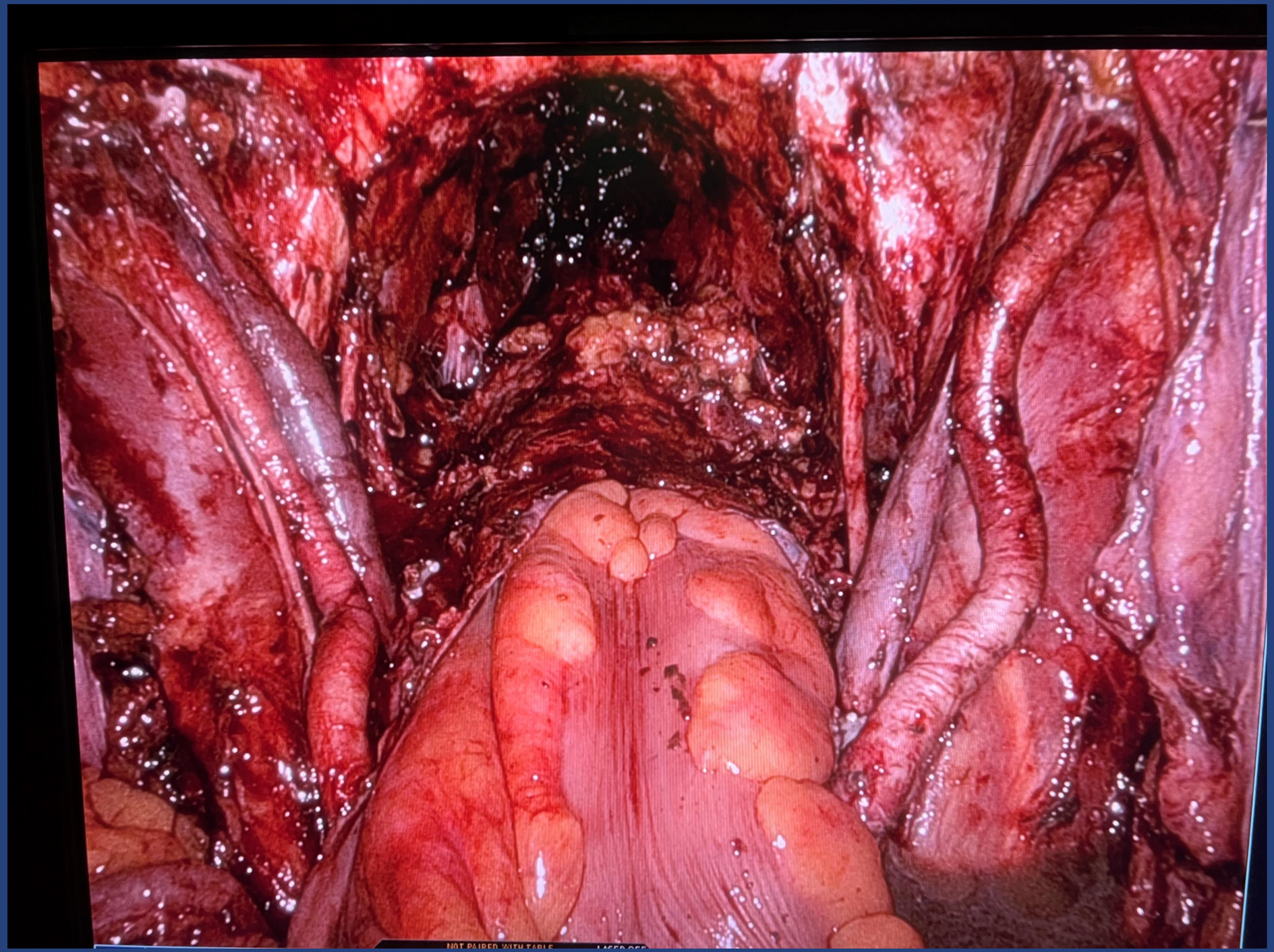
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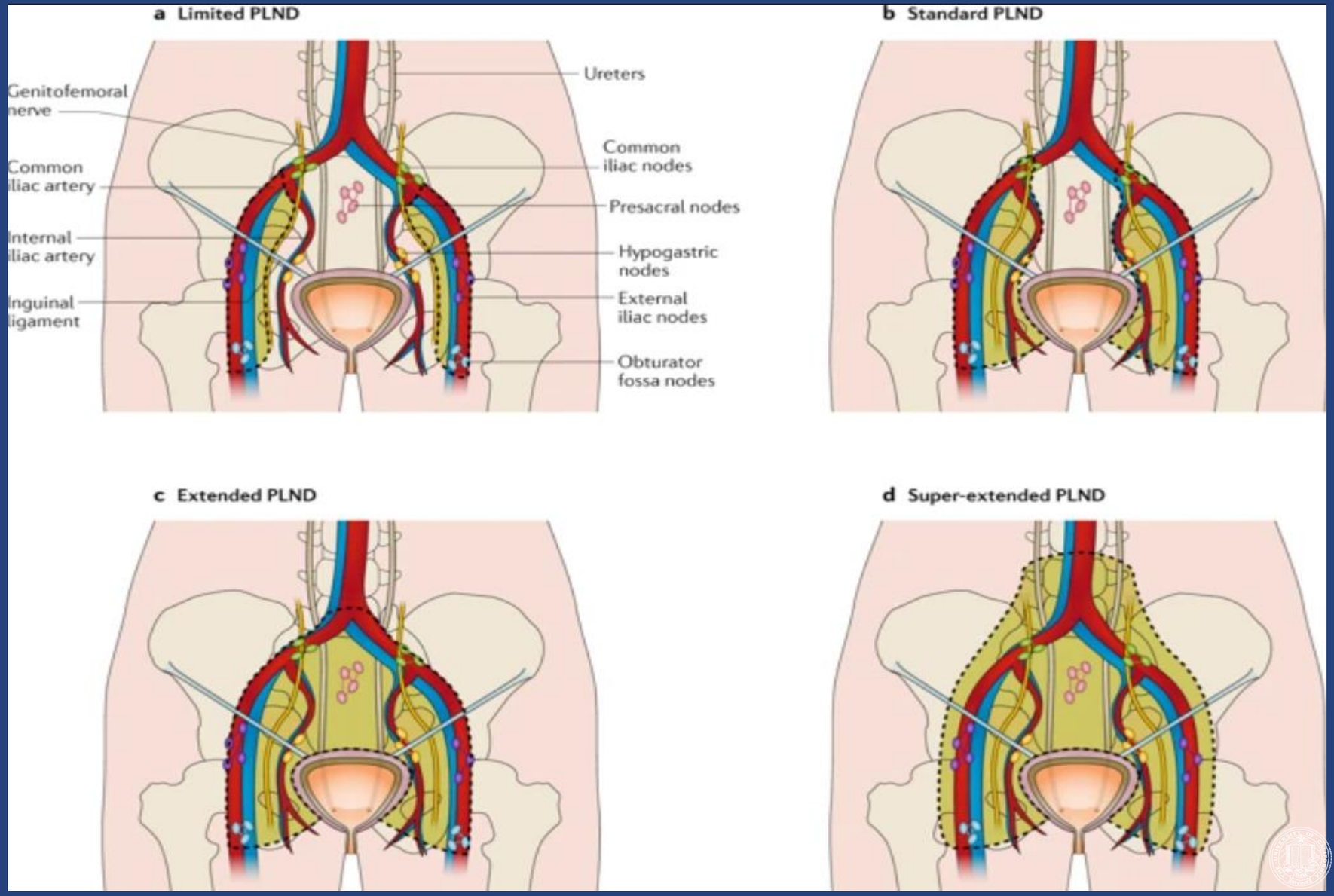
Lymph Node Dissection



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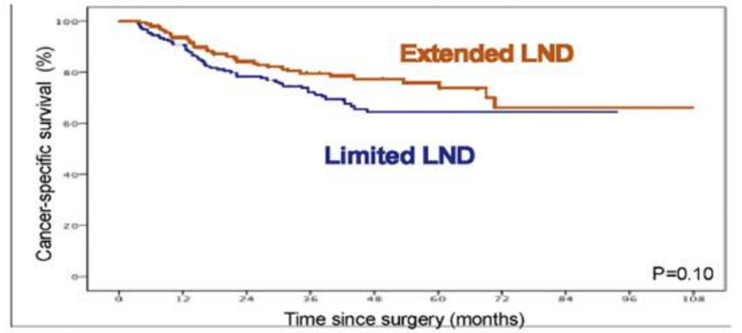
Extended Versus Limited Lymph Node Dissection in Bladder Cancer Patients Undergoing Radical Cystectomy: Survival Results from a Prospective, Randomized Trial

- LEA Trial (2006- Completed 2015); 401 patients
- No benefit of SE-LND over S-LND in RFS (65% vs 59%, p=0.36), CSS (76% vs 65%, p=0.1), OS (59% vs 50% p=0.12)
- Median nodes Standard- 19, Median Nodes SE 31

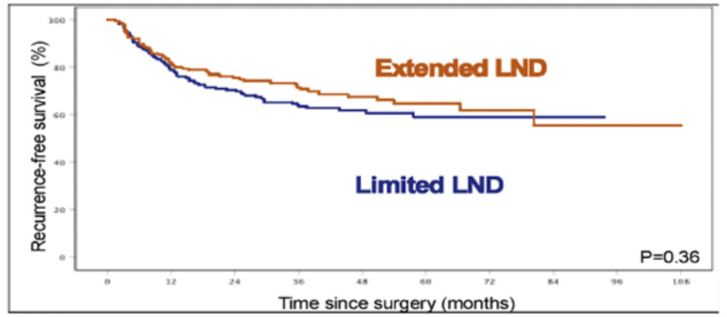
B Cancer-specific survival



Number at risk

Extended LND	198	144	119	88	58	37	14	8	1	1
Limited LND	203	145	110	86	55	38	20	6	0	0

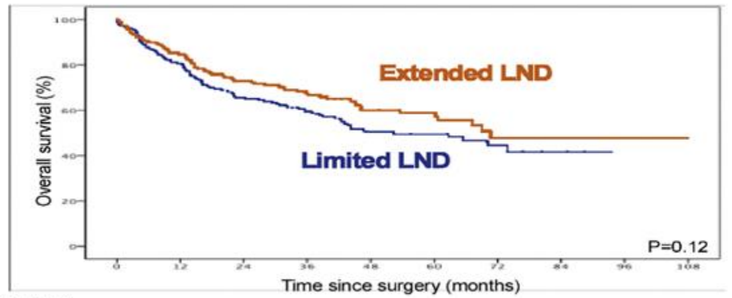
A Recurrence-free survival



Number at risk

Extended LND	198	127	108	81	53	34	14	8	1	1
Limited LND	203	127	101	79	54	35	20	6	0	0

C Overall survival



Number at risk

Extended LND	198	144	119	88	58	37	14	8	1	1
Limited LND	203	145	110	86	55	38	20	6	0	0

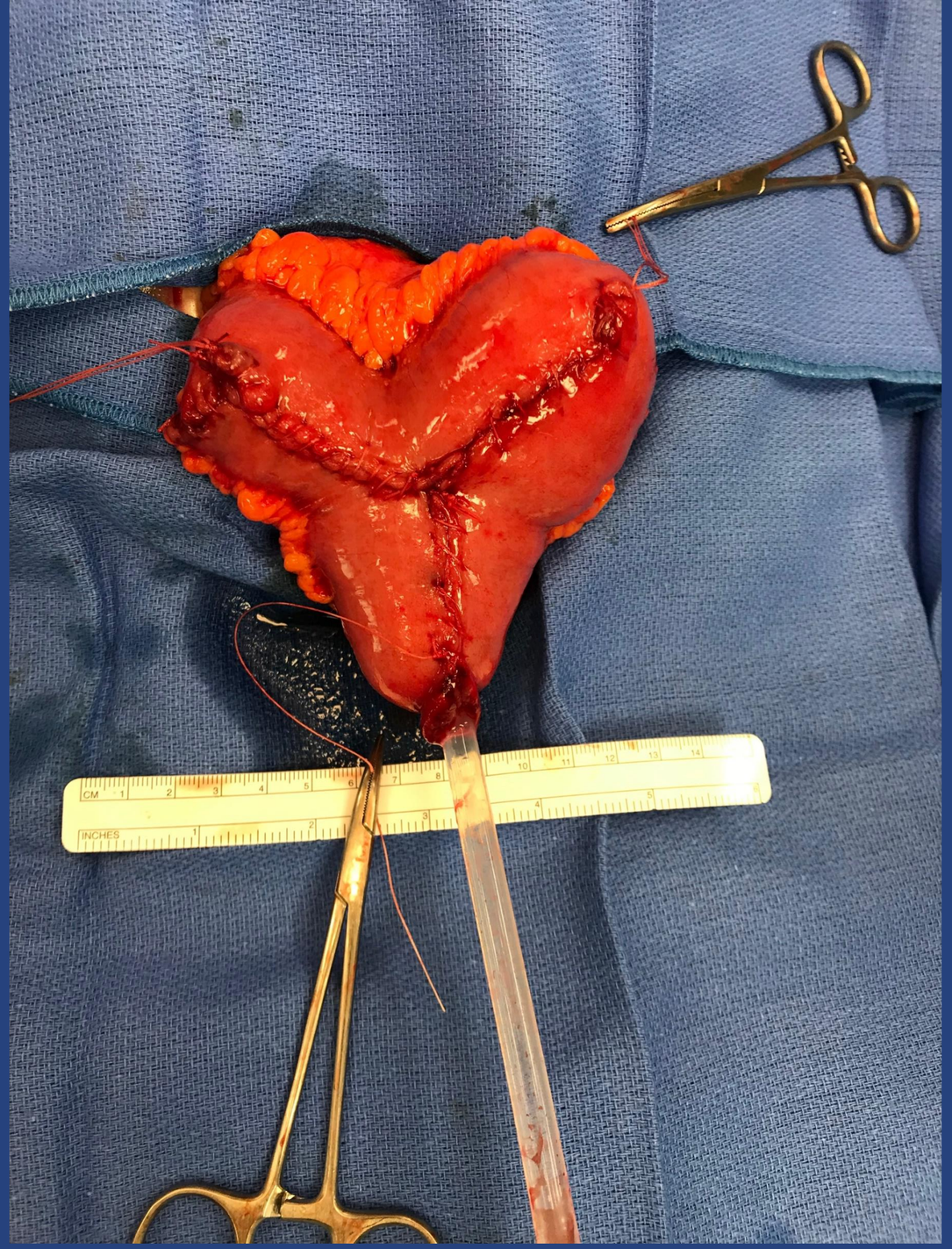
- SWOG S1011
  - Standard vs extended; Primary outcome RFS; Secondary OS, LN counts
  - Extended dissection increased toxicities
  - No benefit of extended by:
    - DFS or OS

Table 1 Comparison of the LEA and SWOG-1011 trial

Characteristics	LEA	SWOG-1011
Identifier*	NCT01215071	NCT01224665
Status	Completed	Ongoing
Comparing	S-LND *vs.* SE-LND	S-LND *vs.* SE-LND
Tumor stage	T1–T4a	T2–T4a
Primary endpoint	RFS at 5 years	RFS at 3 years
Estimated enrollment (n)	450	620
Intention-to-treat (n)	401	–
Per-protocol (n)	363	–
Use of NAC	None	56%
Use of adjuvant chemotherapy	14%#	Optional
Moment of randomization	Pre-operatively	Intra-operatively
Quality check LND	None	Intra-operative photos

*, study details available on https://clinicaltrials.gov; #, optional in patients with pT3–4 and pN+ disease. LND, lymph node dissection; S-LND, standard LND; SE-LND, super extended LND; RFS, recurrence free survival; NAC, neoadjuvant chemotherapy.

Muilwijk, T 2019



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