Urologic Oncology Trends

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Charleston Area Medical Center

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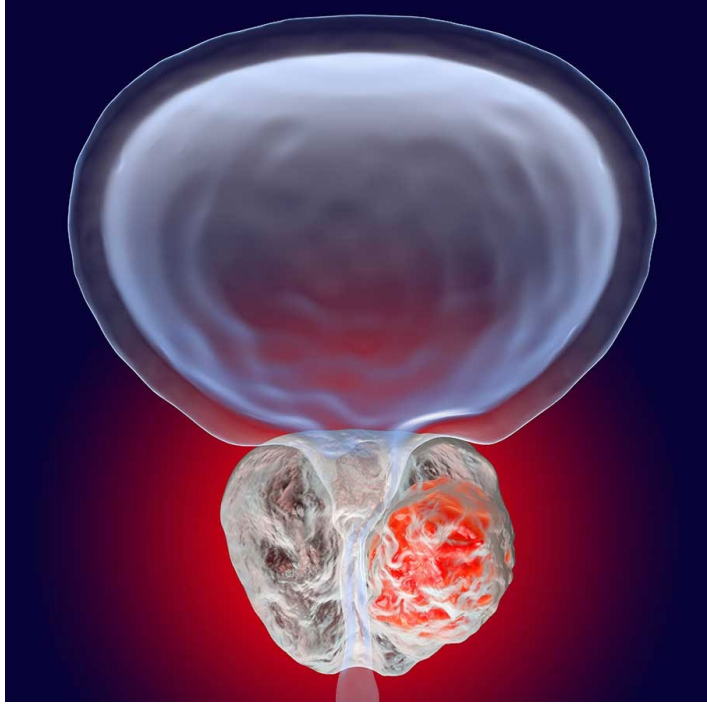
Overview



- Prostate Cancer #3 WV (288,300 dx, 34,700 deaths)
- Bladder Cancer #5 WV (82,290 dx, 16,710 deaths)
- Kidney Cancer #7 WV (81,800 dx, 14,890 deaths)
- Penile/Testicular Cancer
- Adrenal Cancer

- I have nothing to disclose!

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Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA: A Cancer Journal for Clinicians* 2023; 73(1):17-48.

https://oeps.wv.gov/cancer/documents/data/burdenreport2022.pdf (wv.gov)

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Prostate Cancer Screening

- Still recommended!
- DRE utility questioned
- PSA, PHI, 4K, SelectMDX
- ConfirmMDx, PCA3
- Oncotype, Prolaris, Decipher
- Multiparametric 3T MRI
- PSMA Pet

https://www.prostatemarkers.org/map

Localized Prostate Cancer Treatments

- Robotic Single-Port
- Robotic Retzius Sparing – “quicker continence”
- IMRT – Stereotactic 5 day
- HIFU – High Intensity Focused Ultrasound

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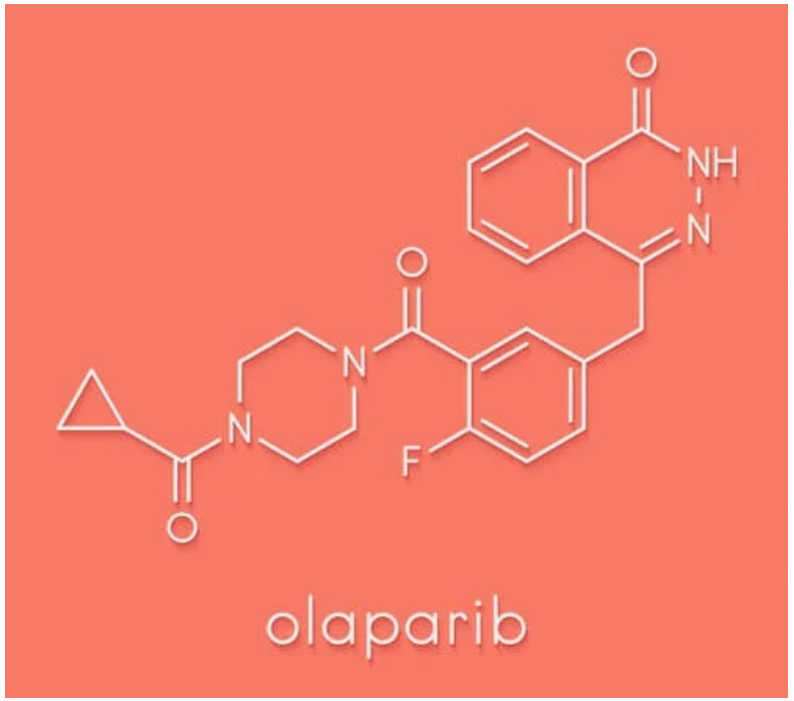
Advanced Prostate Cancer Treatment

- ADT – LHRH agonists/antagonists including oral relugolix
- Cyp17 inhibitor (Abiraterone)
- 2nd Generation Anti-Androgens
  - Enzalutamide, Apalutamide, Darolutamide
- Chemo – Docetaxel, Cabazitaxel, Mitoxantrone, Estramustine, Carboplatin
- Vaccine – Sipuleucel-T
- Immune checkpoint inhibitors – Pembrolizumab/Dostarlimab
- PARP Inhibitors – Rucaparib, Olaparib, Talazoparib, Niraparib
- Radiopharmaceuticals – Radium-223
- PSMA-targeted radioligand therapy – lutetium-177-PSMA-617



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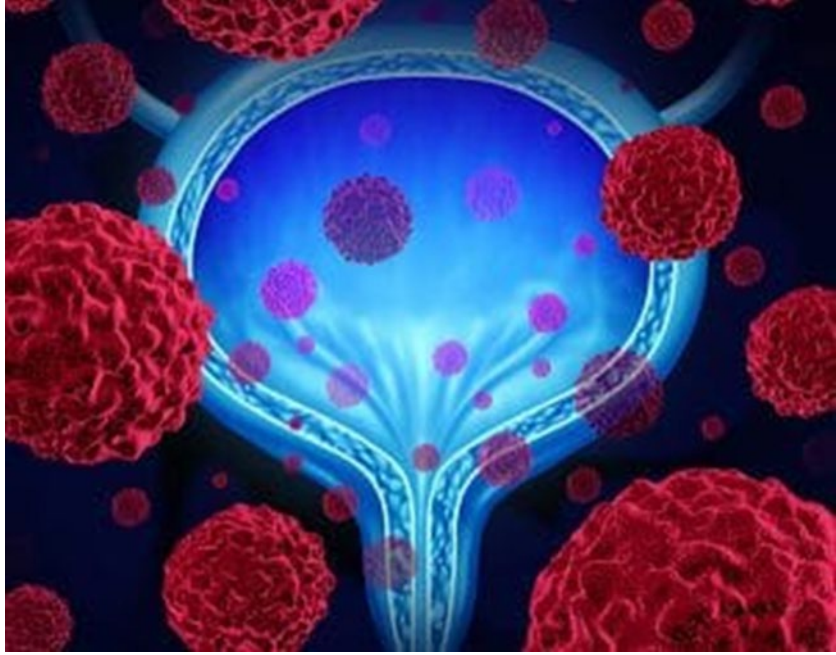
Bladder Cancer

- Digital imaging in office/OR
- Flourescent imaging – Cysview (Blue Light Flourescence) and Narrow-band-imaging
- Bipolar TURBT/Laser TURBT
- Immediate post-procedure chemotherapy – Gemcitabine
- Intravesical therapy: BCG, Gemcitabine/Docetaxol, Nadofarogene
- Intravenous PD-1/PD-(L)1 inhibitors

Adstiladrin

- Nadofaragene firadenovec is a replication-deficient recombinant adenovirus that delivers human interferon alfa-2b cDNA into the bladder epithelium as a novel intravesical therapy for BCG-unresponsive non-muscle-invasive bladder cancer (99% had received at least 2 courses of BCG prior to enrollment)
- 55 (53·4%) of 103 patients with carcinoma in situ (with or without a high-grade Ta or T1 tumour) had a complete response within 3 months of the first dose
- This response was maintained in 25 (45.5%) of 55 patients at 12 months
- Micturition urgency was the most common grade 3-4 study drug-related adverse event (Two patients, both grade 3), and there were no treatment-related deaths
- 3-year data from CS-003 showed 14/55 still remained high-grade recurrence free - median complete response duration of 9.7 months



Boorjian SA, Alemozaffar M, Konety BR, et al. Intravesical nadofaragene firadenovec gene therapy for BCG-unresponsive non-muscle-invasive bladder cancer: a single-arm, open-label, repeat-dose clinical trial. Lancet Oncol. 2021 Jan;22(1):107-117.

Boorjian SA, Narayan VM, Konety BR, et al. Efficacy of intravesical nadofaragene firadenovec-vncg for patients with bacillus Calmette-Guérin-unresponsive carcinoma in situ of the bladder: 36-month follow-up from a phase 3 trial. Presented at: 2023 Society of Urologic Oncology Annual Meeting; November 28-December 1, 2023; Washington, DC. Abstract 164.

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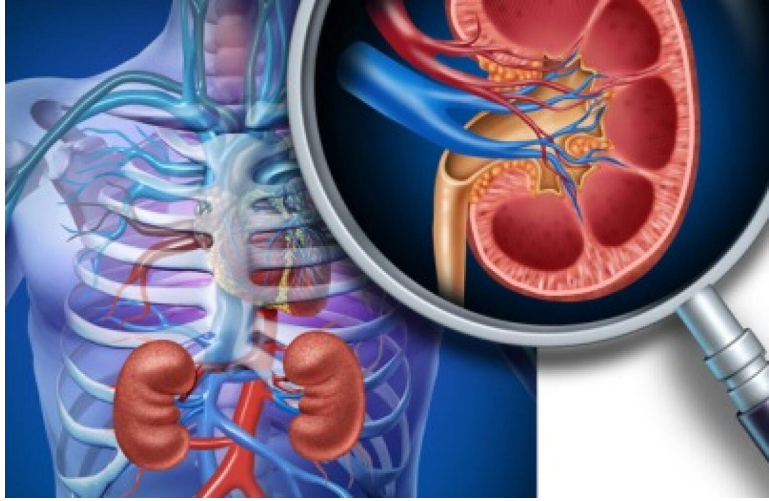
Management of BCG-unresponsive NMIBC

- Cystectomy (Preferred)
- Chemo-radiation
- Intravesical therapy: Mitomycin, Gemcitabine, Valrubicin, Gem-Doce, Nadofarogene
- IV PD-1/PD-(L)1 inhibitors - Pembrolizumab
- Clinical Trial (PD-1i w/ BCG, newer agents)

Cytoreductive Nephrectomy in the immunotherapy era



- Historically
  - SWOG 8949, noted a median overall survival (OS) of 11.1 months in the patient group who received combined CN and interferon a-2b versus 8.1 months in the subgroup who received interferon a-2b alone.
  - EORTC 30947, demonstrated a significant OS benefit following CN and interferon a-2b compared with interferon a-2b alone (17 vs. 7 months)
- However… results in SURTIME, although exploratory, suggest that a deferred CN approach, in which CN is only offered if the disease does not progress after initial VEGFR-TT, is superior to immediate CN
- Carmena - Sunitinib alone was not inferior to nephrectomy followed by sunitinib in patients with metastatic renal-cell carcinoma who were classified as having intermediate-risk or poor-risk disease. NEJM 8/2018

Mickisch GH, Garin A, van Poppel H, et al.; European Organisation for Research and Treatment of Cancer (EORTC) Genitourinary Group. Radical nephrectomy plus interferon-alfa-based immunotherapy compared with interferon alfa alone in metastatic renal-cell carcinoma: a randomised trial. *Lancet*. 2001;358:966–70.

Bell H, Cotta BH, Salami SS, Kim H, Vaishampayan U. "PROBE"ing the Role of Cytoreductive Nephrectomy in Advanced Renal Cancer. Kidney Cancer J. 2022 Mar 15;6(1):3-9. doi: 10.3233/kca-210010. PMID: 35310961; PMCID: PMC8929722.

Gross EE, Li M, Yin M, Orcutt D, Hussey D, Trott E, Holt SK, Dwyer ER, Kramer J, Oliva K, Gore JL, Schade GR, Lin DW, Tykodi SS, Hall ET, Thompson JA, Parikh A, Yang Y, Collier KA, Miah A, Mori-Vogt S, Hinkley M, Mortazavi A, Monk P, Folefac E, Clinton SK, Psutka SP. A multicenter study assessing survival in patients with metastatic renal cell carcinoma receiving immune checkpoint inhibitor therapy with and without cytoreductive nephrectomy. Urol Oncol. 2023 Jan;41(1):51.e25-51.e31.

- Multicenter retrospective cohort study consisted of 367 patients (CN+ST n = 232, ST alone n = 135).
- Overall, patients who underwent CN+ST had longer median OS (56.3 months) compared to the ST alone group (19.1 months)
- Multivariable analyses demonstrated a 67% reduction in risk of all-cause mortality in patients who received CN+ST vs. ST alone ($P < 0.0001$)
- CN was independently associated with longer OS in patients with mRCC treated with ICI in any line of therapy.

The Role of Cytoreductive Nephrectomy in Metastatic Renal Cell Carcinoma: A Real-World Multi-Institutional Analysis

Pooja Ghatalia,[1*†] Elizabeth A. Handorf,[2*] Daniel M. Geynisman,[1*] Mengying Deng,[2] Matthew R. Zibelman,[1] Philip Abbosh,[3] Fern Anari,[1] Richard E. Greenberg,[3] Rosalia Viterbo,[3] David Chen,[3] Marc C. Smaldone,[3] Alexander Kutikov[3] and Robert G. Uzzo[3]

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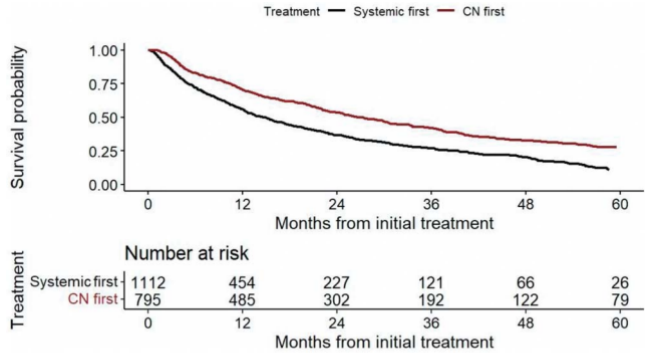

Figure. Adjusted Kaplan-Meier OS in all patients using sensitivity analysis.

- Journal of Urology, July 2022
- 1,910 patients with mRCC, 972 (57%) received systemic therapy, 605 (32%) received upfront CN, 142 (8%) delayed CN and 191 (10%) CN alone
- 433 (23%) patients received immunotherapy-based therapy
- The adjusted mOS was significantly improved in first-treatment, landmark and time-varying covariate analysis (mOS 26.6 vs 14.6 months, 36.3 vs 21.1 months and 26.1 vs 12.2 months respectively) in patients undergoing CN
- Among patients receiving CN and systemic therapy, the timing of systemic therapy relative to CN was not significantly related to overall survival

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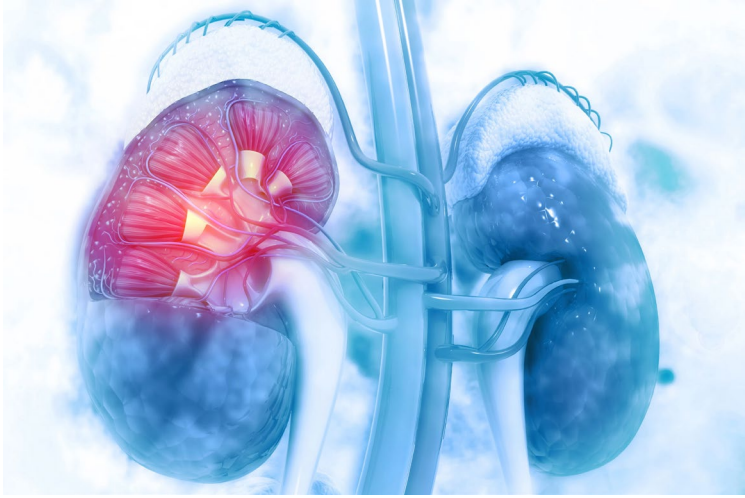
To cytoreductive nephrectomy or not?



- Yes….sometimes…depends
  - Remove large burden of disease? Oligometastatic disease easy to manage w/ ablation/surgery/radiation
  - Younger with excellent performance status
- Still very controversial
  - Some ongoing prospective trials evaluate the outcomes of ICI containing therapy in combination with or without CN, out of which PROBE (NCT04510597), NORDICSUN (NCT03977571), or Cyto-KIK (NCT04322955) may answer some questions with regard to the choice between immediate versus deferred CN in the immunotherapy era.
- Timing/order of nephrectomy and systemic therapy doesn't seem to matter…but benefit may be seen from both
- At CAMC, recently, we tend to treat systemically first

Standard vs extended lymphadenectomy for radical cystectomy

- Lymph node dissection at time of cystectomy always recommended
  - Even in clinically node negative patients, up to 25% are pathologically +
- Retrospective data support extended lymphadenectomy
  - 2014 meta-analysis summarized 5yr recurrence free survival 62% vs 55% in favor of extended vs standard node dissection
- 2 phase 3 randomized trials (LEA AUO AB 25/02 and SWOG S1011)
  - Both concluded no difference in RFS or OS
  - S1011 also concluded a higher rate of Grade 3-5 adverse events and 90 day mortality in extended lymphadenectomy group
- Based on these prospective trials, patients DO NOT benefit from routine extended lymphadenectomy
- Some benefit may exist in select groups – clinical N2-3, pT3-T4
  - More studies needed

Dawson V, Sinha M, Smith J, Somani BK, Douglas J. The role of extended lymph node dissection in patients undergoing radical cystectomy. Turk J Urol. 2021 Feb;47(Supp. 1):S27-S32. doi: 10.5152/tud.2020.20376. Epub 2020 Oct 9. PMID: 33052839; PMCID: PMC8057354.

Lerner, SP, et al. SWOG S1011: A phase III surgical trial to evaluate the benefit of a standard versus an extended lymphadenectomy performed at time of radical cystectomy for muscle invasive urothelial cancer.. *JCO* 41, 4508-4508(2023).DOI:10.1200/JCO.2023.41.16_suppl.4508

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