

Radical Cystectomy vs Bladder Preservation; past, present, and future

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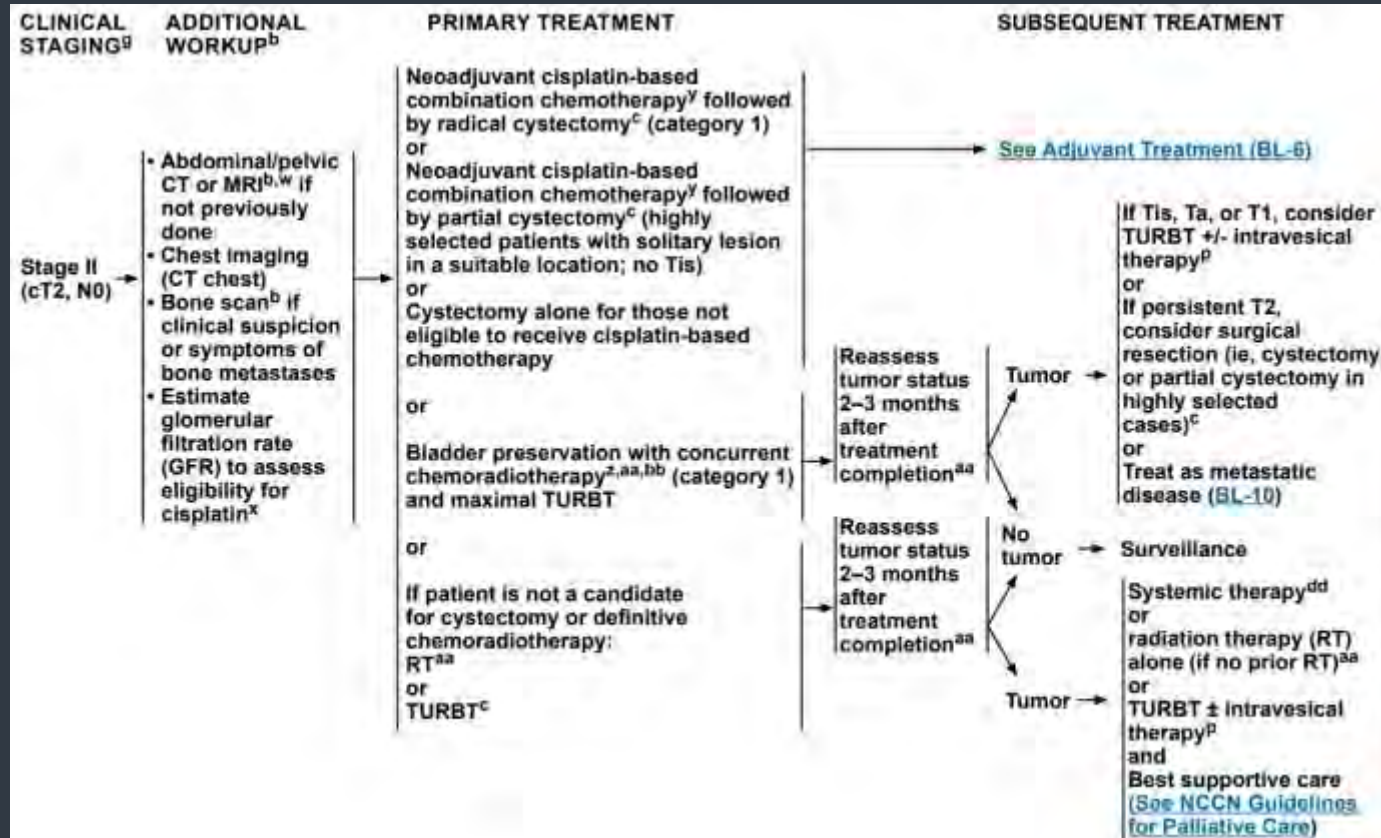
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Outline

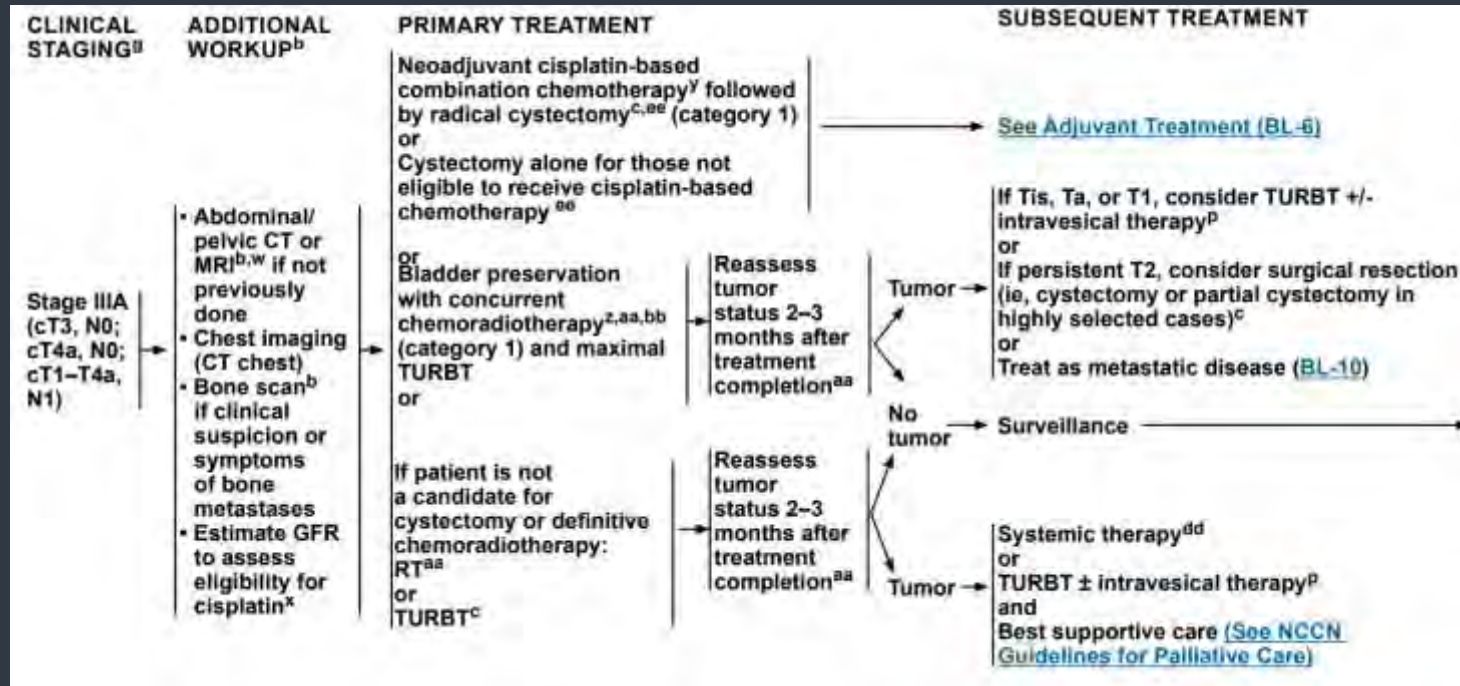
- Treatment options for localized muscle-invasive bladder cancer
- Overall culture surrounding treatment paradigms and why
- Evolution of our understanding of treatment outcomes when comparing treatment
- Where we are at currently
- What we still need to investigate



Treatment Options (T2 N0 M0)

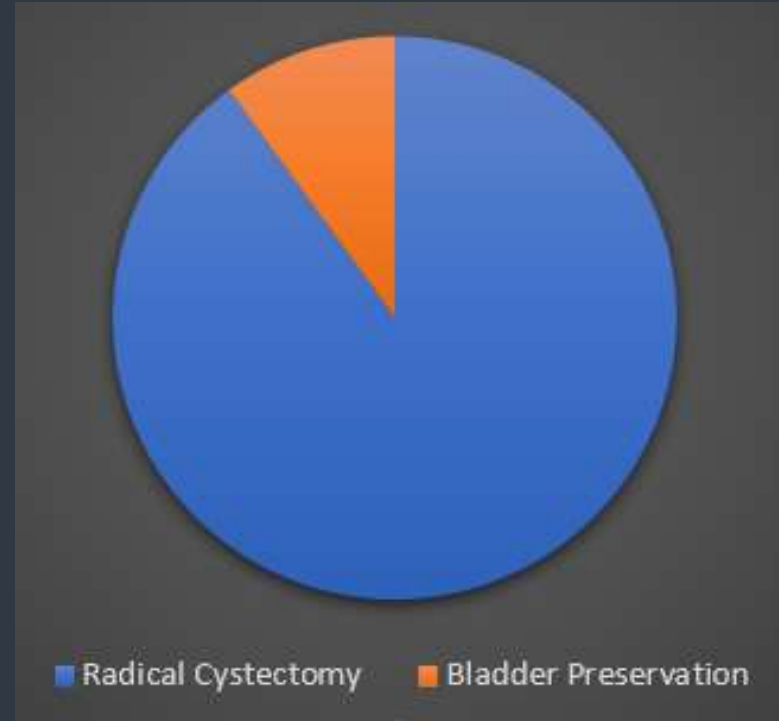


Treatment Options (T3-4a N0-1 M0)



What actually occurs

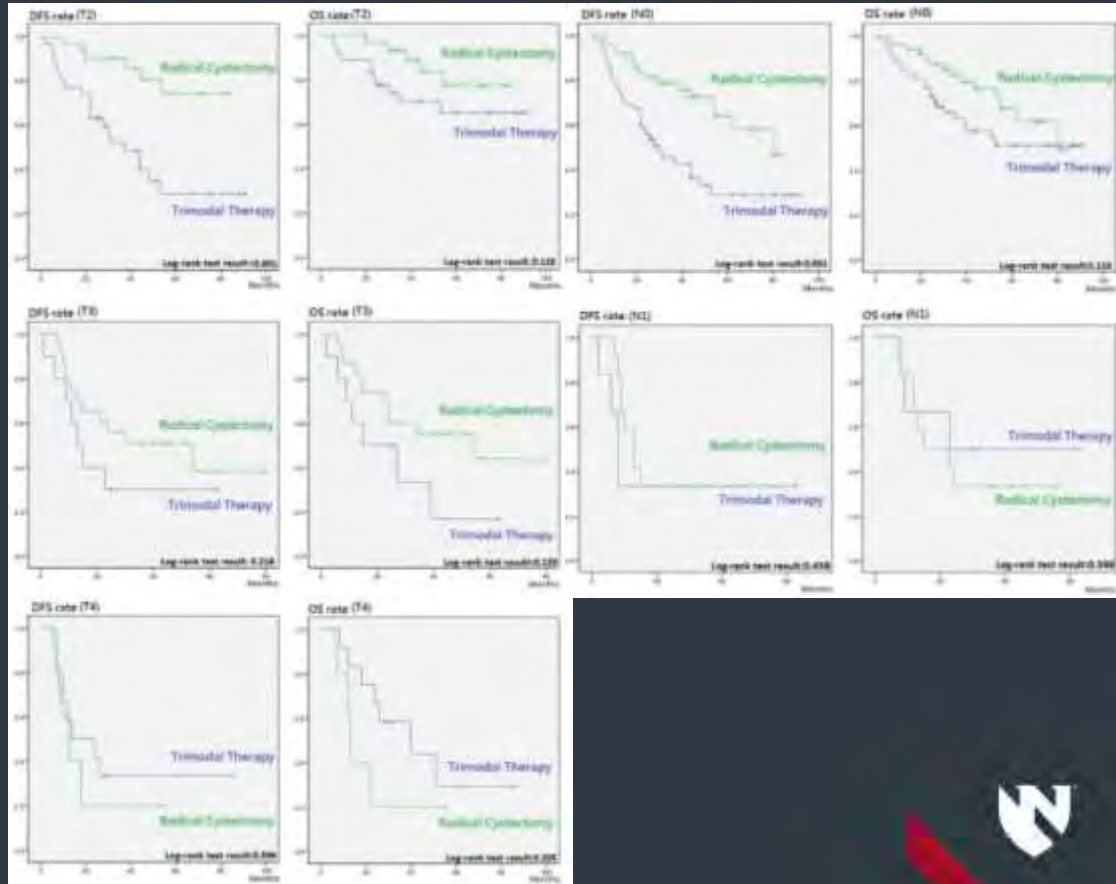
- A NCDB analysis of patients aged 40-79 with T2-3c N0 UC
 - 2006-2015
 - 2048 pts; 1812 pts underwent RC (88.5%) while only 236 pts (11.5%) underwent BP (PMID: 35058142)
- 2020 VA database analysis of pts treated for T2-4 N0-3 UC
 - 2000-2015
 - 1927 pts; 1775 pts underwent RC (92.2%) while only 152 pts (7.8%) underwent BP (PMID: 34337540)



Why this paradigm?

Representative Study:

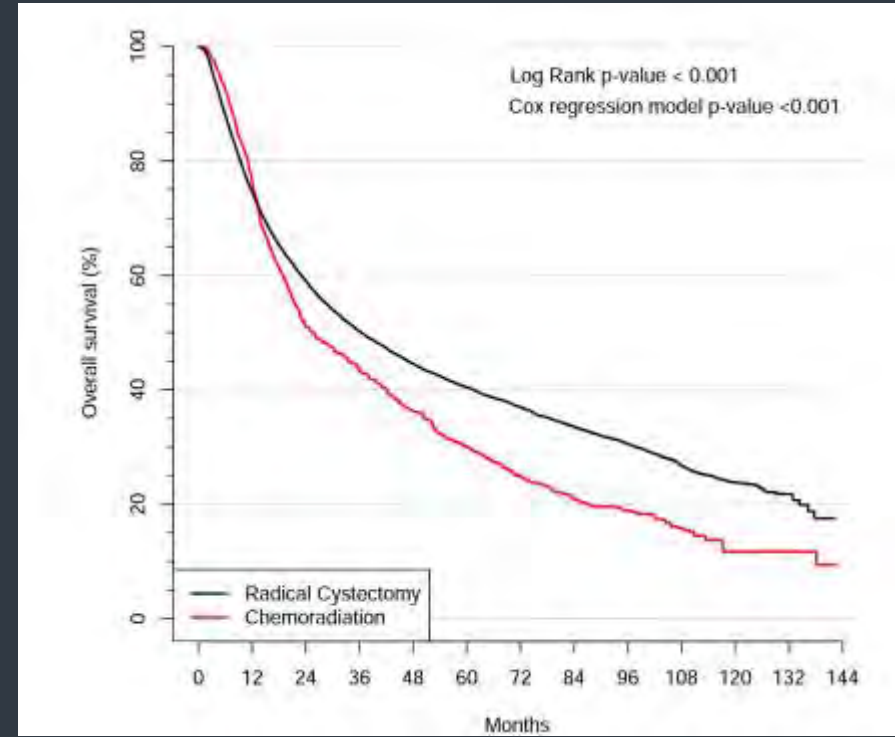
- Single institutional analysis (Taiwan) comparing BP and RC (Tseng et al, Uro Sci 2021)
 - 119 pts, stratified per tumor stage; 58 BP, 61 RC
 - 3y DFS- 44.1% vs 69.7% (RC wins; $p=0.003$)
 - On subgroup analysis, only holds true if T2N0
 - 3y OS- 61.7% vs 72.5% ($p=0.226$)



Why this paradigm?

Representative Study:

- 2019 NCDB Study (PMID: 31401220):
 - 15,854 pts with RC, 2,083 pts with BP
 - Propensity matched
 - T-stage still discordant between groups
 - OS higher with RC (HR:1.18, $p < 0.001$)



Why this paradigm?

- 2014 cost analysis (abstract only) comparing RC to BP using Medicare reimbursement data (Value in Healthcare 2014)
 - Focus on upfront costs
 - BP was \$6,788 less expensive but resulted in 1.2 fewer QALY, reaching a cost of \$5,680 per QALY
- 2022 SEER study on long-term care costs (PMID: 35168881)
 - Cost of treatment at 2 years: \$372,839 (BP) vs. \$191,363 (RC)
 - Cost of treatment at 5 years: \$424,570 (BP) vs. \$253,651 (RC)
 - Difference driven by outpt costs in follow-up (2y: \$318,221 vs \$100,900; 5y: \$367,092 vs. \$146,561)



Issues with past data

- **Confounders:**
 - Most BP pts are those who were not candidates for RC or had overall worse disease (higher comorbidity score, more N+, more T4)
- **Outcomes:**
 - Most looked at DFS (confounded by local recurrence between groups), and OS (confounded by above), but not Cancer Specific Survival
- **Treatments:**
 - Most past data were either RT alone or used substandard concurrent chemo (not true of presented studies but true of many others that have fed into overall acceptance)



Why this paradigm?

SPARE trial: direct comparison of RC and BP

- Multicenter trial in UK comparing RC to SBP after neoadj chemo
- T2-3N0; randomized after 3c neoadj chemo (gem/cis q3wk) but before cystoscopy, if \leq T1 at that time, proceeded to 4th cycle of chemo then RC or BP (If T2+, went to RC)
- Designed to show non-inferiority of SBP; planned 1015 pts with initial feasibility to be shown by 110 pts over first 3 years
- **Plagued by poor accrual and non-compliance with protocol (45 pts over 30 months (25 RC, 20 BP) with 6/25 RC pts actually getting BP); so stopped early**



New Data

2022 NCDB analysis
(PMID: 35058142)

- 2006-2015
- T2-3 N0 pts aged 40-79;
UCC only
- 1812 pts got RC, 236 got BP
- Propensity matched (no discordance between any variable)
- No difference in OS

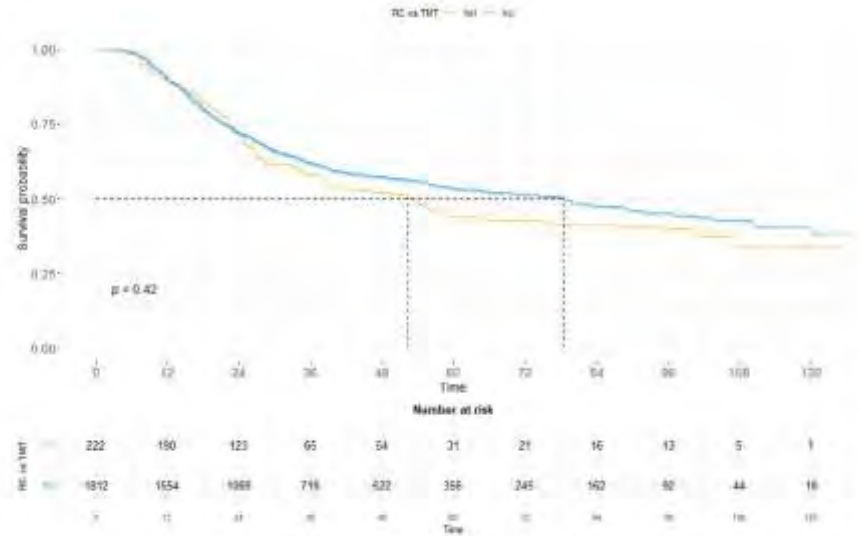


Fig. 1. Association of RC and TMT with OS after sIPW-adjustment. OS = overall survival; RC = radical cystectomy; sIPW = stabilized inverse probability of treatment weights; TMT = trimodality therapy.

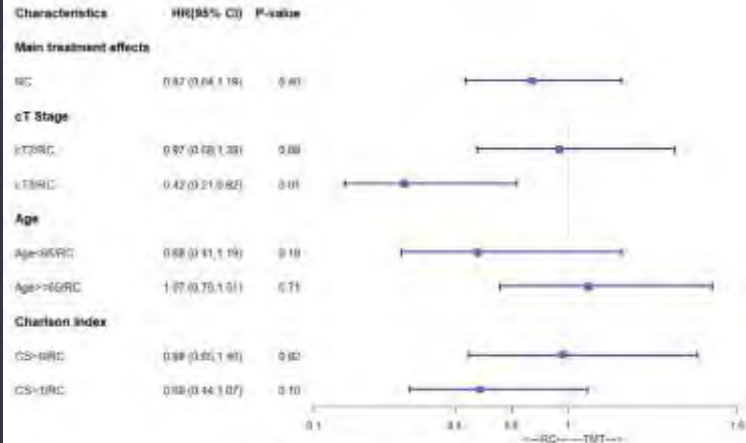


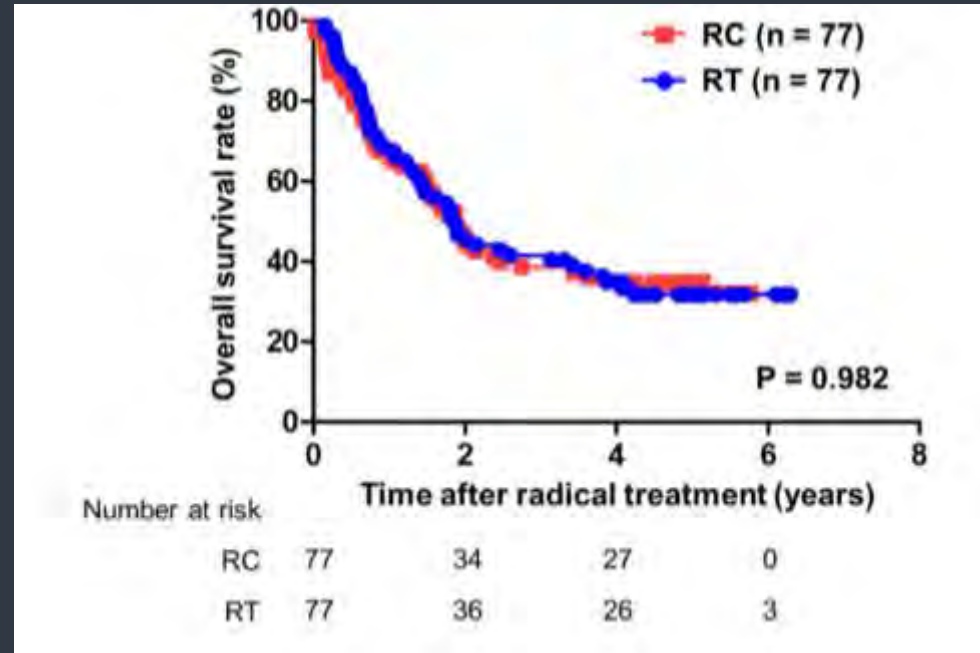
Fig. 2. Forest plot for heterogeneity of treatment effects.



New Data

2023 Japanese Cancer Registry (PMID: 36896218)

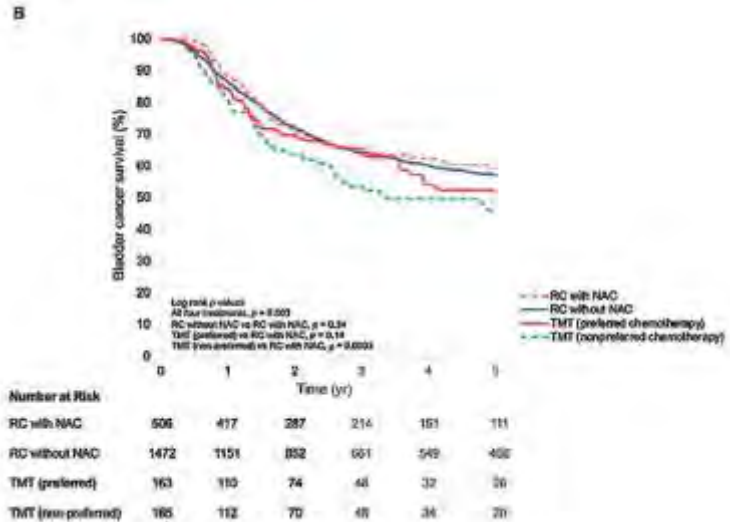
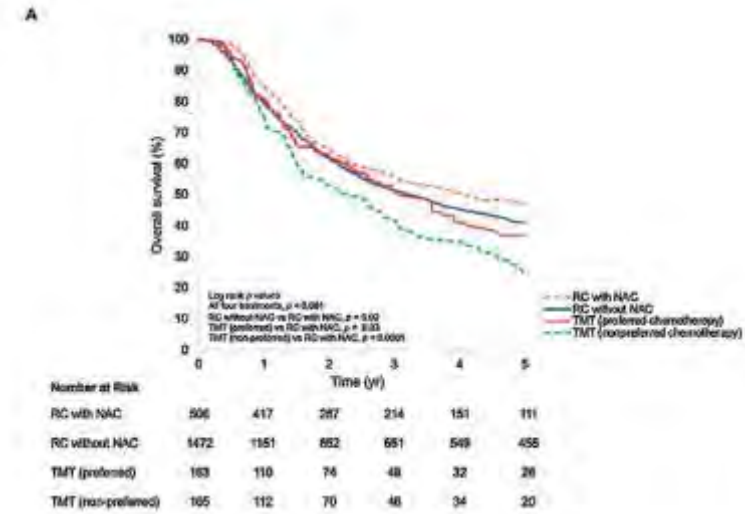
- 2013-2015
- T2-3 N0-3 pts aged 37-98; UCC only
- 241 pts got RC, 92 got BP
- Propensity matched (77 pts per group, no discordance between any variable)
- No difference in OS



New Data

2020 VA database analysis of pts treated for T2-4 N0-3 UC (PMID: 34337540)

- 2013-2015
- T2-4a N0-3 pts aged 52-89; UCC only
- 1472 pts got NAC-RC, 506 pts got RC, 163 pts got BP with preferred chemo, and 165 pts got BP with non-preferred chemo
 - BP was in those who couldn't get/refused RC
- Worse OS in BP but no difference in CSS



New Data

Radical cystectomy versus trimodality therapy for muscle-invasive bladder cancer: a multi-institutional propensity score matched and weighted analysis

Alexandre R Zlotta, Leslie K Ballas, Andrzej Niemierko†, Katherine Lajkosz†, Cynthia Kuk, Gus Miranda, Michael Drumm, Andrea Mari, Ethan Thio, Neil E Fleshner, Girish S Kulkarni, Michael A S Jewett, Robert G Bristow, Charles Catton, Alejandro Berlin, Srikala S Sridhar, Anne Schuckman, Adam S Feldman, Matthew Wszolek, Douglas M Dahl, Richard J Lee, Philip J Saylor, M Dror Michaelson, David T Miyamoto, Anthony Zietman, William Shipley, Peter Chung, Siamak Daneshmand, Jason A Efstathiou**

Published June 2023 in Lancet Oncology

Closest thing we may ever get to a RCT



Lancet Oncology; June 2023

Design:

- Retrospective analysis of 722 pts diagnosed with muscle invasive UCC; 440 RC, 282 BP; ALL eligible for both approaches
- T2-4 N0; all solitary tumors < 7 cm, no bilateral hydroneph, no extensive or multifocal CIS
- Treated across 3 centers; USC, Princess Margaret, MGH
- Primary endpoint MFS; secondary endpoints included OS, CSS, and DFS

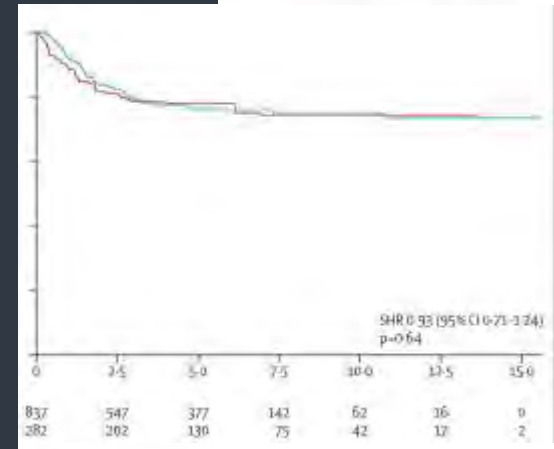


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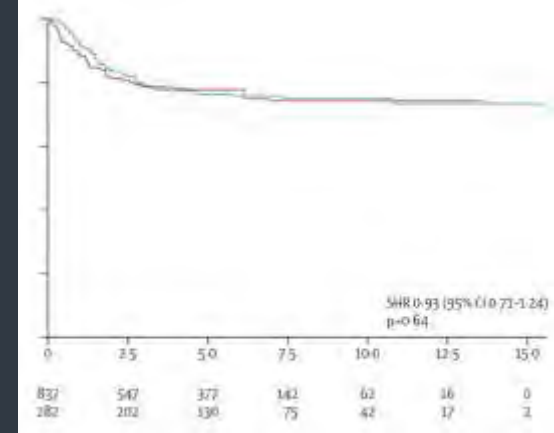
Results: (BP vs RC; using propensity matched data)

- 5y MFS: 74% vs 74%; p=0.64
- 5y CSS: 85% vs 83%; p=0.06
- 5y DFS: 76% vs 76%; p=0.37
- 5y OS: 77% vs 72%; p=0.01

MFS

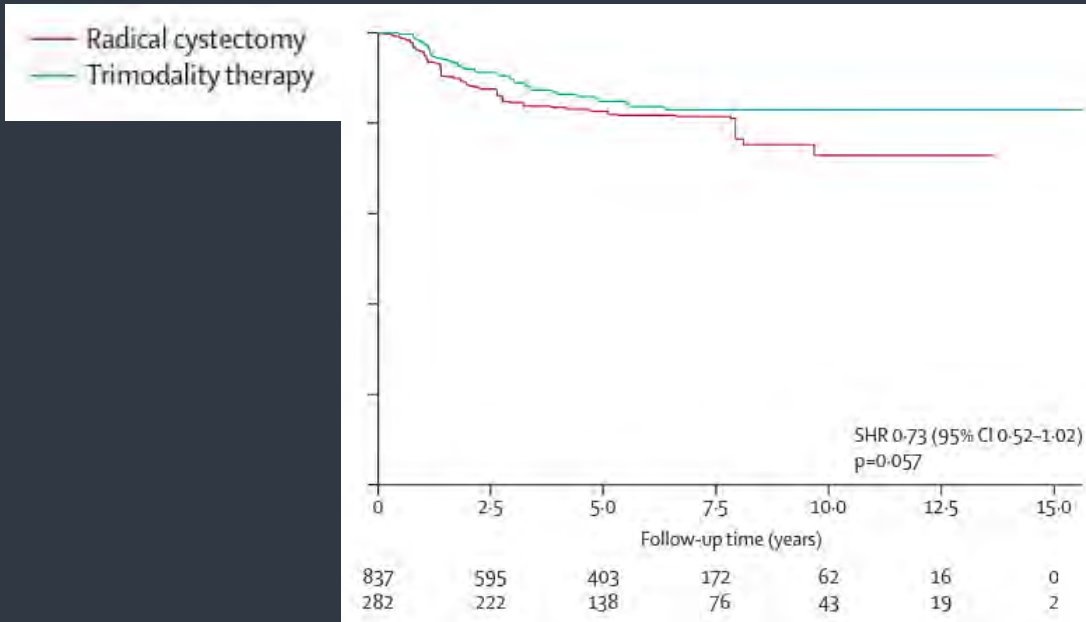


DFS

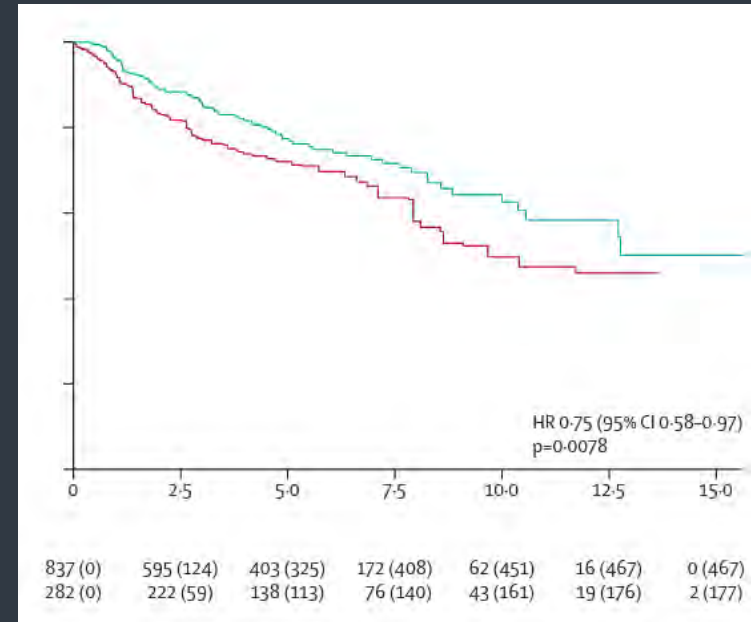


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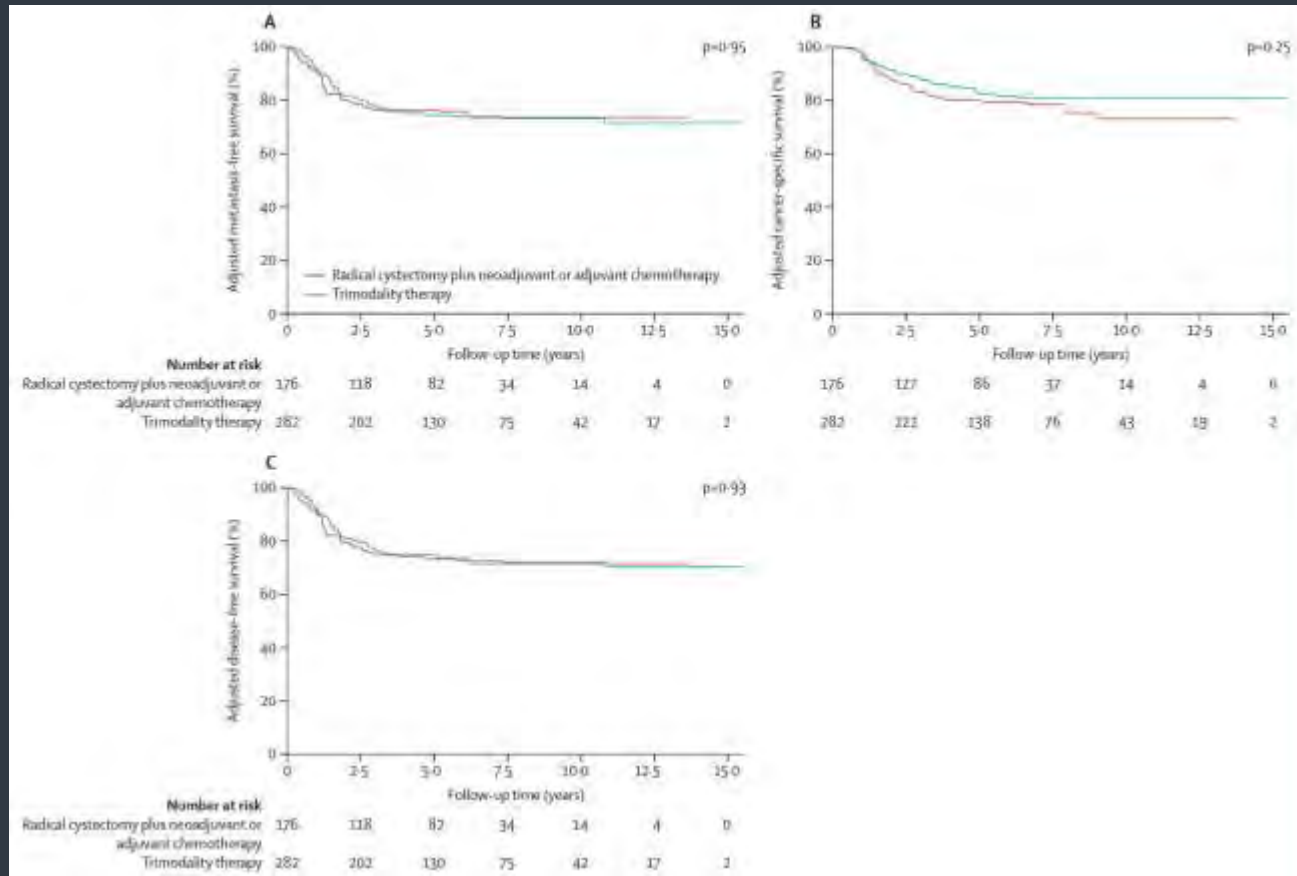
CSS



OS



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Culture Change?-where are we now

- More of a push across both Radiation Oncology and Urology to start to consider BP as a true first-line option in discussions and at scientific meetings
- Unclear how rapidly true referral patterns may change



Future Directions

- Still cannot deny the more extensive follow-up needed with BP...can we make this more efficient or cost effective?
 - cDNA or urine cytology instead of routine imaging and cystoscopies?
- Await NRG GU001 to see if adjuvant RT in high-risk patients after RC may further improve outcomes



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