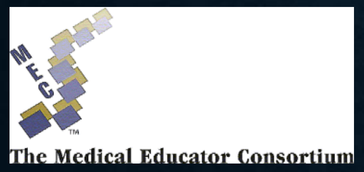
RALPH DE VERE WHITE, MD

STATE OF THE ART IN GENITOURINARY CANCERS

RELEVANT FINANCIAL RELATIONSHIPS IN THE PAST TWELVE MONTHS BY PRESENTER OR SPOUSE/PARTNER.

GRANT/RESEARCH SUPPORT: NCI
STOCK SHAREHOLDER: IMAGIN MEDICAL PRODUCTS

THE SPEAKER WILL DIRECTLY DISCLOSURE THE USE OF PRODUCTS FOR WHICH ARE NOT LABELED (E.G., OFF LABEL USE) OR IF THE PRODUCT IS STILL INVESTIGATIONAL.



Topics To Be Covered:

- PSA Screening
- Lowering mortality for UC
  - NMIUC: Following standard of care
  - MIUC: More realistic approach to therapy

Prediction in 2012 After USPSTF Recommended Against PSA Screening

There would be an increase in:

- Advanced Disease at Presentation
- Prostate Cancer Mortality

Prostate Cancer Death Rate

Death	Year
34,900	1993
29,000	2004
27,560	2006

Population growth 11%

24% Drop in per capita death rate

PSA: Stage Migration

	Pre PSA	Post PSA
D2 at RX	30%	3%
Node Positive	22%	2%
Margin Positive	30%	15%
T1C	10%	84%

- **Adjusted rates of metastatic PCa incidence for NHW men significantly increased by 4.3% since 2010**

CONCLUSIONS ON PSA SCREENING

- Continue to screen appropriate patients.
- Talk to patients concerning active surveillance PRIOR to biopsy.

Primary and Recurrent UC

*Non muscle invasive (NMI)

Intravesical BCG

- BCG superior to TUR alone with regard to tumor recurrence[1,2]
  - 31% net benefit

Increases progression-free survival at 10 yrs[4] by 25%

TUR + BCG = 62%

TUR + delayed or no BCG = 37%

1. Brake M, *Urology* 2000; 55: 673-678.
2. Hurle R, *Urology* 1999; 54: 258-263.
3. Mack K, *J Urol* 2001; 165: 401-403.
4. Herr H, *J Clin Oncol* 1995; 13; 1404

Repeat TUR of T1 Cancers

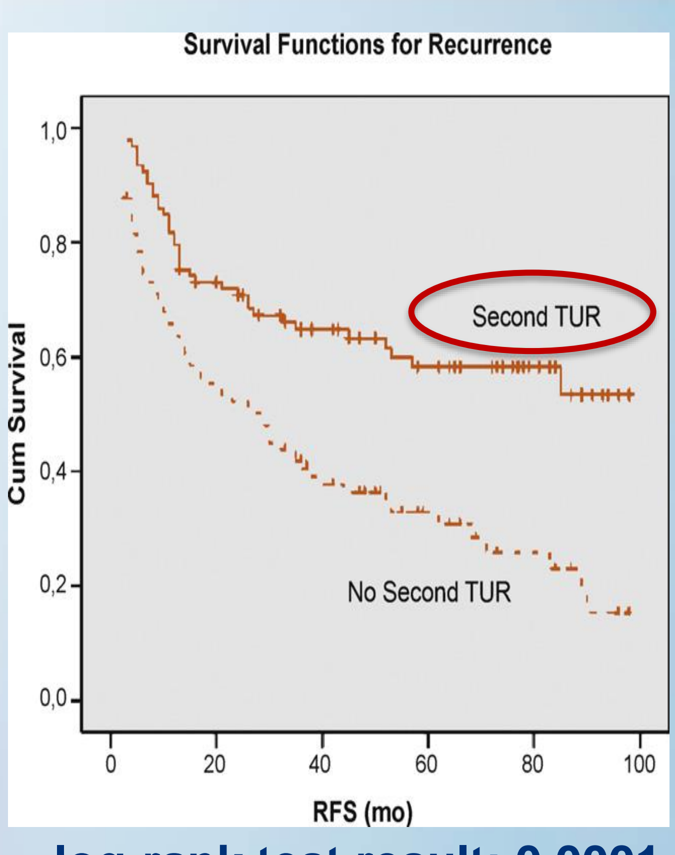
- 48% Persistent NMIBC
- 30% Upstaged to MIBC

Herr HW. J Natl Compr Cancer Netw. 2015 13. 14111

RE TUR of T1 NMIBC

Improved:

Recurrence Free Survival   Progression Free Survival



log-rank test result: 0.0001

Mean Follow-Up: 31.5 Months

	Group 1	Group 2
Second TUR	Yes	No
Recurrence	26%	63%
Grade 3	60%	90%
Progression	4%	12%

DIVRIK RT. J Urol 2005

UCDAVIS COMPREHENSIVE CANCER CENTER

Repeat TURBT T1 & BCG For High Risk

- 14,302 patients T1 NMIUC
  - 15% Repeat TURBT
  - 10% Received BCG

NABBOUT P. AUA 2015

Questions/Challenges

- Guidelines strongly supported by AUA/SUO
  - Home study courses
  - Instructional courses
  - Plenary sessions
  - State of the art talks
  - Featured Articles
  - Re-certification
  - Urology Care Foundation
- Rated #1 Benefit by AUA members

In 80-90% of our patients, they are not followed.

Muscle Invasive UC ≥ T2

- 20% of initial tumors
- 8% of all tumors
- 80% of UC deaths
- 40-50% Response to chemotherapy

Improving Survival

- Clinical Trials/Research
- Evidence based medicine
- Standard of care

Recognizing realities of care

DSS No improvement in 25 Years

Muscle Invasive Urothelial Cancer
Most Effective Therapy

- Neoadjuvant Chemotherapy
- Radical Cystectomy
- Pelvic Lymph Node Dissection

Therapy for M.I.U.C 28,691 Patients 04-08 NCDB

Curative Intent

64%

Observation

15%

Cumulative percent: 0, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100

60%

19%

≤50, 51-60, 61-70, 71-80, 81-90, >90

Age group, yr

Missing, Observation, Chemotherapy, Radiotherapy, Surgery

(Gray J.P EUR GRO 63(2013) 823-829

Median age at diagnosis is 73 years.

Complication Rate Post Cystectomy (CUAJ 2013)

Diversion	Conduit	Neobladder
Complication	54%	51%

Hospital Volume and 90-day Mortality (BJU 2014)

Overall Mortality: 7.2%

Number of Cases:	Mortality:
<10	8.0% (52% of Hospitals)
≥20	5.7% (32% of Hospitals)

169 Cases RC + ERAS Protocol USC (WJU 2017)

Complications: Major 24% ER Visit 38% Readmit 30%

Death 4% (7 patients)

N Engl J Med. 2003 Aug 28;349(9):859-66.

Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer.

Grossman HB1, Natale RB, Tangen CM, Speights VO, Vogelzang NJ, Trump DL, deVere White RW, Sarosdy MF, Wood DP Jr, Raghavan D, Crawford ED.

Survival by Pathologic Stage at Cystectomy

M-VAC and cystectomy, pT0 (14 deaths; median survival, NR)
Cystectomy, pT0 (6 deaths; median survival, 11.3 yr)
M-VAC and cystectomy, RD (76 deaths; median survival, 3.8 yr)
Cystectomy, RD (94 deaths; median survival, 2.4 yr)

pT0 85% 5-yr survival

Cystectomy 10%

M-VAC 38%

+16mo

M-VAC (RD)

MS: 3.8 yrs

Cystectomy (RD)

MS: 2.4 yrs

Survival (%)

100, 80, 60, 40, 20, 0

0, 24, 48, 72, 96, 120, 144, 168

Months after Randomization

Benefit by Stage

cT3/cT4	3.5 years
cT2	2.5 years

Risk	0	24	48	72	96	120	144
... and cystectomy, pT0	48	43	40	37	26	12	2
Cystectomy, pT0	18	17	15	12	10	4	1
M-VAC and cystectomy, RD	105	69	52	38	20	11	4
Cystectomy, RD	136	71	52	37	27	14	6

60 Patients MIBC NAC Followed by TUR
Median Follow-Up 60 Months

Patient Group	Overall Survival	Cancer-Specific Survival
All Patients (60 Patients)	65%	73%
>cT0 Following NAC – Immediate Cystectomy (27 Patients)	51%	53%
cT0 Following NAC – No Recurrence or Cystectomies (17 Patients)	83%	100%
cT0 Following NAC – +Recurrence (15 Patients)	66%	73%

Survival Local Regional Disease 38% (2017)

YAP Urology Practice 7/20/17

UCDAVIS COMPREHENSIVE CANCER CENTER

Systematic Review and Meta-Analysis on the Efficacy of Chemotherapy with Transurethral Resection of Bladder Tumors as Definitive Therapy for Muscle Invasive Bladder Cancer (2017)

Results

Meta-Analysis 10 Papers, 266 PT's

OS At 5 Years Estimated To Be:

72% [95% CL 64% - 82%]

75% UC Davis

Therapy for Muscle Invasive Bladder Cancer
Meta-Analysis (2018)

Trimodality (TMT)	RC +/— NAC (3.2%)
3,402 PT's	26,891 PT's
10 Year Survival Rates	
OS 31%	35%(+4%)
DSS 51%	58%(+7%)
T2 DSS 69%	79(+10%)

"Quality of evidence for results of this study was moderate to very low"

(Fahmy, J URO ONC 36(2018) 43-53)

To Improve Survival in MIUC

- More patients have to receive treatment with curative intent.
- Treatment needs to be tailored to what is possible for that patient and treating institution.