Asco-GU 2018 San Francisco

Maurizio Brausi

SIU
SOCIETÀ ITALIANA di UROLOGIA
FONDATA NEL 1908

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ASCO-GU 2018 : Bladder Cancer Program

- **2 General Sessions:**
  * Current and future directions of MIBC : 4 lectures + 1 selected abstract
  * Multimodality approach to locally advanced BC : 3 lectures (case discussion) + 1 selected abstract
- **2 Keynote lectures**
- **Poster Sections: 139 posters**
  . 9 UUT Tcc
  . 17 NMIBC
  . 113 MIBC
- **2 Symposia**

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Immunotherapy in Bladder Cancer : Asco-GU 2018

- ***Immunotherapy in NMIBC: State of the art and new developments***
  R Colombo
- Debater/opinion leader
  Bassi
- Clinical case (Brausi) with Colombo and Bassi + audience

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Urothelial TCC of Upper Urinary Tract

- Treatment of High risk and muscle invasive TCC of UUT:
  The role on neo-adiuvant and adjuvant chemotherapy after the new data from ASCO-GU 2018
  POUT study
  Necchi
- Debater: Bassi

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Muscle Invasive Bladder Cancer

- ***Bladder Sparing procedures:*** State of the art and Asco-Gu news Brausi
- Discussant: Bassi
- Clinical case (Colombo): Bassi, Brausi, Necchi + Audience

- ***Immunotherapy in MIBC:*** Agents and available + new Trials A.Necchi
  Discussion with panel and audience
- ***The Future in MIBC: Genomic Atlas :*** Brausi

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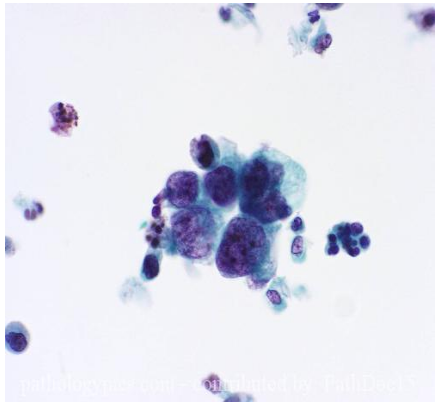
- Have a Nice Discussion !!!

Clinical Case

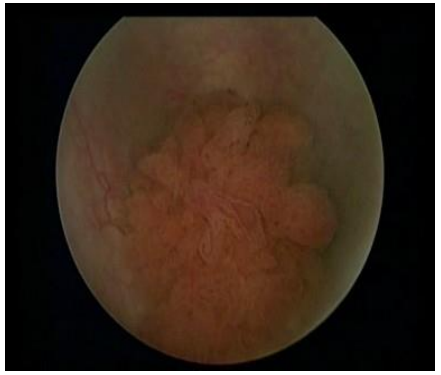
Maurizio A Brausi

Clinical Case

- LE 73 yr, smoker (15 sig./day since 30 yrs)
  09.'96 disuria, urge and one episode of macro-hematuria.
- Cytology positive
  US: lesion of 1.6 cm in the L lat. bladder wall Prostate: 4.5 x4.8 cm. No nodules. Psa = 3.5 ng/ml



- *09.96* Urethrocystoscopy (anest.): 1 papillary lesion in the L lat. wall of 1.5cm + 2 lesions of 0.5 and 0.4 cm in the post wall and left trigone. No other suspicious areas
  Treatment: TUR of the lesions + deep biopsy of tumor bed. Fulguration of surrounding areas (1-2 cm)

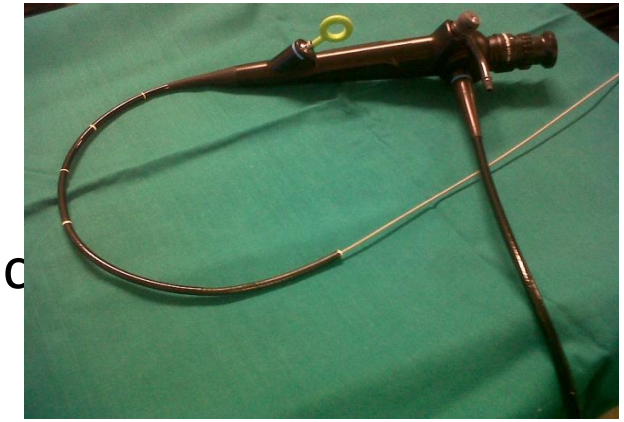


Clinical Case

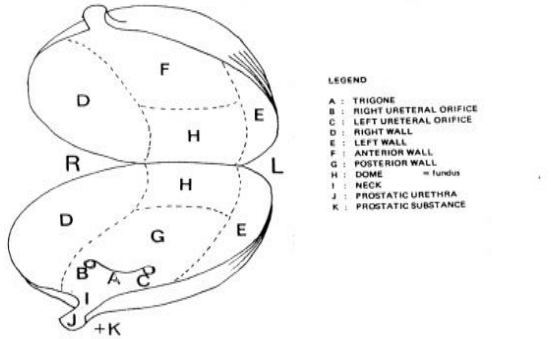
- ***Path Report:***
  1. Transitional cell carcinoma grade 2 confined to the mucosa. No infiltration of lamina propria. Muscle present with no infiltration.
- *2 and 3 TCC confined to the mucosa*
- ***Staging:*** ***Primary multiple TaG2***

Clinical Case

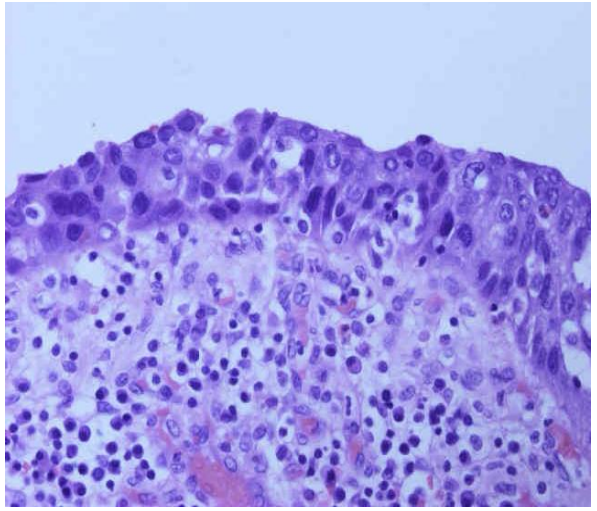
- *10.96* Pat. randomized in EORTC prot. 30911
  (Epi vs BCG vs BCG +INH).
  Epi 50 mg x 6 with maintenance 3 years.
  F-Up: No side effects. No recurrence (Cyto + Cysto: neg)
- *04.2006* Disuria, UTI, nocturia (4) I-PSS 18.
  3 cytology : displasia. Psa = 3.7ng/ml
- ***US:*** Enlarged prostate x3. No nodules or firm areas.
  Suspicious lesion on the R wall. Cytology : +
- ***Flexible uretro-cystoscopy:*** stenosis (13F) of bulbous urethra. Prostate of 4.7 x 5 cm .
  2 small papillary lesions on the R+ sup. wall 1 and 0.8 c



Clinical case



- *10.06* Uro- CT = Negative
- *11.06 TUR of the 2 lesions and bladder mapping according to Eortc (7 biopsies).*
- ***Path Report**. **Ta G2 + Cis in 1 fragment (L lat wall).***
- *12.07* BCG x 6 with maintenance (3 years). After 4 instillations patient (83 yr) had severe disuria, macroscopic hematuria, fever > 38°.
  He wanted to stop BCG.



Clinical Case

- *02.07* MMC + EMDA x 6 with maintenance, once a month for 12 months
- *06.07* Local side effects : disuria and burning
  Cytology : mild dysplasia . Cysto: Negative
  Bladder capacity reduced (< 150cc)
- *10.07* Cytology: Neg
  Cystoscopy (No anesthesia) : red velvet areas on the L trigone and post. wall: cold cup biopsies
- ***Path Report: mild dysplasia + inflammation***

Clinical Case

- *02.08* UTI treated with chinolones.
  Disuria with nocturia >5. Urge incontinence (2 pads/day)
- Cytology: neg. Cystoscopy: urethal stenosis (13F) reduced bladder capacity (100cc) with enlarged prostate (Dutasteride + Tamsulosin).
- *04.08* Uro-CT: thikness of the bladder wall with R hydro (Grade 1). No bladder or metastatic lesions
- *08.08* Stable. Cytology and cysto negative. UTI cured by antibiotics.
  QoL really affected…..

Comments

- Should we treat these patients more aggressively after recurrence ?
- How can we improve their quality of life ?
- Is radical cystectomy an option ?
- Is an enlarged prostate a contra-indication for BCG? (UTI)
- Age: is it important for deciding between immuno and chemo?

Bladder Sparing Approach to MIBC

- ASCO-GU 2018

- Maurizio Brausi

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Bladder Preservation: Goals

1. Avoid major surgery (death rate 0-7%)
2. Obtain favorable oncological outcome
3. Maintain physiological voiding
4. Preserve potency (QoL)
5. Preserve ejaculation and fertility

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Risk of Bladder Sparing Strategies

A delay in RC increases the risk of lymphnode metastases

Nodes positive rate of 26% when RC becomes necessary because of treatment failure vs 15% when RC is perfomed immediately
(EUA Guideline 2008)

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Strategies for Bladder Preservation: History

Neoadjuvant Chemo + Tur + Re-staging Tur

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MSKCC Experience : 10 yr FU

N Pts. = 111 received neo-adjuvant M-Vac + TUR

PT0 = 60/111 (54%)

The majority of them had long term survival with bladder preservation

(Herr et al: J Clin. Onc. '98)

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Chemo For Bladder Preservation

Neo-adjuvant M-Vac in cT2-T4 N0M0 BC

N Pts. = 104 treated with TUR after M-Vac

Results: 49/104 (49%) were T0.
Responding pts underwent Re-Tur or Partial C

Median Survival = 7.5 yrs

60% of pts. (M-Vac+ TUR) are alive at mean F-Up of 56 mo.

44% of pts. treated with TUR alone maintained their bladder

(Sternberg et al Cancer '03)

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MSKCC Experience

(Herr, Eur Urol 2008)

N pts. = 63 (decline to recive RC) for PT0 after Cis-Platin based chemo + TUR

Results: (median F-up = 86 mo)

40/63 (64%) survived : 54% of them maintained their bladder

The most significant treatment variable predicting better survival was:
pT0 on Re-staging TUR before starting chemotherapy

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MSKCC Experience

Results

23/63 pts (36%) died of disease

19/63 relapsed with MIBC

Over 90% of surviving pts. had solitary, small, low stage (pT2) invasive tumours completely resected

83% of them survived with no relapse

(Herr Eur Urol 2008)

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TURBT and twice-daily RT + paclitaxel-cisplatin or fluorouracil-cisplatin with selective BP and A- chemo for pts. with MIBC (RTOG 0233) Randomised Multicenter phase II Study

- ***Methods :***
  93 cT2-T4a patients recruited/ elegible from 2002-2008 in 24 US institutions
- *Median Age 65*
- ***Stage cT2 in 95% of the pts. cT3-T4 in 5%***
- ***PS : 0 in 90% , 1 in 10%***
- *Results : median F-up 5 yrs.*
  5-yrs bladder intact survival: 65% in Paclitaxel group
  71% in the Fluorouracil group

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RTOG 0233 Randomised Study on BP

- ***Toxicity***
  P-Group : 34/40 pts. (85%) toxicity during adjuvant chemo
  F-Group: 19% Grade 3-4 toxicity in induction + 26% Grade 3-4 in consolidation + 11% Grade 3-4 after RT. Total toxicity : 56%.
  1 patient died of toxicity in this group.
  Finally 13% and 6% of pts in P and F Group stopped treatment for toxicity

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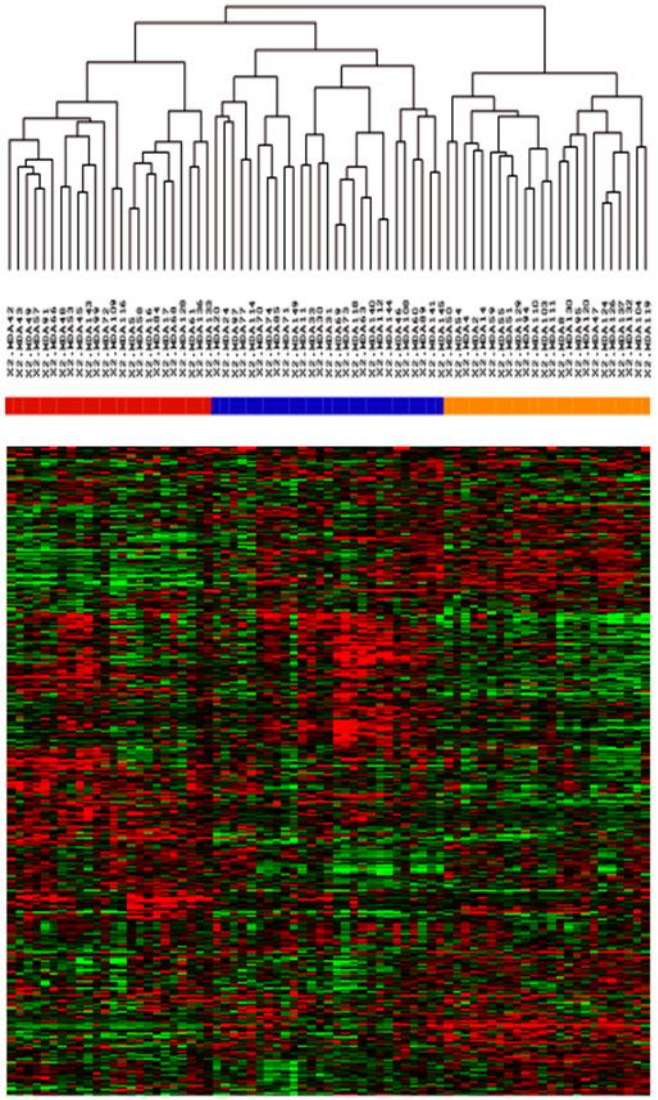
Use of Molecular Markers in Bladder-Preservation Therapy: ASCO-GU 2018

- Lecture by Peter Hoskin (09.02.2018)
- Poster



Translation of Biomedical Research Into Clinical Practice

- RTOG investigated the outcome of 73 pts. treated in 4 bladder preserving protocols (overexpression of HER2)
- **Results:** In pts treated with TT the **Overexpression** of **HER2** (ERBB2) correlated significantly with a reduced CR (50% vs 81% p= 0.026)
  (Chakravarti A et al Int J Rad Onc 2005)

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Other Molecular Markers

- MRE11 is one of the DNA damage –signaling proteins activated in the process of DNA double strand break repair (Meiotic REcombination 11 homolog)
- MRE11 espression was evaluated in MIBC pts. treated with definitive RT or RC
- Results: High MRE11 protein expression by the tumor predicted for improved outcome with RT but not by RC
- Conclusions: MRE11 overexpression is a predictive molecular marker of improved CSS after RT for MIBC (Choundury et al Cancer Res 2010)

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MRE11 and TIP60 in RC vs RT

- The expression of MRE11 and Tat-Interactive protein 60 (TIP60) were evaluated in 435 pts who received RC in Denmark
- ***Results:***
  Elevated expression of TIP60 was significantly correlated with DSS in RC but not in RT pts. (opposite of MRE11)

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MRE11 and TIP60 in Combinations

- ***TIP60 and MRE11 were used in combination in pts. who received RC or RT***
- **Results:** low MRE11 expr + high TIP60 exp = better DSS in favour of RC (p=0.01)
  high MRE11 expr + low TIP60 expr = better DSS in favour of RT (p=0.012)
- **Conclusions:** MRE11 and TIP60 are interesting predicting markers. Need validation in prospective trials
  (Laurberg at al BJU Int 2012)

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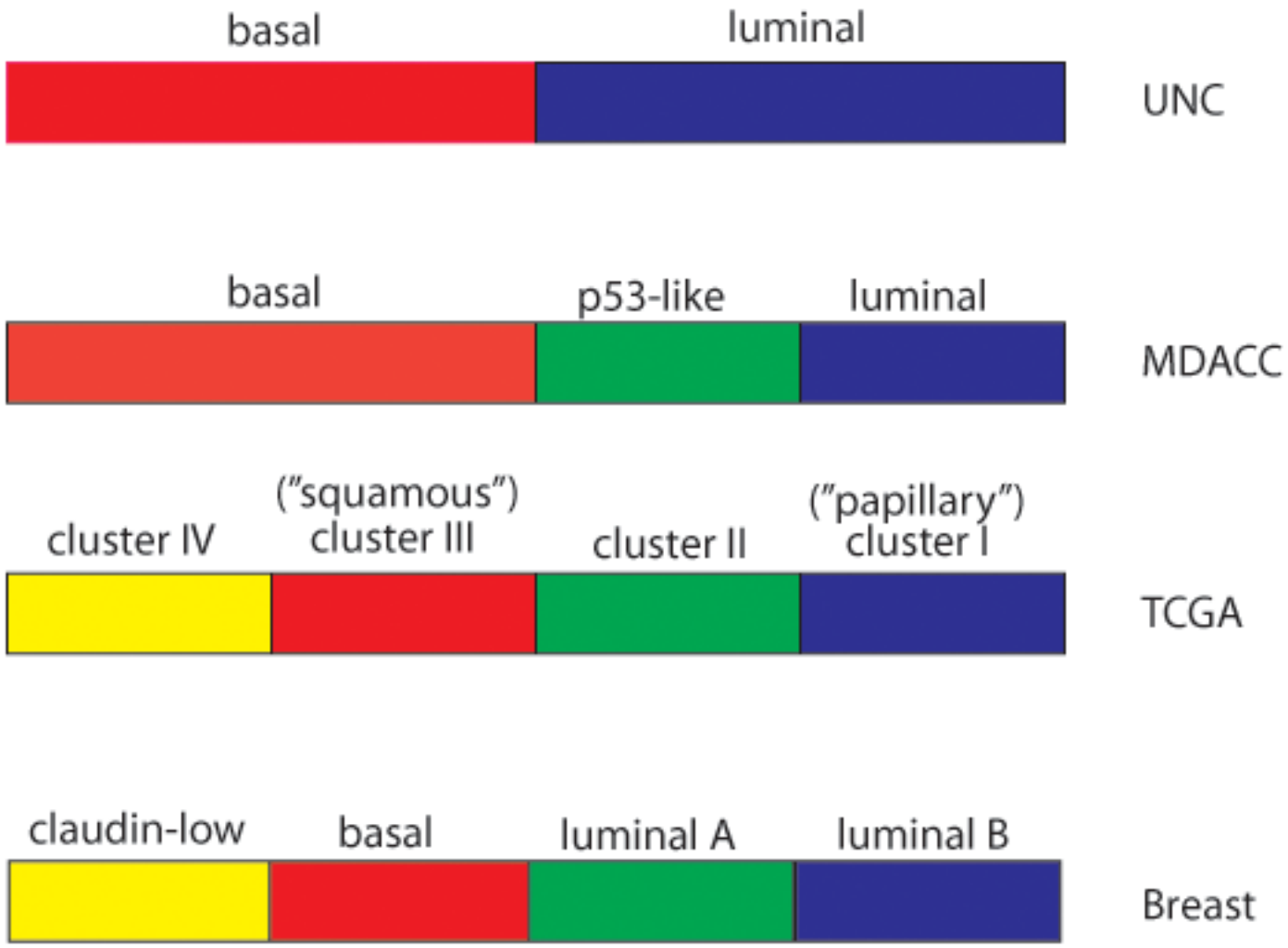
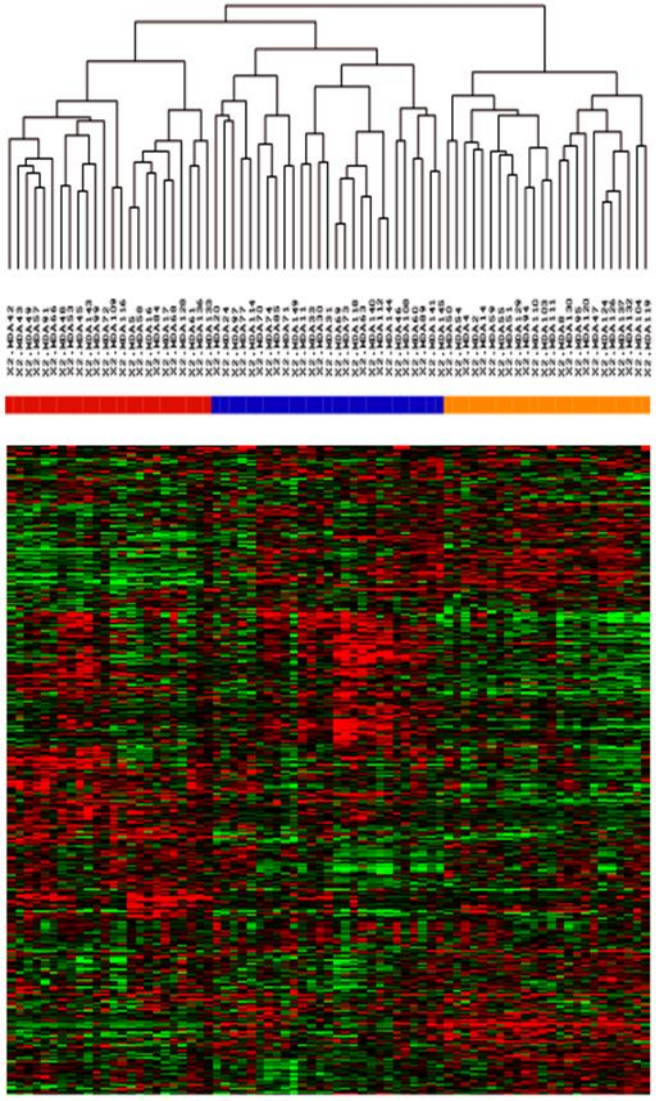
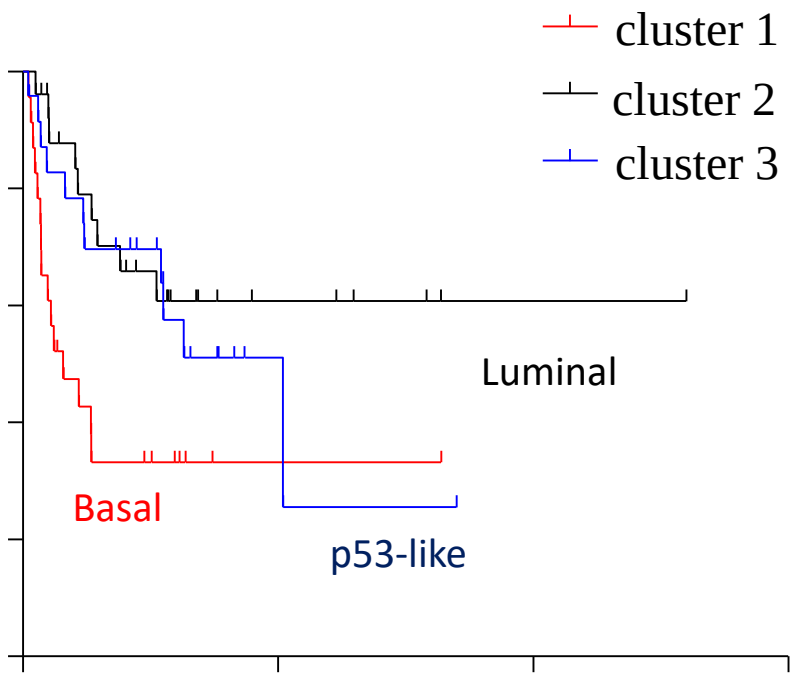
Genomic efforts identified intrinsic subtypes of MIBC that reflect breast cancer biology



MDACC: 3 molecular subtypes of MIBC



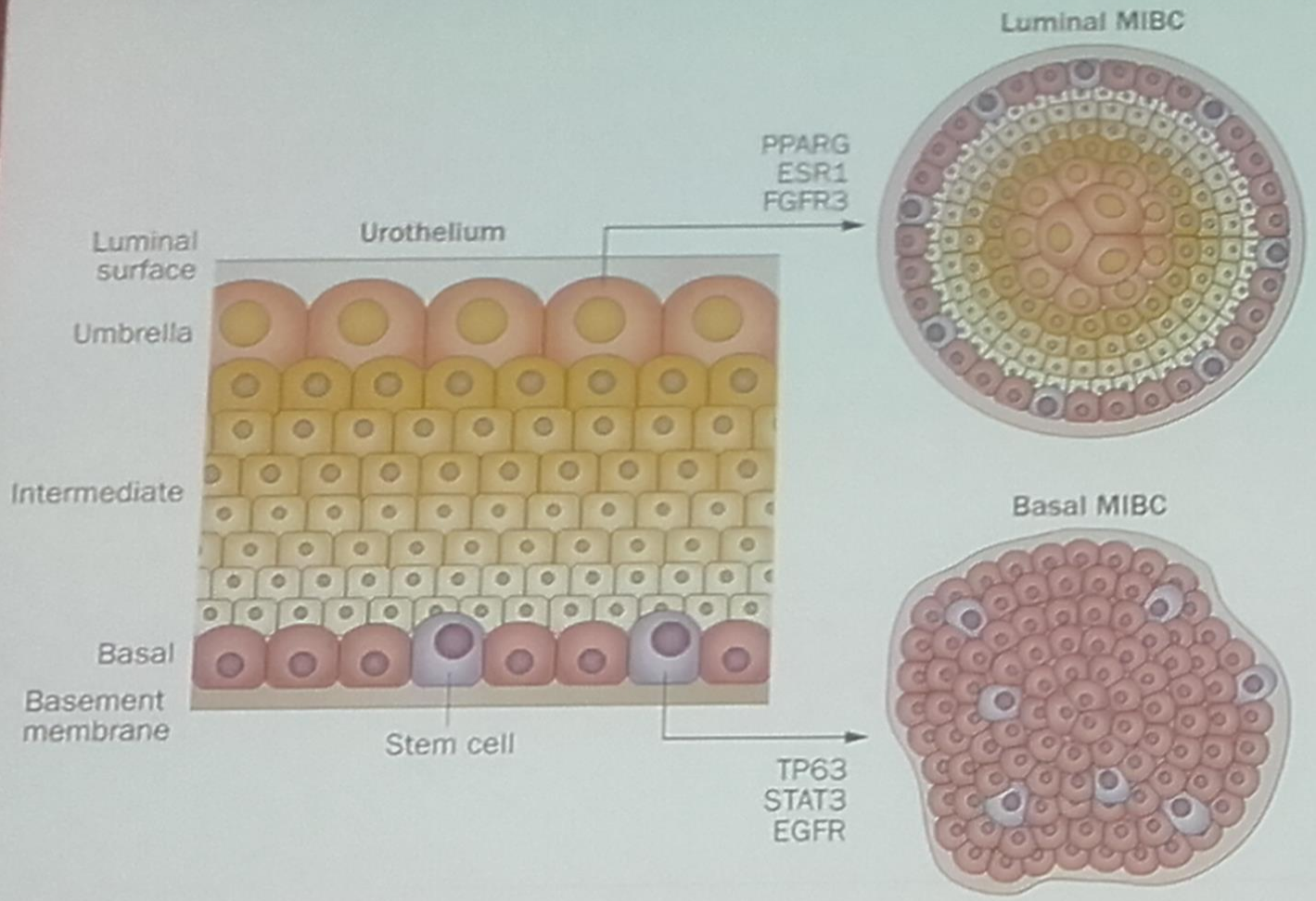


Validated in 3 independent cohorts.

Choi et al, Cancer Cell 2014

Molecular Subtypes

Karmanos CANCER INSTITUTE
Wayne State University



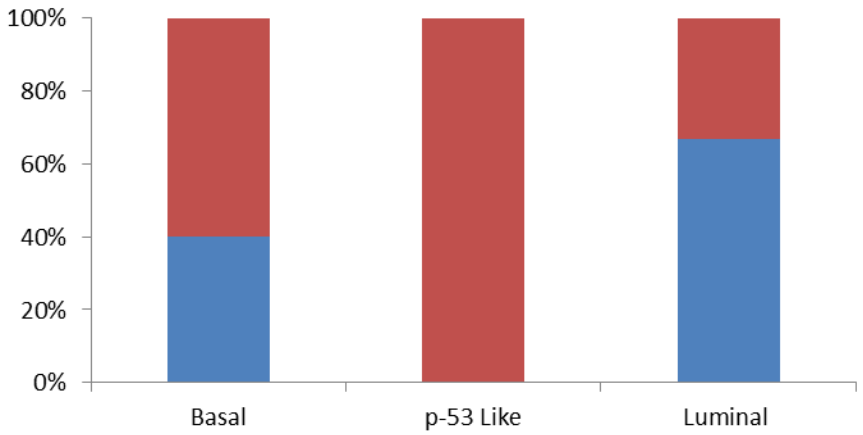
- Basal versus Luminal
  - GSC, UNC, MDA, TCGA, Lund

- Basal tumors most sensitive to neoadjuvant chemotherapy

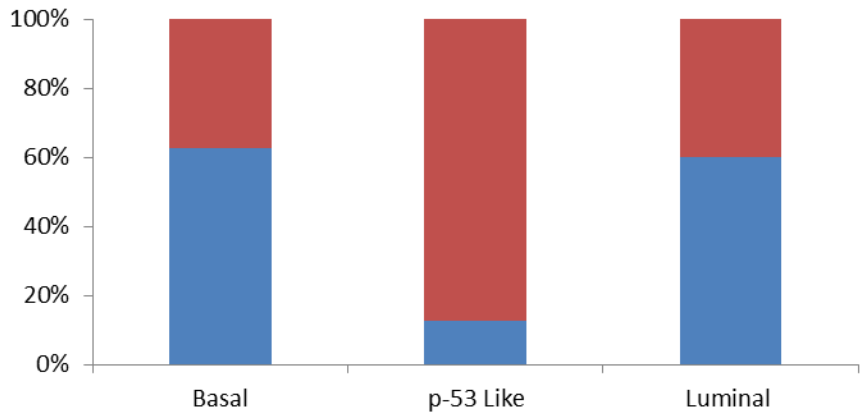
https://media.nature.com/full/nature-assets/nrurol/journal/v11/n7/images/nrurol.2014.129-f2.jpg

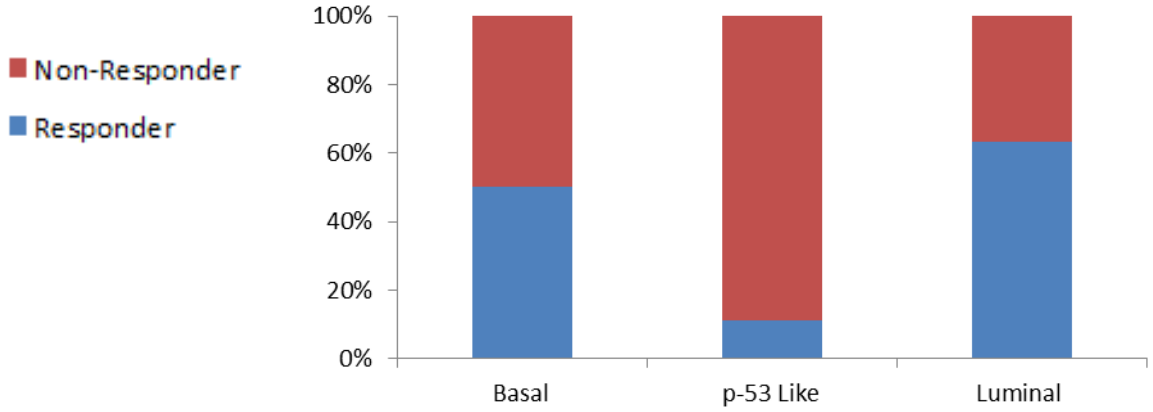
p53 pathway activation is associated with cisplatin resistance

MDACC Discovery (p=0.018)



MDACC Validation (p=0.014





Choi et al, Cancer Cell 2014

Trimodality Treatment of MIBC: *ASCO-GU 2018* Results from lectures and Debates *(Peter Hoskin 2018)*

- Bladder sparing is offered more and more often in the US and Europe to patients with localised BC
- Tertiary centers should have protocols of bladder preservation to offer to their patients
- MDT in this setting is a must
- ***The Use of molecular markers to predict response (HER2, MRE11, TIP60,Molecular Subtypes,P-53 like)is the way but not ready yet in standard practice***

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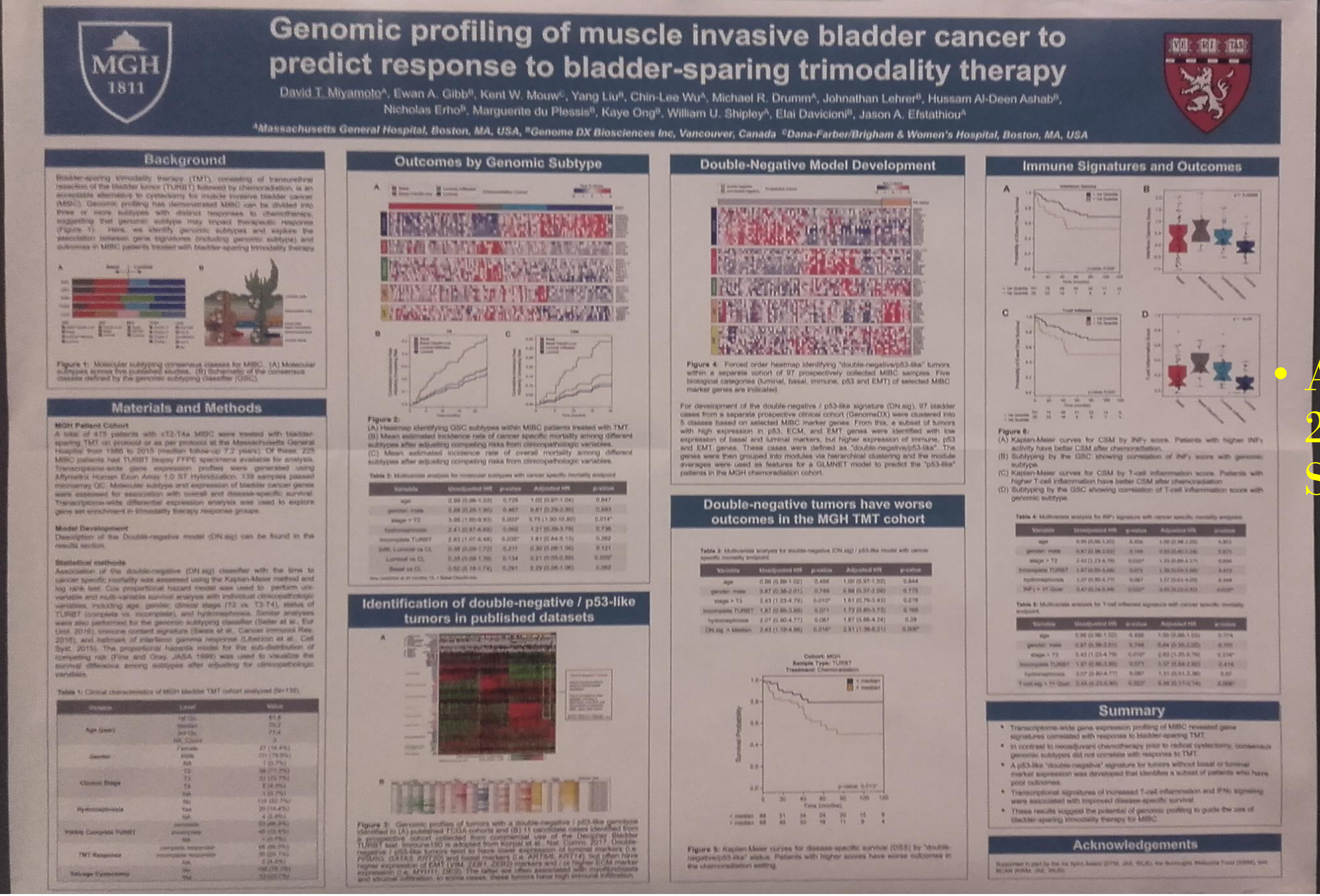

- Asco-Gu 2018 S. Francisco

Recent Clinical Studies

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RC Compared to Combined Modality Treatment for MIBC: A Systematic Review and Metanalysis (2017)

- *Metanalysis of 8 studies with about 9,000 pts*
- *Results: No difference in OS , DSS*

- *Limitations*
  * *Retrospective studies*
  * *A consistent N of pts. Underwent salvage RC in the majority of the studies*
  * *Chemotherapy was not always used*
  * *Selection bias: pts receiving RT were older with more co-morbidities **

  (Vashistha et al Int J Rad Onc. 2017)

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Propensity Score Analysis of RC vs TMT in the Setting of a Multidisciplinary BC Clinic *(Kulkarni et al J Clin Onc 2017)*

- Retrospective study including 112 patients:
  RC : 56
  TMT : 56
  Statistical Method: Propensity Score Analysis to reduce at minimum the differences between the 2 groups
- *Patients were stratifies according to: TURBT , T stage, IDN, Cis and co-morbidities*
- ***Results:*** NO diffeence in OS and DSS

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European Association of Urology

Long-term Outcomes After Bladder-preserving Tri-modality Therapy for Patients with Muscle-invasive Bladder Cancer: An Updated Analysis of the Massachusetts General Hospital Experience

Nicholas J. Giacalone [a,b], William U. Shipley [a], Rebecca H. Clayman [a], Andrzej Niemierko [a], Michael Drumm [a], Niall M. Heney [c], Marc D. Michaelson [d], Richard J. Lee [d], Philip J. Saylor [d], Matthew F. Wszolek [c], Adam S. Feldman [c], Douglas M. Dahl [c], Anthony L. Zietman [a], Jason A. Efstathiou [a,]*

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Abstract

Background: Tri-modality therapy (TMT) is a recognized treatment strategy for selected patients with muscle-invasive bladder cancer (MIBC).
Objective: Report long-term outcomes of patients with MIBC treated by TMT.
Design, setting, and participants: Four hundred and seventy-five patients with cT2–T4a MIBC were enrolled on protocols or treated as per protocol at the Massachusetts General Hospital between 1986 and 2013.
Intervention: Patients underwent transurethral resection of bladder tumor followed by concurrent radiation and chemotherapy. Patients with less than a complete response (CR) to chemoradiation or with an invasive recurrence were recommended to undergo salvage radical cystectomy.
Outcome measurements and statistical analysis: Disease-specific survival (DSS) and overall survival (OS) were calculated using the Kaplan-Meier method.
Results and limitations: Median follow-up for surviving patients was 7.21 yr. Five- and 10-yr DSS rates were 66% and 59%, respectively. Five- and 10-yr OS rates were 57% and 39%, respectively. The risk of salvage cystectomy at 5 yr was 29%. In multivariate analyses, T2 disease (OS hazard ratio [HR]: 0.57, 95% confidence interval [CI]: 0.44–0.75, DSS HR: 0.51, 95% CI: 0.36–0.73), CR to chemoradiation (OS HR: 0.61, 95% CI: 0.46–0.81, DSS HR: 0.49, 95% CI: 0.34–0.71), and presence of tumor-associated carcinoma in situ (OS HR: 1.56, 95% CI: 1.17–2.08, DSS HR: 1.50, 95% CI: 1.03–2.17) were significant predictors for OS and DSS. When evaluating our cohort over treatment eras, rates of CR improved from 66% to 88% and 5-yr DSS improved from 60% to 84% during the eras of 1986–1995 to 2005–2013, while the 5-yr risk of salvage radical cystectomy rate decreased from 42% to 16%.
Conclusions: These data demonstrate high rates of CR and bladder preservation in patients receiving TMT, and confirm DSS rates similar to modern cystectomy series. Contemporary results are particularly encouraging, and therefore TMT should be discussed and offered as a treatment option for selected patients.
Patient summary: Tri-modality therapy is an alternative to radical cystectomy for patients with muscle-invasive bladder cancer, and is associated with comparable long-term survival and high rates of bladder preservation.

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0302-2838/

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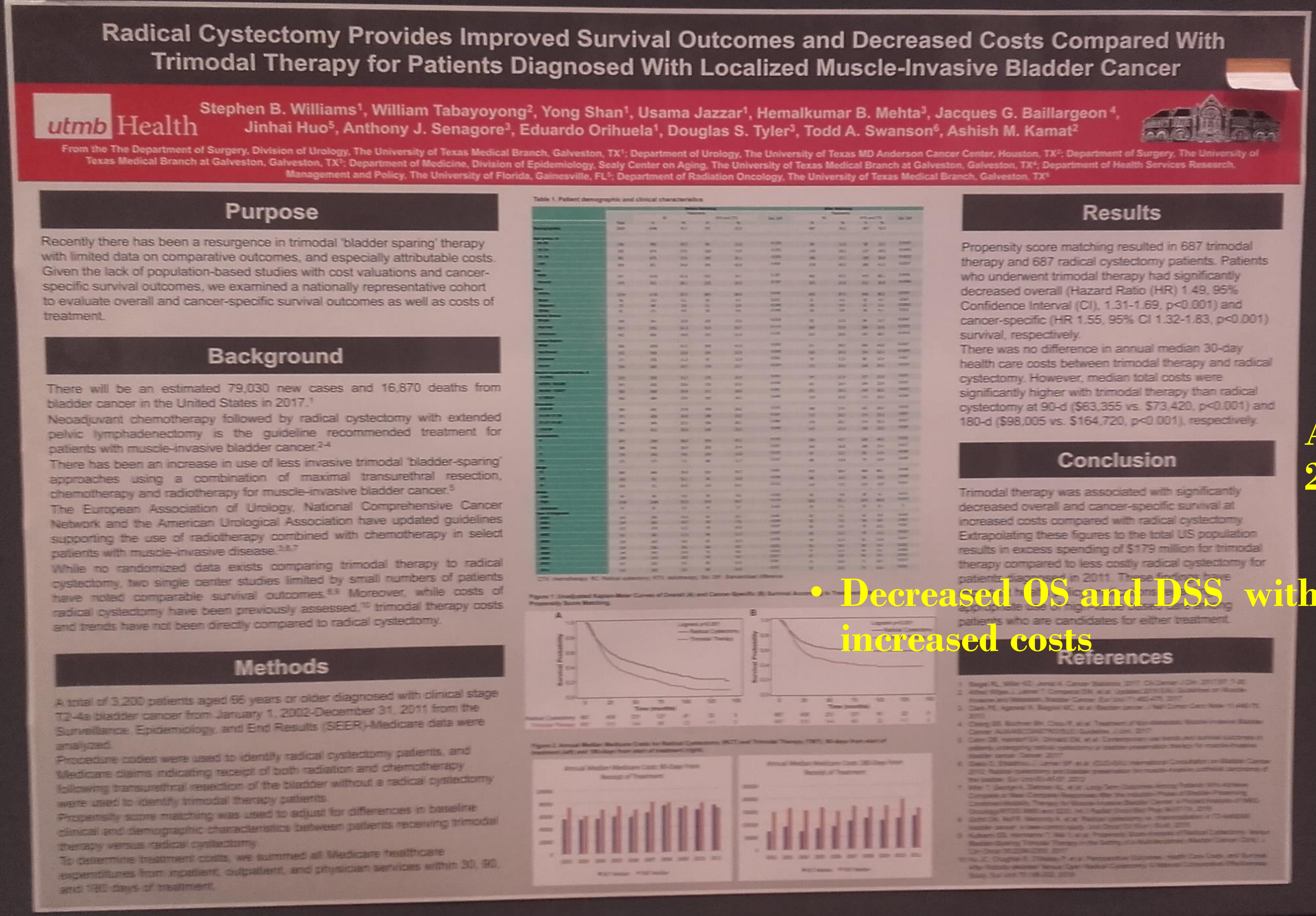
- 475 pts. with T2-T4a BC enrolled in MGH between 1986 to 2013.
  Methods: TURBT + RT and Chemo
  CR: re-TUR and F-UP No CR : Cystectomy
- *Results:* (median F-Up 7.21 yrs)
  . 5-yr DSS = 66% 10-yr DSS = 59%
  . 5-yr OS = 57% 10-yr OS = 39%
  RC rate at 5-yr = 29%
  Multivariate analysis:
  T2, CR to C/RT , Cis predictors for OS- DSS
  '86-'95 5-yr DSS = 60% vs 84% '00-'13
  5-yr risk of Salvage RC
  '86-'95 = 42% vs 16% '00-'13
- *Conclusions:*
  TMT should be discussed and offered to selected pts. with MIBC as treatment option

EAU Guideline 2017. Multimodality Treatment

- ***«Offer multimodality treatment as an alternative in selected, well informed and compliant patients, especially for whom cystectomy is not an option»***

- ***In highly selected patient population, long-term survival rates of multimodality treatment are comparable to those of early cystectomy. Delay in surgical therapy can compromise survival rates***
- ***…. Costs of TMT vs RC ??***

European Association of Urology



Asco-GU 2018

- Decreased OS and DSS with TMT and increased costs

Conclusions

- *Treatment for localized BC should be decided according to prognostic factors (clinical, pathological and biomolecular)*
- ***Neoadjuvant chemo (cisplatin based) + RC and extended LND performed by an experienced surgeons in a high volume institution remains the golden standard treatment.***
  (Brausi …Esou 2018)

Conclusions

BP is recommended only in selected, well informed and compliant pts in whom RC is not considered for clinical or personal reasons.

A T0 status after the first TUR or Chemo is a prognostic positive variable

Tur alone or chemo alone are not recommended as primary treatment of localized BC for BP strategy

A multimodality treatment (Tur + Chemo or RT, TUR+ RT +Chemo) is the best choice

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Conclusions : Factors Associated with BP

1. *Clinical Stage (pT2)*
2. *Tumor size (<3-5 cm)*
3. *Absence of Hydronephrosis*
4. *Absence of palpable mass after TUR*
5. *Unifocal Disease, NO CIS*
6. *Downstaging to PT0 after chemo +TUR : the best*

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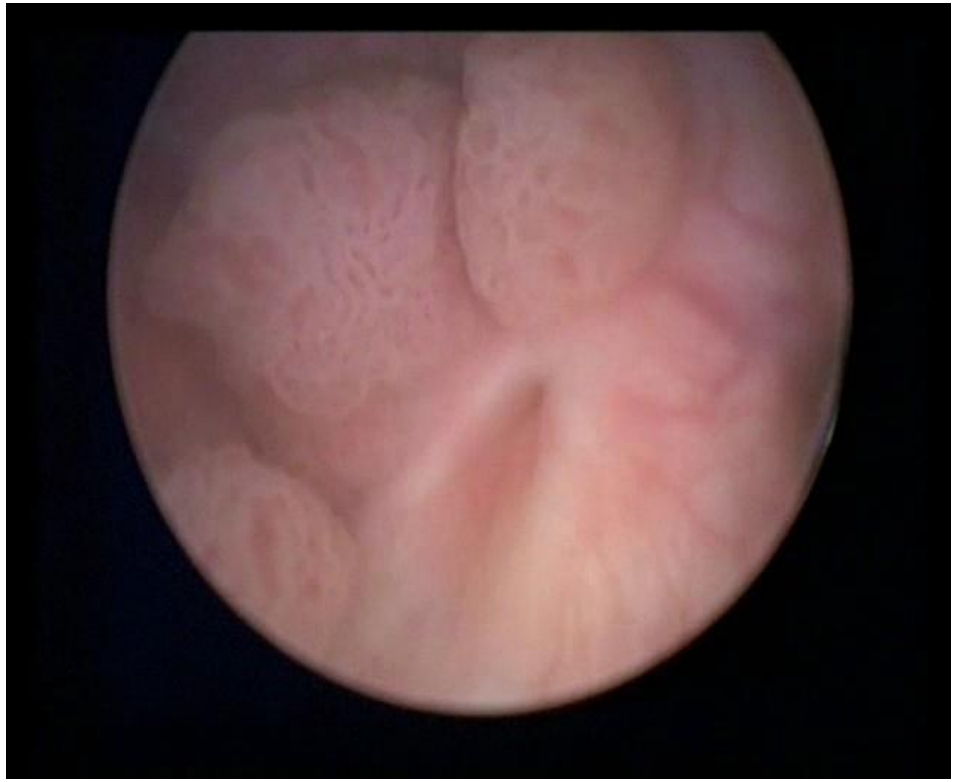
CLINICAL CASE

65-yr old pt. with 3 solid tumors.

02.18 TURBT + Bladder mapping.
Path report: T1cHGTcc No Cis. LVI. DM present with 1 focus of Tcc in the DM

What do you suggest ?



Bladder Cancer : The Future

- *The Cancer Genomic Atlas :*
- Is a collaborative project between the NCI and NHGRI.
  TCGA has generated comprehensive maps of key genomic changes in 33 different type of cancer including 10 rare tumours.
- TCGA is really an example of multidisciplinary research
  Goal: to create an atlas of genomic changes using an integrated multiplatform analysis and have all the data available in the public domain for researchers worlwide to use

The Cancer Genomic Atlas : MIBC

- TCGA has resulted in discovery of novel cancer mutation and better understanding of pathways and mechanisms involved in cancer development.
- ***In a group of 412 MIBC mutational changes were found in 58 genes. A high-mutation subset with a 5-year survival rate of 75% was identify by mutation signature clustering, whereas mRNA expression clustering yelded 5 expression-based sub-types that were associated with OS and may explain response to treatment.***

The Cancer Genomic Atlas: MIBC

- The research provided a more precise definition of expression-based molecular subtypes and mutation signature-based subtypes. This has implications from the biological standpoint and potentially from the therapeutic standpoint by affecting the response to chemotherapy and immuno-oncology agents
- Another finding was that mRNA and long noncoding RNA further modify the expression based subtypes

The Cancer Genomic Atlas

- There are important questions that still need to be answered:
  1. How do we take TCGA findings into the clinic and apply them to other patient population. Are these findings truly generalizable?
  2. How do we take next-generation sequencing into the clinic so that we can use them in a user-friendly way?
- The very final goal is to arrive a precision medicine-based aproach to treating invasive bladder

Lerner Set Baylor College ASCO-GU 2018

Materiale

- *Genome*
- *UUTcc*
- *Multimodality Treatment of MIBC*
- *Immunotherapy in MIBC*

Biomarkers in MIBC

- Biomarkers for selecting patients who undergo chemotherapy before cystectomy
- Basal cell sub-type and Luminal cell sub-Type
- Basal cell sub-type tumors have more benefit from adjuvant chemo
- NOXEN model predict response to NAC in individual patients
- Alteration in DNA repair genes may define patients who will likely to respond

Peter Black Canada ASCO-GU 2018

Check Point Inhibitors in Urothelial TCC

- Check point-Inhibitors determine 20- 25% RR in metastatic disease
- Indications : * Metastatic disease (second line after chemo)
  * Cis-Platinum inelegible patients or Platinum refractory disease (first line)
- *PEMBROLIZUMAB* the only one that showed efficacy vs chemo in randomised-prospective study (Bellmunt et al NEJM 2016)
- Atezolizumab (neg in bladder),.....Nivolumab, Durvalumab, Avelumab,***Pembrolizumab***
- PD-L1
- Biomarkers : not useful

NMIBC

- Two important studies design on immunotherapy :
- 1. ALT-803 + BCG vs BCG alone in high risk Tcc of the bladder
- 2. A multicenter clinical trial of intravesical BCG in combination with ALT-803 in patients with BCG-unresponsive NMIBC

RTOG Protocol 0524: Phase I/II In Pts with MIBC Not fit for Surgery

- Daily RT + weekly Paclitaxel and the HER2 targeted ab Trastuzumab given to pts. whose tumors overexpress HER2.
- 70 patients recruited : results still pending
  (Mitin et al Curr Urol Rep 2013)

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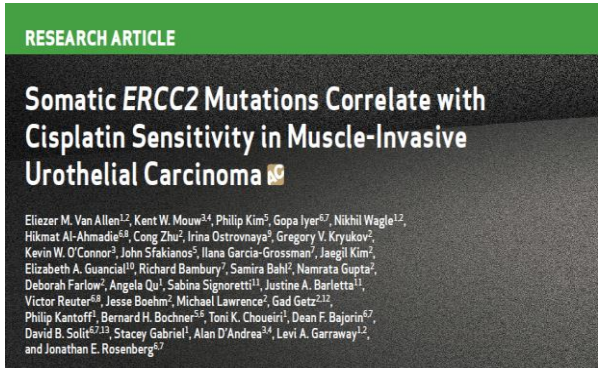
Genetic Alterations Predicting Response to Chemotherapy

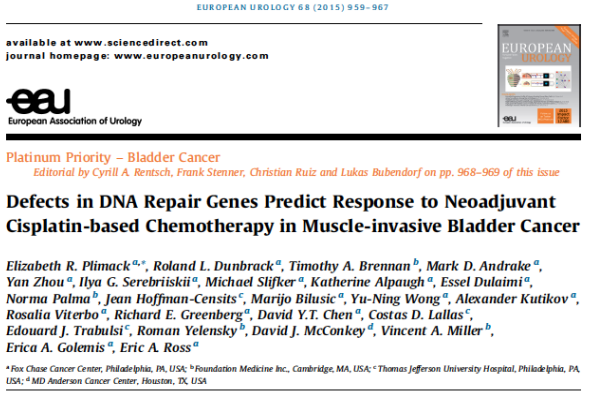
- *ERBB2 mutations characterize a subgroup of muscle invasive bladder cancers with excellent response to neo-adjuvant chemotherapy*
  Groenendijk FH et al Eur Urol 2016;69:384
- *Alterations in ATM, RB1 and FANCC correlates with survival after NAC*
  Van Allen, Cancer Discov 2014, Plimack, Eur Urol 2015



RESEARCH ARTICLE

Somatic *ERCC2* Mutations Correlate with Cisplatin Sensitivity in Muscle-Invasive Urothelial Carcinoma

Eliezer M. Van Allen[1,2], Kent W. Mouw[3,4], Philip Kim[5], Gopa Iyer[6,7], Nikhil Wagle[1,2], Hikmat Al-Ahmadie[6,8], Cong Zhu[2], Irina Ostrovnaya[9], Gregory V. Kryukov[2], Kevin W. O'Connor[3], John Sfakianos[5], Ilana Garcia-Grossman[7], Jaegil Kim[2], Elizabeth A. Guancial[10], Richard Bambury[7], Samira Bahl[2], Namrata Gupta[2], Deborah Farlow[2], Angela Qu[1], Sabina Signoretti[11], Justine A. Barletta[11], Victor Reuter[6,8], Jesse Boehm[2], Michael Lawrence[2], Gad Getz[2,12], Philip Kantoff[3], Bernard H. Bochner[5,6], Toni K. Choueiri[3], Dean F. Bajorin[6,7], David B. Solit[6,7,13], Stacey Gabriel[1], Alan D'Andrea[3,4], Levi A. Garraway[1,2], and Jonathan E. Rosenberg[6,7]



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European Association of Urology

Platinum Priority – Bladder Cancer

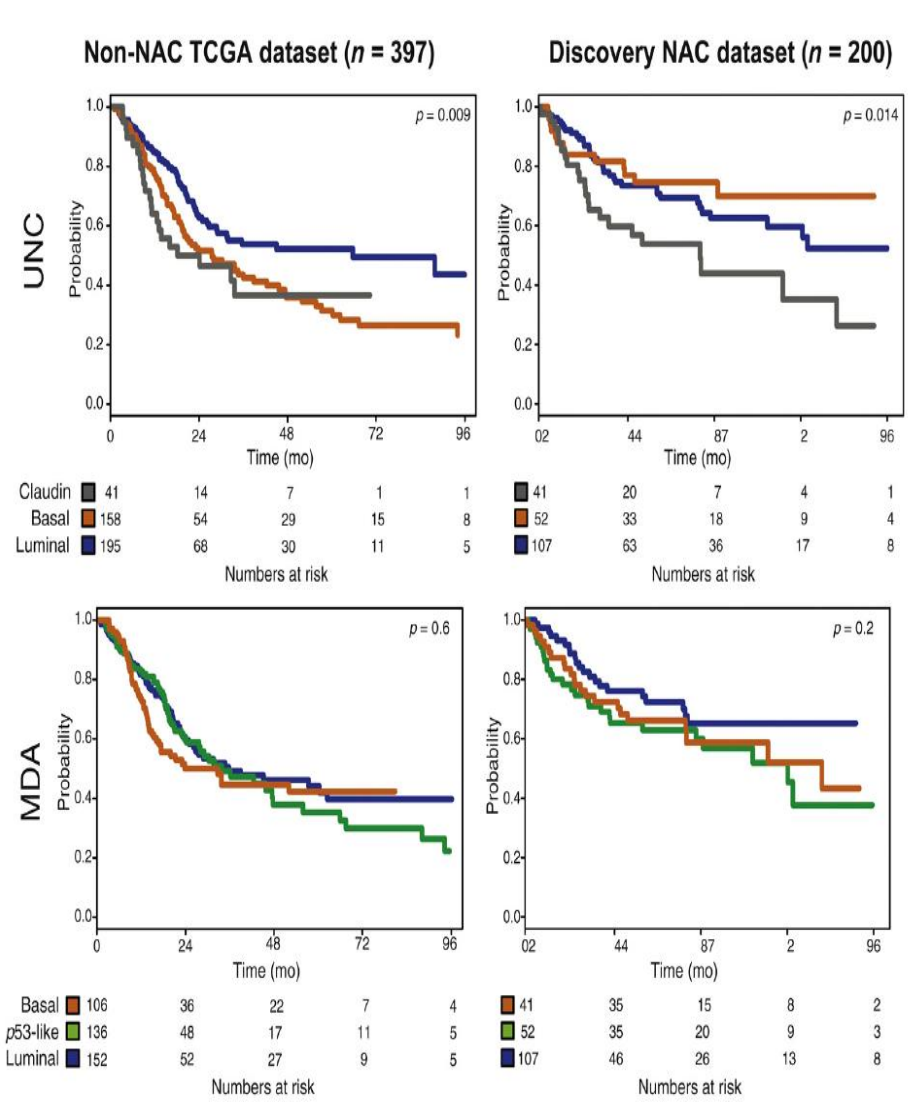
Editorial by Cyrill A. Rentsch, Frank Stenner, Christian Ruiz and Lukas Bubendorf on pp. 968–969 of this issue

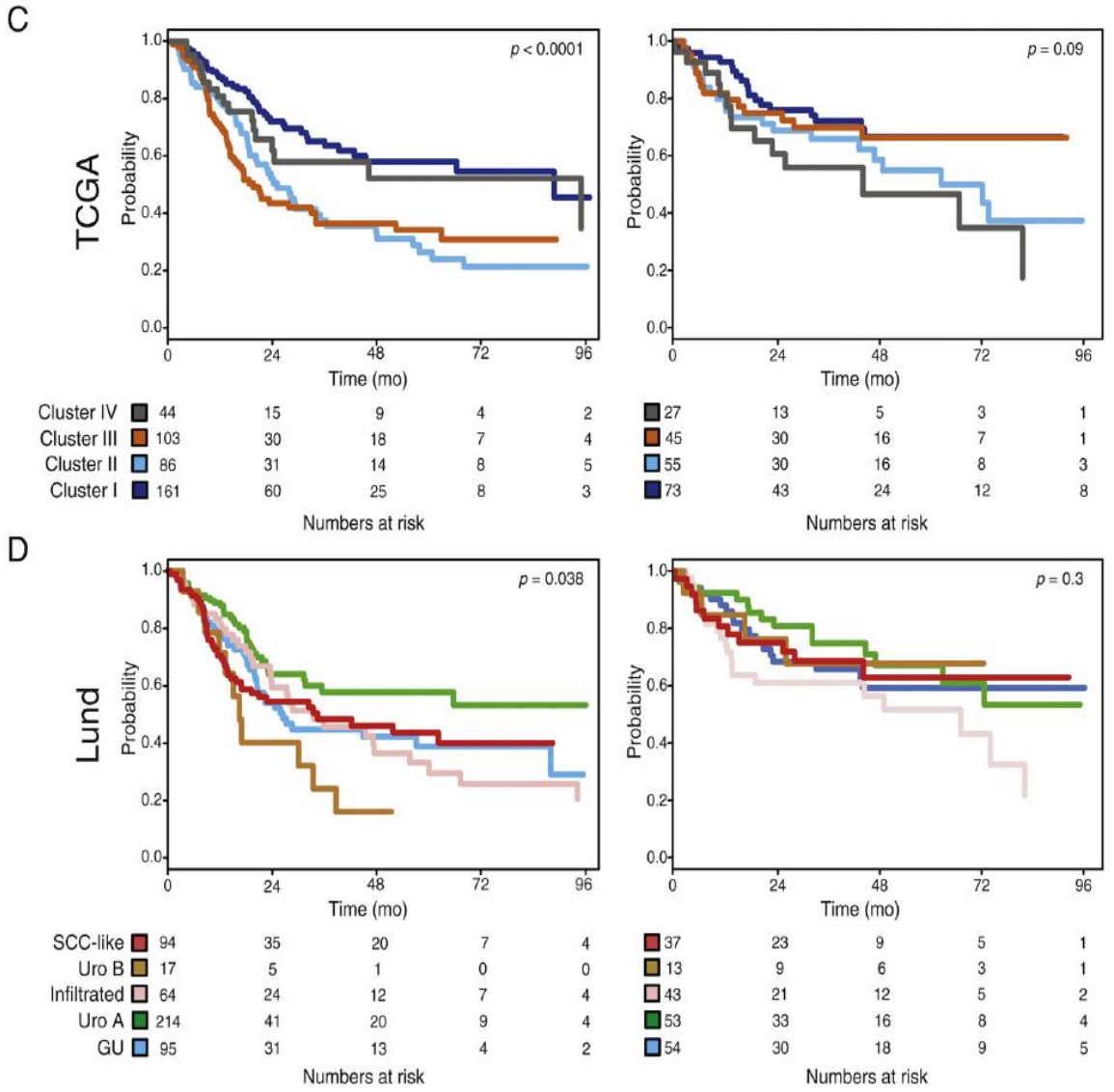
Defects in DNA Repair Genes Predict Response to Neoadjuvant Cisplatin-based Chemotherapy in Muscle-invasive Bladder Cancer

Elizabeth R. Plimack[a,], Roland L. Dunbrack[a], Timothy A. Brennan[b], Mark D. Andrake[a], Yan Zhou[a], Ilya G. Serebriiskii[a], Michael Slifker[a], Katherine Alpaugh[a], Essel Dulaimi[a], Norma Palma[b], Jean Hoffman-Censits[c], Marijo Bilusic[a], Yu-Ning Wong[a], Alexander Kutikov[a], Rosalia Viterbo[a], Richard E. Greenberg[a], David Y.T. Chen[a], Costas D. Lallas[c], Edouard J. Trabulsi[c], Roman Yelensky[b], David J. McConkey[d], Vincent A. Miller[b], Erica A. Golemis[a], Eric A. Ross[a]*

[a] Fox Chase Cancer Center, Philadelphia, PA, USA; [b] Foundation Medicine Inc., Cambridge, MA, USA; [c] Thomas Jefferson University Hospital, Philadelphia, PA, USA; [d] MD Anderson Cancer Center, Houston, TX, USA

Impact of Molecular Subtypes in Muscle-invasive Bladder Cancer on Predicting Response and Survival after Neoadjuvant Chemotherapy





Seiler et al., Eur Urol. 2017 Apr 5.]

Bladder Spaing Approach : Review of the Literature

(Ploussard et al Eur Urol 2014)

- TUR BT + RT + Chemo (most used)
- Dose of Radiotherapy : varies

- Type of Chemotherapy: Should be cisplatin based

Bladder Sparing Trimodality Treatment

(Efstathiou et al Eur Urol 2012)

- ***Bladder Sparing Trimodality Approach:***
  Maximal TURBT + RT (40Gy) and concurrent Chemo (Cisplatin based):
  Re-TURBT and Assessment of Response
- Incomplete Response = Radical Cystectomy
- Complete Response = Chemo + RT to 65 Gy
- Single Institutions in North America and Europe + multiinstitutional studies enrolled > 1200 pts with MIBC in bladder preserving protocols

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Bladder Sparing Trimodality Treatment

(Efstathiou et al Eur Urol 2012)

- **Material and methods:**
  348 pts. treated from'86 to 2006.
  Up-dated F-Up : 7.7 yrs
- **Results:** CR = 72% (to induction therapy). 102/348 pts (29%) had salvage RC (60: IR, 42 Recurrent Invasive T)
  5 yr- DSS = 64%, 10yr-DSS = 59% , 15yr-DSS = 57%
  5-yr- OS = 52%, 35%, 22%.
  In CRs the Recurrence rate at 10 years was: 29% (NMIBC),16% (MIC),
  Recurrence rate: Pelvic recurrence (11%) Distant mets (32%)
  In patients who had visibly complete TURBT 22% required RC vs 42% incomplete TURBT ($p < 0.001$)

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Bladder Sparing Trimodality Treatment

- **Conclusions:**
  In long term F-UP, selective BP trimodality therapy is associated with a high rate (71%) of BP and OS rate comparable to that in contemporary RC .
  (Efstathiou et al Eur Urol 2012)

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