6 Questions for Clinical Oncologists

BAUS Oncology

Belfast 2012

Who I don’t give neo-adjuvant chemotherapy to

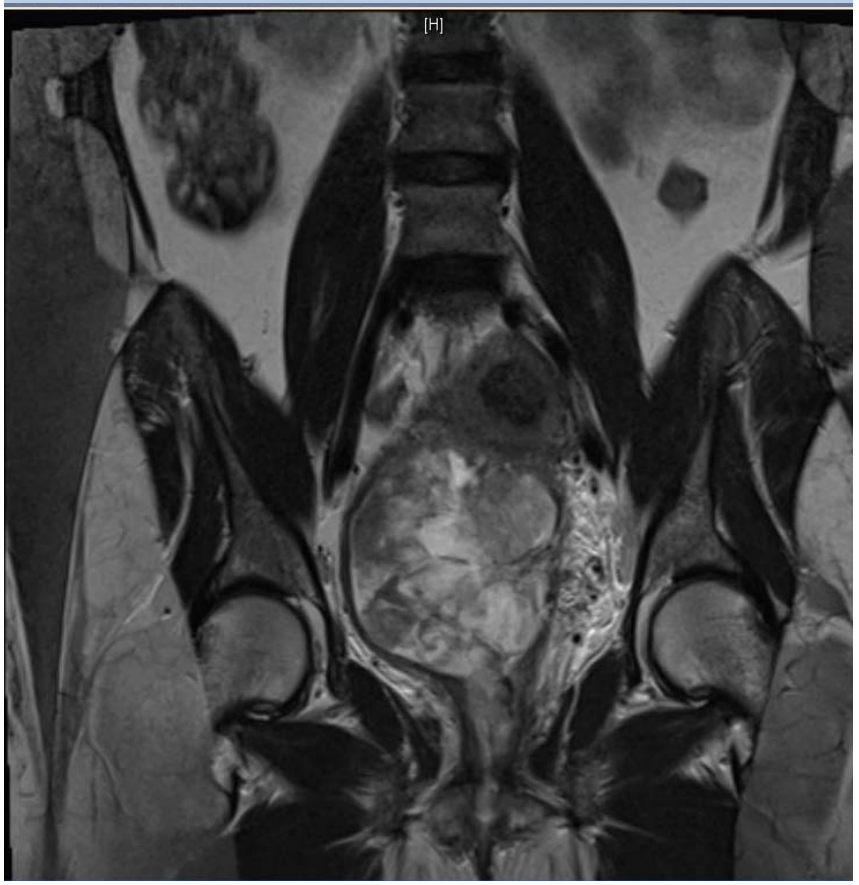
Nick James

Neoadjuvant Chemotherapy?

Presenting Complaint

- 61 yr old female
  - Referred from gynae team
- 1/12 difficulty passing urine:
  - “blockage”
  - Frequency (hourly)
  - Nocturia x 5-6
- Weight loss (2kg)
- WHO PS1
- Ex-smoker

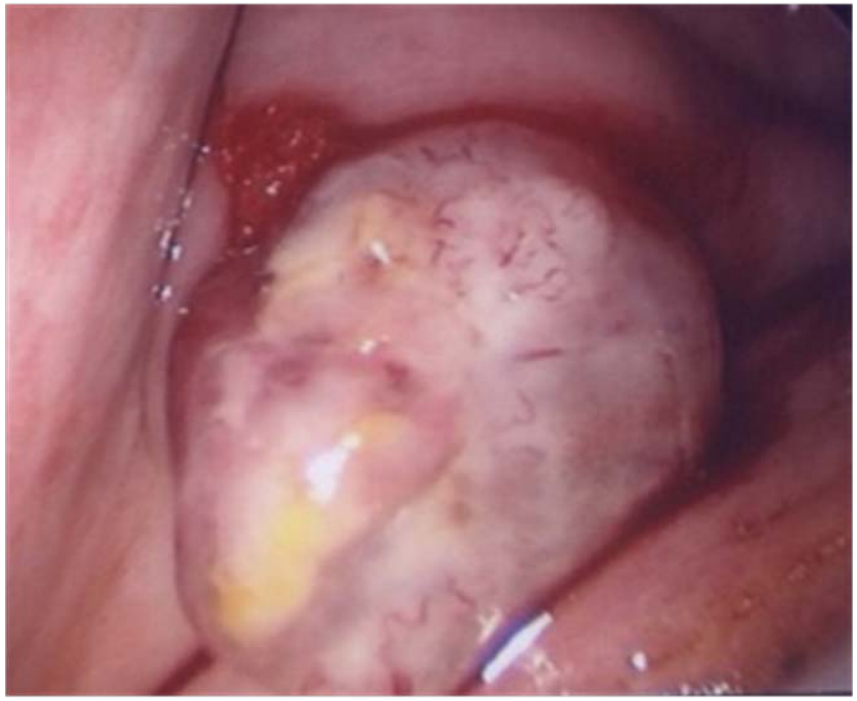
MRI



Neoadjuvant Chemotherapy?

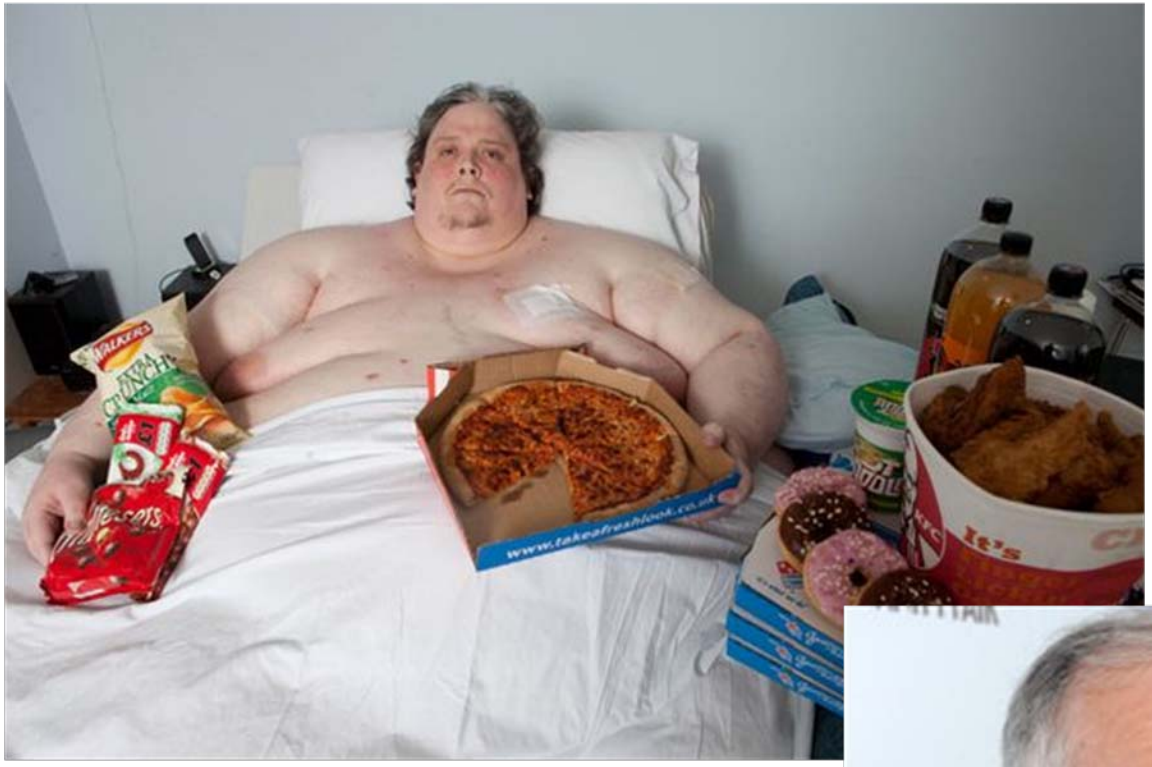
Investigation

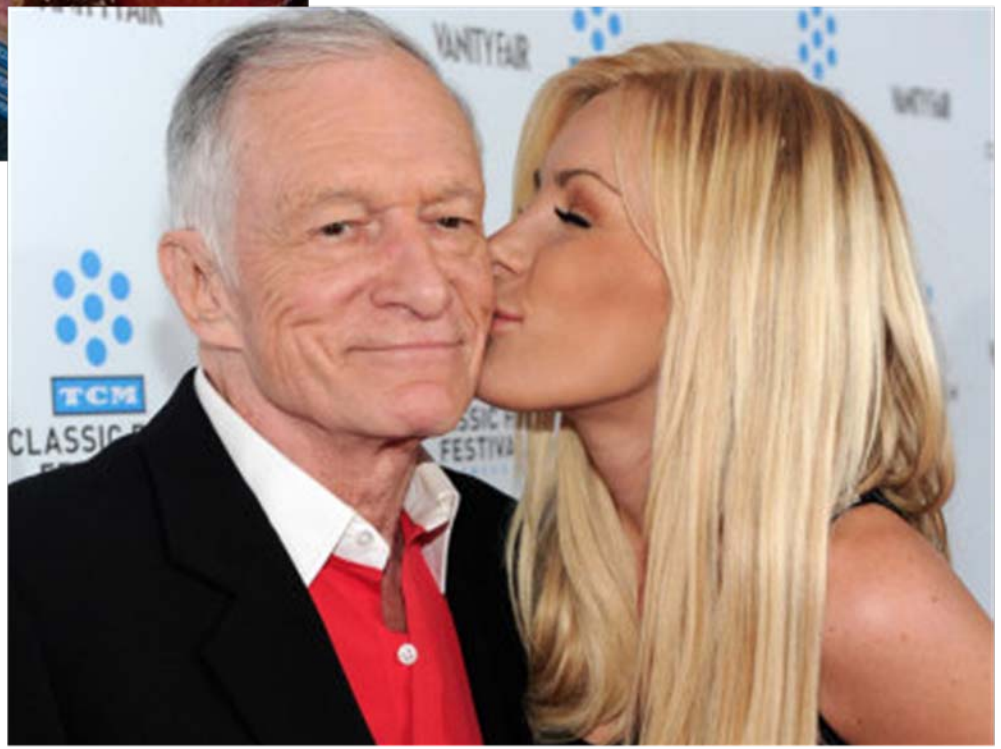
- EUA + Cystoscopy:
  - Peri-urethral polypoid necrotic mass
- Histology:
  - Transitional cell carcinoma
  - Extensive sarcomatoid changes



What about the elderly and unfit?

Alison Birtle


MALTESERS
Maltesers
www.takeafreshlook.co.uk
It's


VANITY FAIR
TCM

Why radiotherapy and surgery patients are not the same

- Median Age:
  - Radiotherapy: 75
  - Surgery: 68

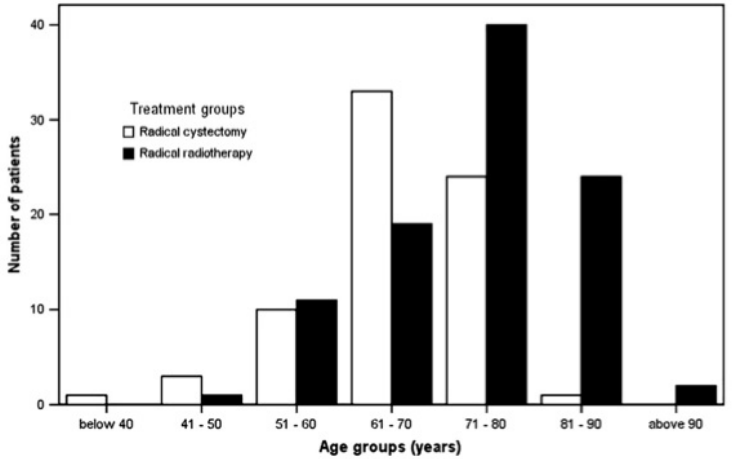
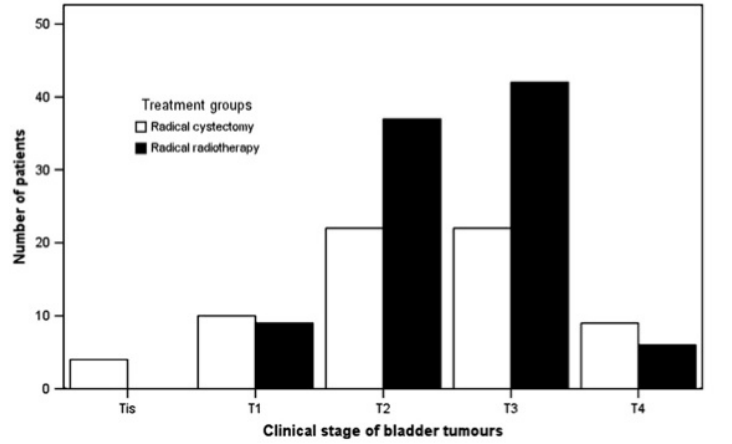


Fig. 1. Age distribution at the time of diagnosis in the radical cystectomy and radical radiotherapy groups.

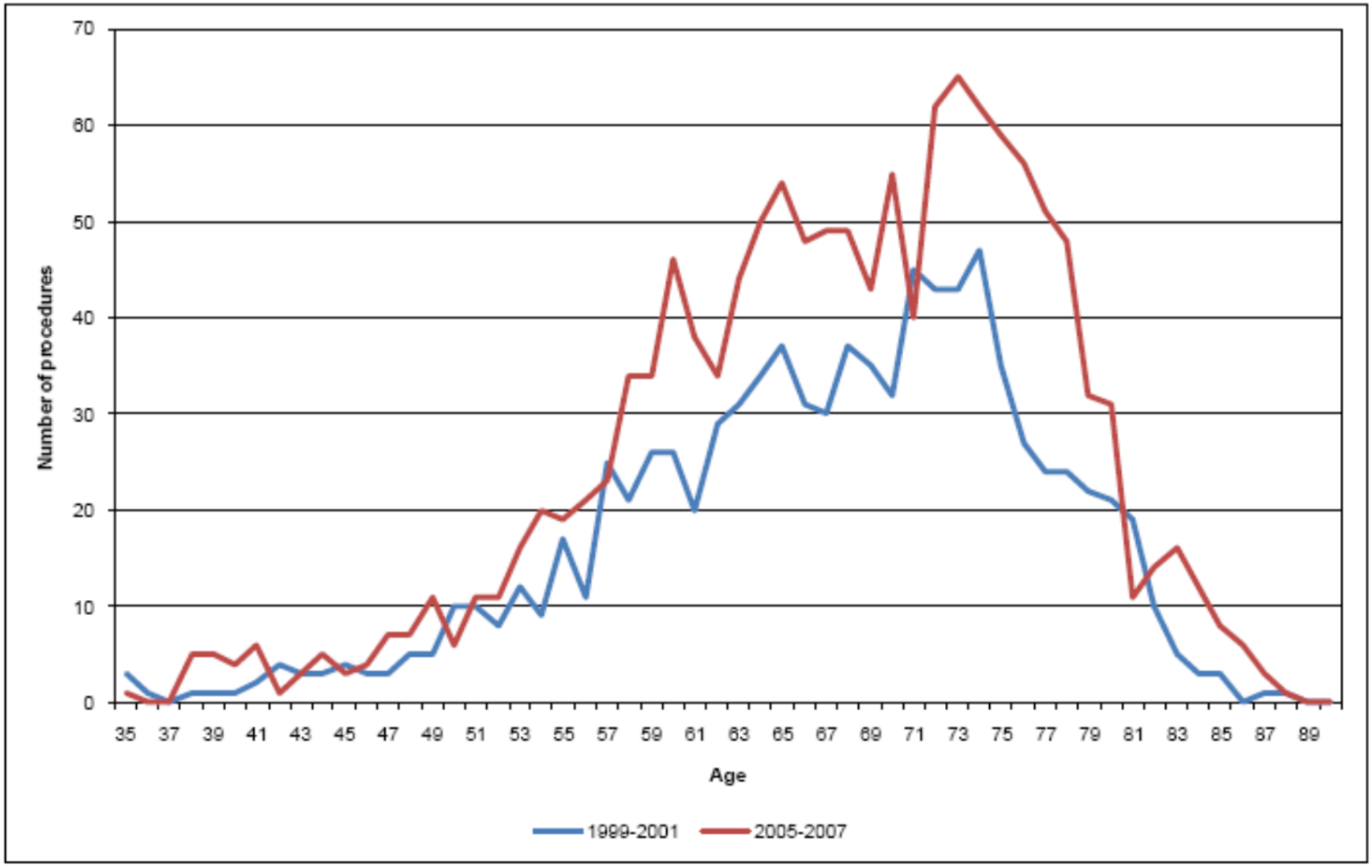
- Clinical Stage:



Distribution of clinical stage of bladder tumors in the radical cystectomy and radical radiotherapy groups.

Kotwal et al 2008 IJROBP 70 456-463

Figure 5: Age at treatment for cystectomy, for muscle-invasive bladder cancer, in England, diagnosed 1999-2001 and 2005-2007.



Source: United Kingdom Association of Cancer Registries; Hospital Episode Statistics; British Association of Urological Surgeons

Bladder cancer in the over 80s

	Median [95%CI]			
	Whole cohort (n=67)	No radiotherapy (n=31)	Radiotherapy (n=36)	
Overall survival (OS)	14.6 [10.3, 22.0]	11.6 [3.4, 14.6]	19.8 [10.3, 31.1]	
Bladder cancer specific survival (BCSS)	24.3 [14.6, 43.2]	14.6 [9.2, 37.4]	31.1 [17.1, 51.2]	
Recurrence free survival (RFS)	26.1 [23.5, 42.4]	23.5 [8.7, NR]	30.4 [25.5, NR]	

Source: Bladder cancer prognosis programme, unpublished data

Chemotherapy or observe pN+

Simon Hughes

No Neoadjuvant Chemotherapy

Adjuvant chemotherapy for invasive bladder cancer (individual patient data) (Review)

Vale CL, Advanced Bladder Cancer Meta-analysis Collaboration

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This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2011, Issue 4

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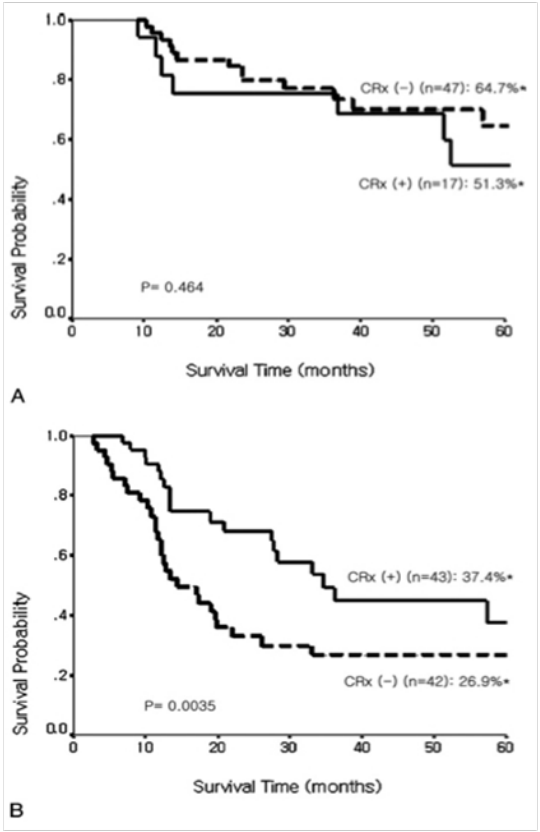
Retrospective Review



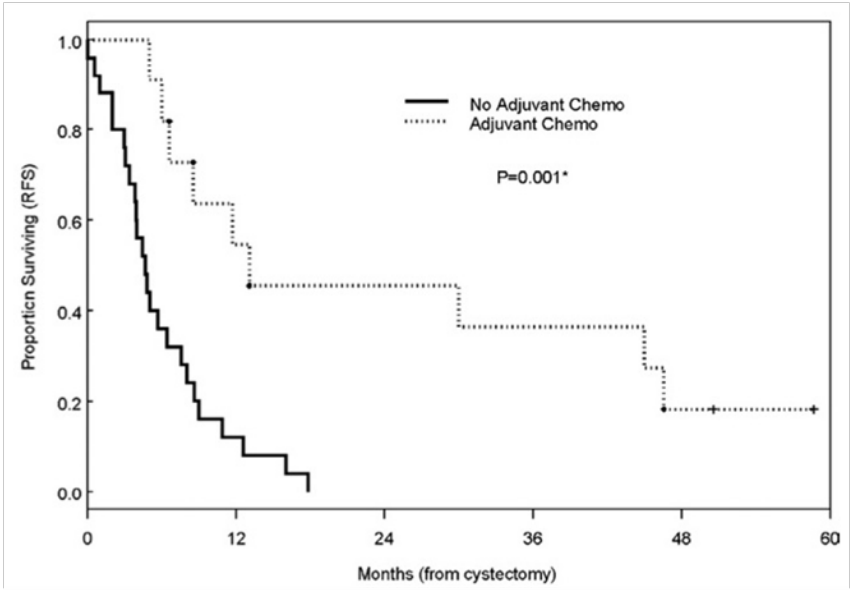
pN-

pN+

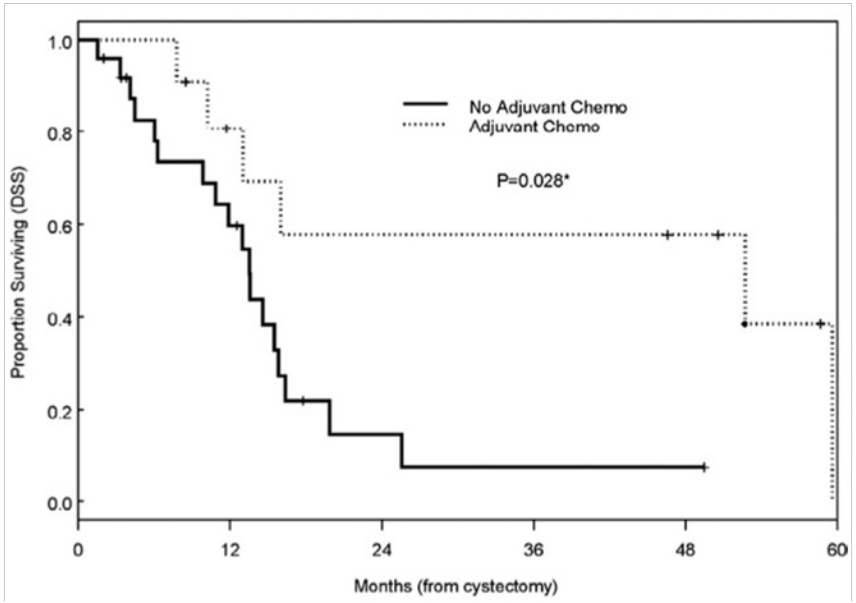
Park J Urol 2007;70:257-262

Post Neoadjuvant Chemotherapy

RFS



DSS

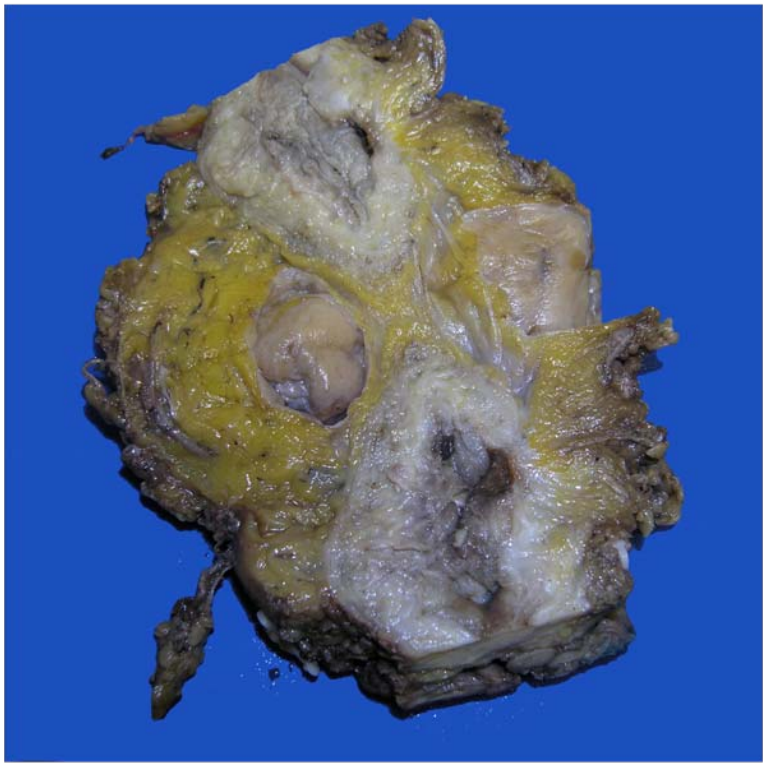


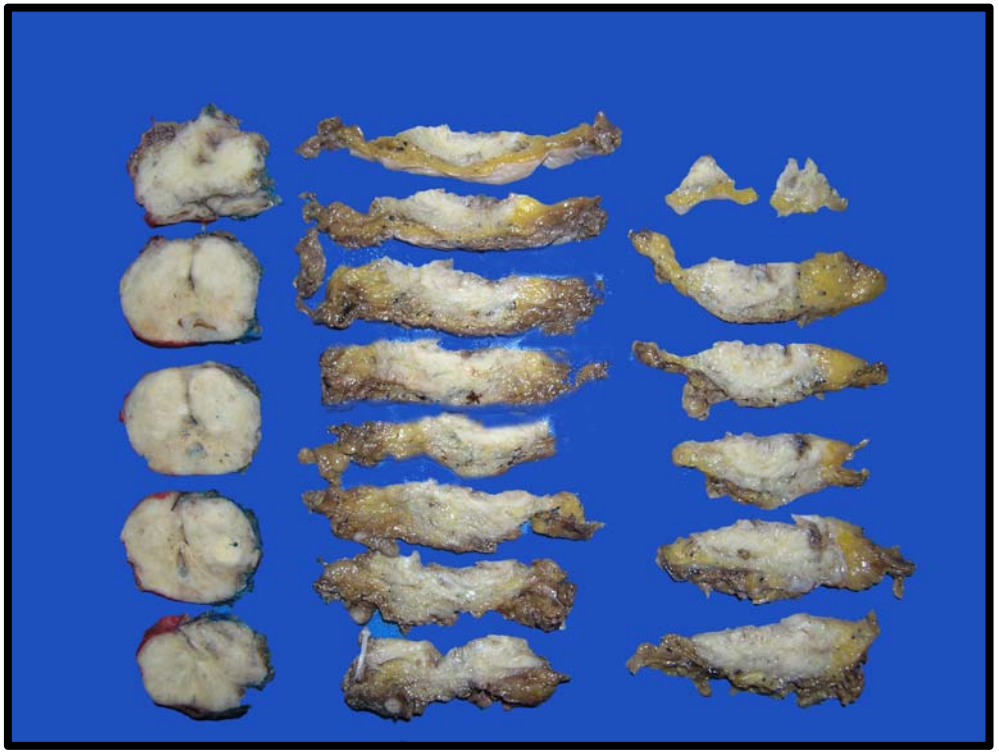
Kassouf Urology 2009;73:147-152

pT0 post neoadjuvant chemotherapy – Still need the cystectomy?

Simon Hughes

pT0 v cT0





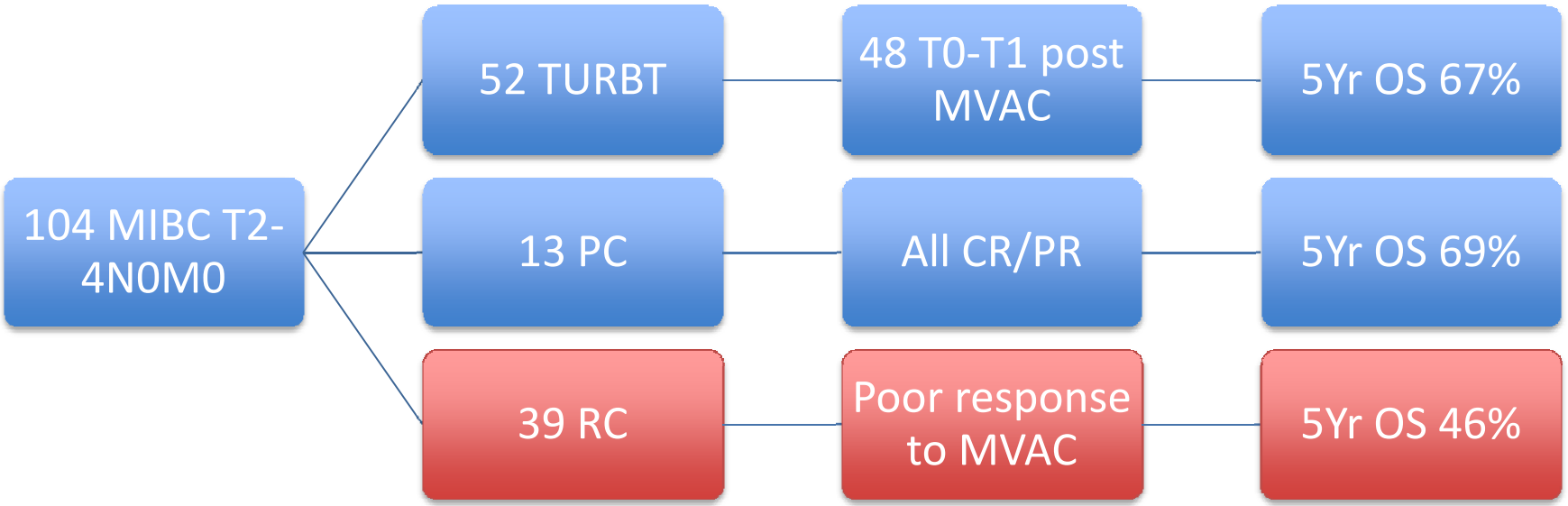
Can Patient Selection for Bladder Preservation Be Based on Response to Chemotherapy?

Cancer 2003;97:1644-52

Cora N. Sternberg, M.D.[1,2]
Vito Pansadoro, M.D.[1]
Fabio Calabrò, M.D.[1,2]
Sylvia Schnetzer[1]
Diana Giannarelli, M.S.[3]
Paolo Emiliozzi, M.D.[1,4]
Francesco De Paula, M.D.[1]
Paolo Scarpone, M.D.[1,5]
Piero De Carli, M.D.[3]
Maurizio Pizzo, M.D.[1]
Andrea Platania, M.D.[6]
Mostafà Amini, M.D.[7]

BACKGROUND. Neoadjuvant chemotherapy for patients with muscle-invasive bladder carcinoma is given to treat micrometastases and to preserve the bladder. The objective of this study was to evaluate the possibility of bladder preservation in patients with muscle-invasive bladder carcinoma who were treated with neoadjuvant methotrexate, vinblastine, doxorubicin, and cisplatin (M-VAC) chemotherapy.
METHODS. One hundred four consecutive patients with T2–T4,N0,M0 transitional cell carcinoma of the bladder were treated with 3 cycles of neoadjuvant M-VAC chemotherapy. After clinical restaging, 52 patients underwent transurethral resection of the bladder (TURB) alone, 13 patients underwent partial cystectomy, and 39 patients underwent radical cystectomy.
RESULTS. The median survival for the entire group was 7.49 years (95% confidence interval, 4.86–10.0 years). Forty-nine patients (49%) were T0 at the time of TURB after

25%:	NMIBC
10%:	MIBC
23%:	Mets
6%:	MIBC + Mets
44%:	Bladder Intact

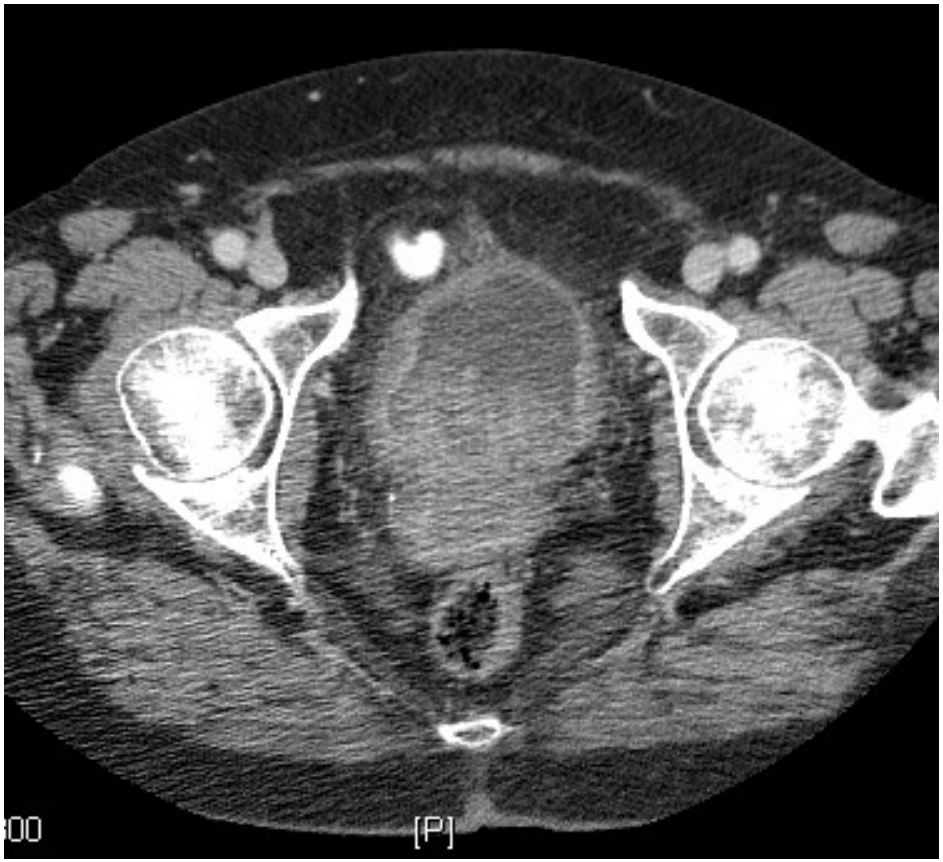


What about the non-TCC histologies?

Alison Birtle

Case

- V fit 90 year old lady
- Recurrent UTIs
- Good bladder function
- Flexi:
  - Tumour
- TURBT:
  - Squamous cell Carcinoma
- EUA:
  - Large mobile mass
- CT: T2/3N0M0



SCC treatment

- Radical cystectomy
  - 5 year survival 33-48%
  - 10 year survival 23 %
- Partial cystectomy –high local recurrence rate
- EBRT “ineffective”
  - data from papers in 1970’s
  - 5 year survival 5-18%

Rundle et al BJUI 2008;54:522-526

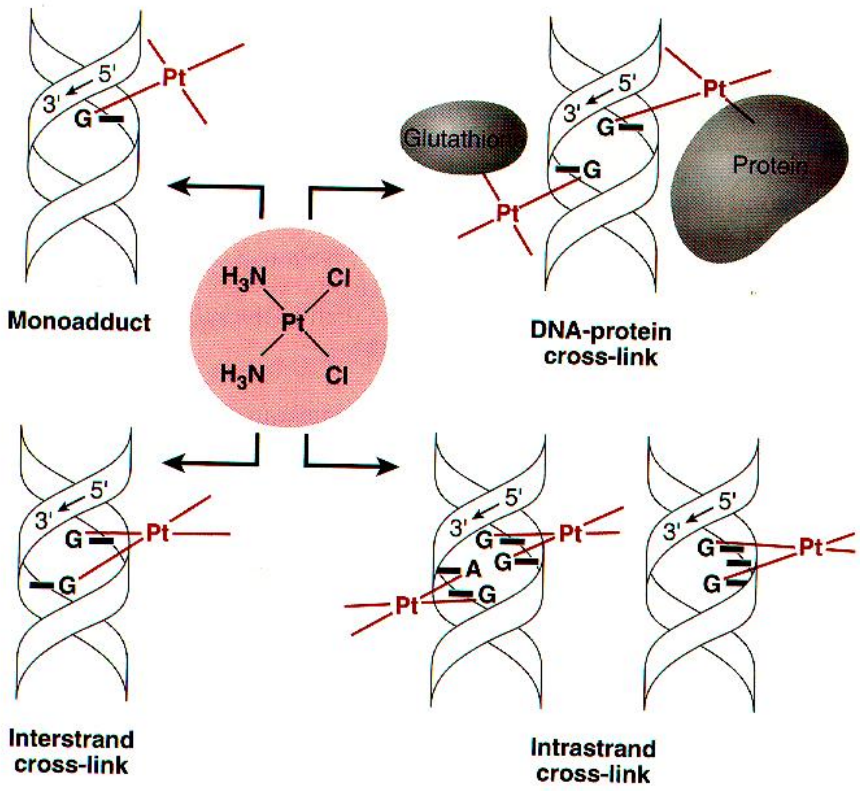
- 114 patients Glasgow 1964-1978
- 92.4% T2-T4
- 8.8% metastatic
- One year survival 23.8%
- 5 year survival 9 %
- 5 year survival after EBRT
  - 16.7% for T2
  - 4.8% for T3
  - (EBRT-understaging effect)

Progress in understanding who might respond to chemotherapy?

Simon Hughes

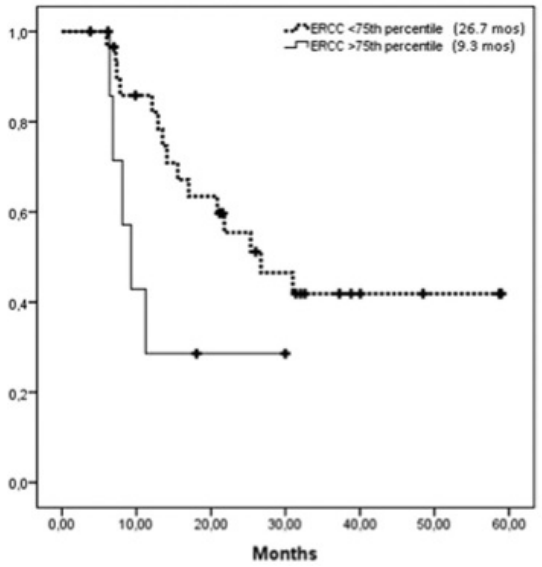
Cytotoxic Chemotherapy

Cisplatin



ERCC1

N = 38	Median DFS	Median OS
Low ERCC1	9.3 mths	9.3 mths
High ERCC1	20.5 mths	26.7 mths
p value	0.186	0.058



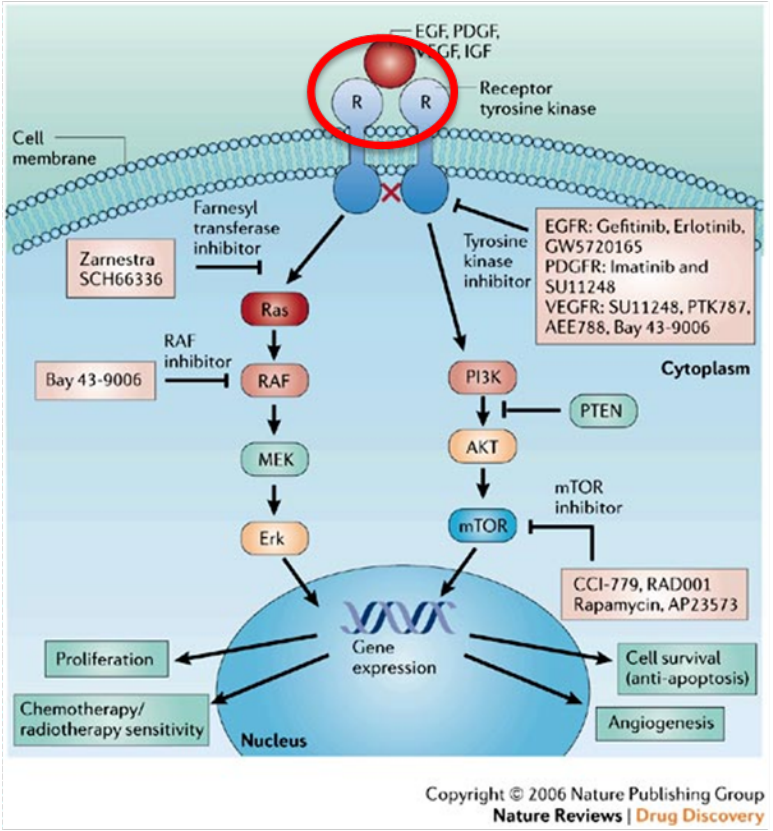
Ozcan 2012; Urologic Oncology *in press*

Targeted agents

Under Investigation

- HER2: Trastuzumab
- EGFR: Cetuximab
- VEGF
- TKI: Lapatinib
- mTOR

Nature Reviews Drug Discovery 2006;5:671-688



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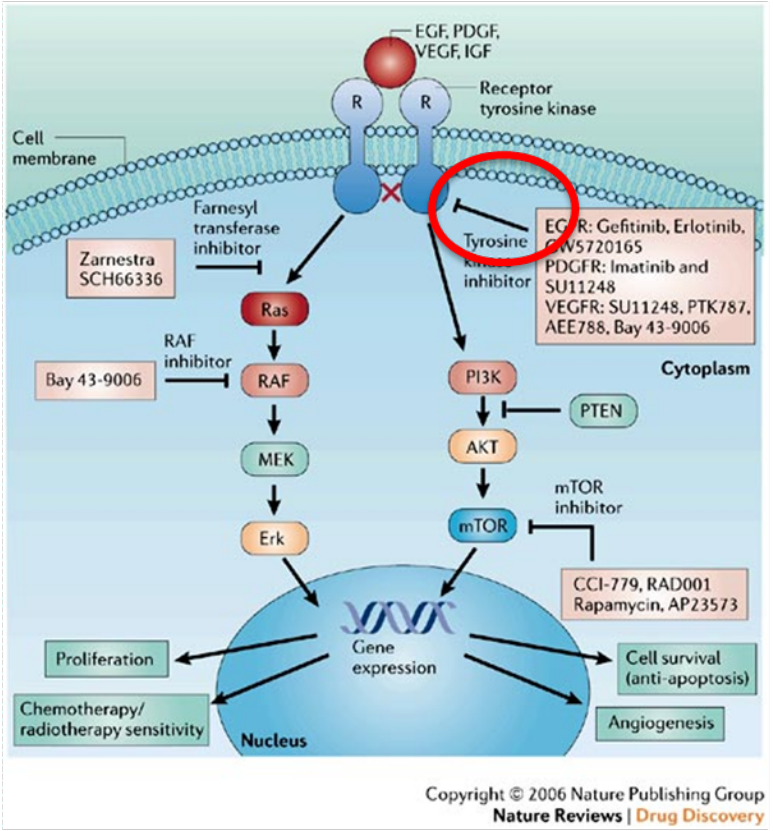

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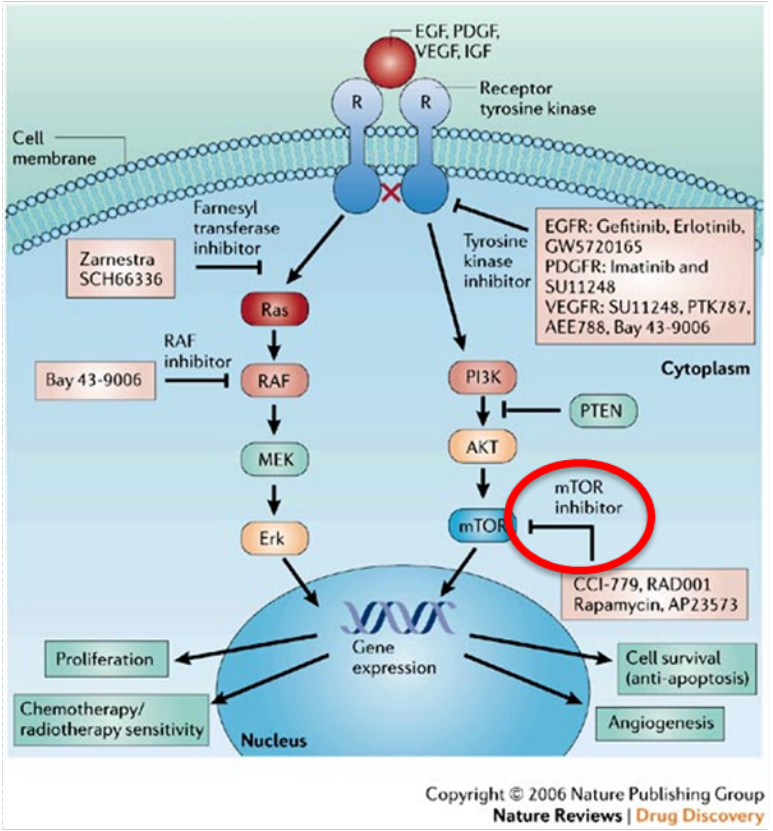

Any Questions?