

# Bladder Cancer: An Unusual Case, continued...

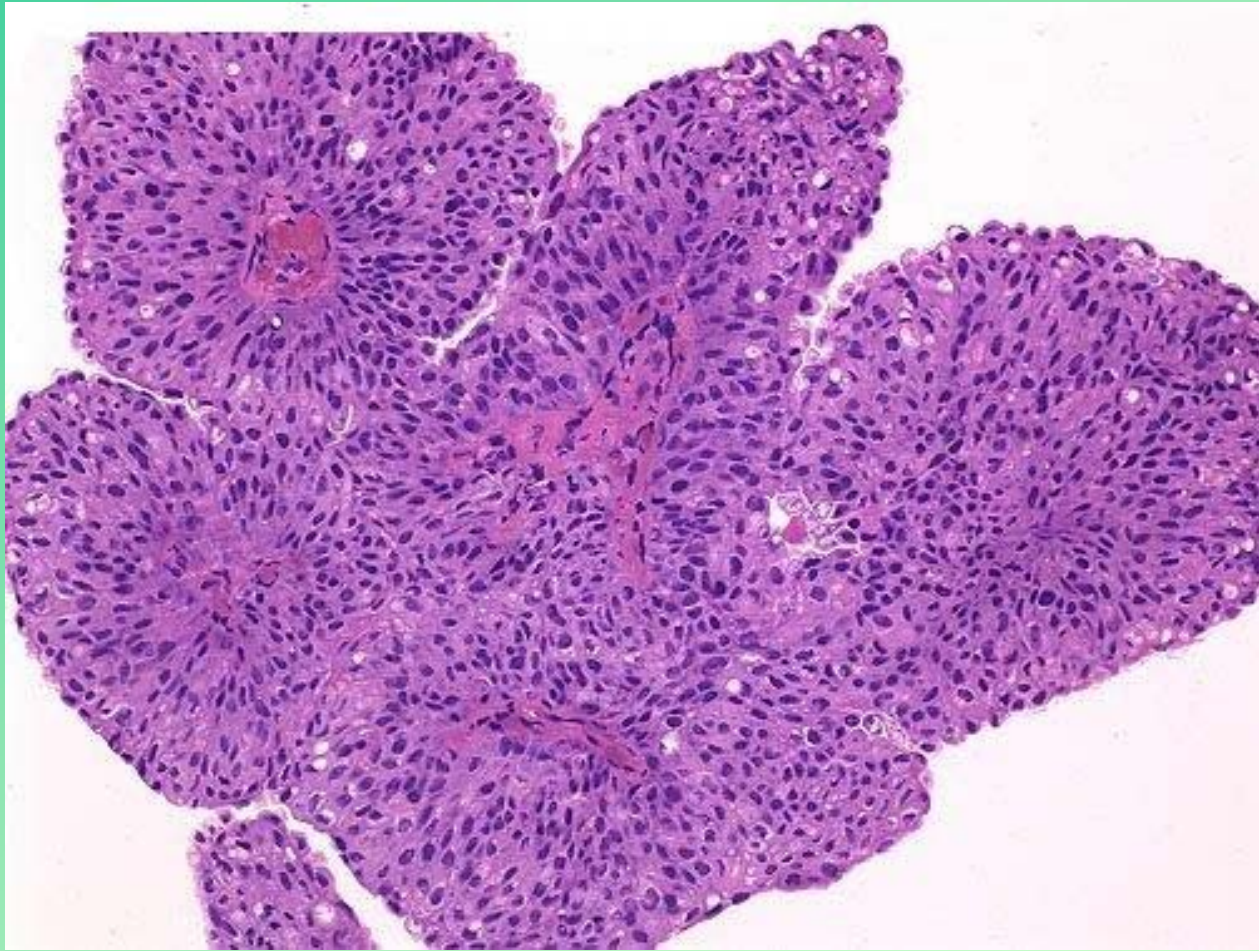
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January 28, 2011

# Case Presentation

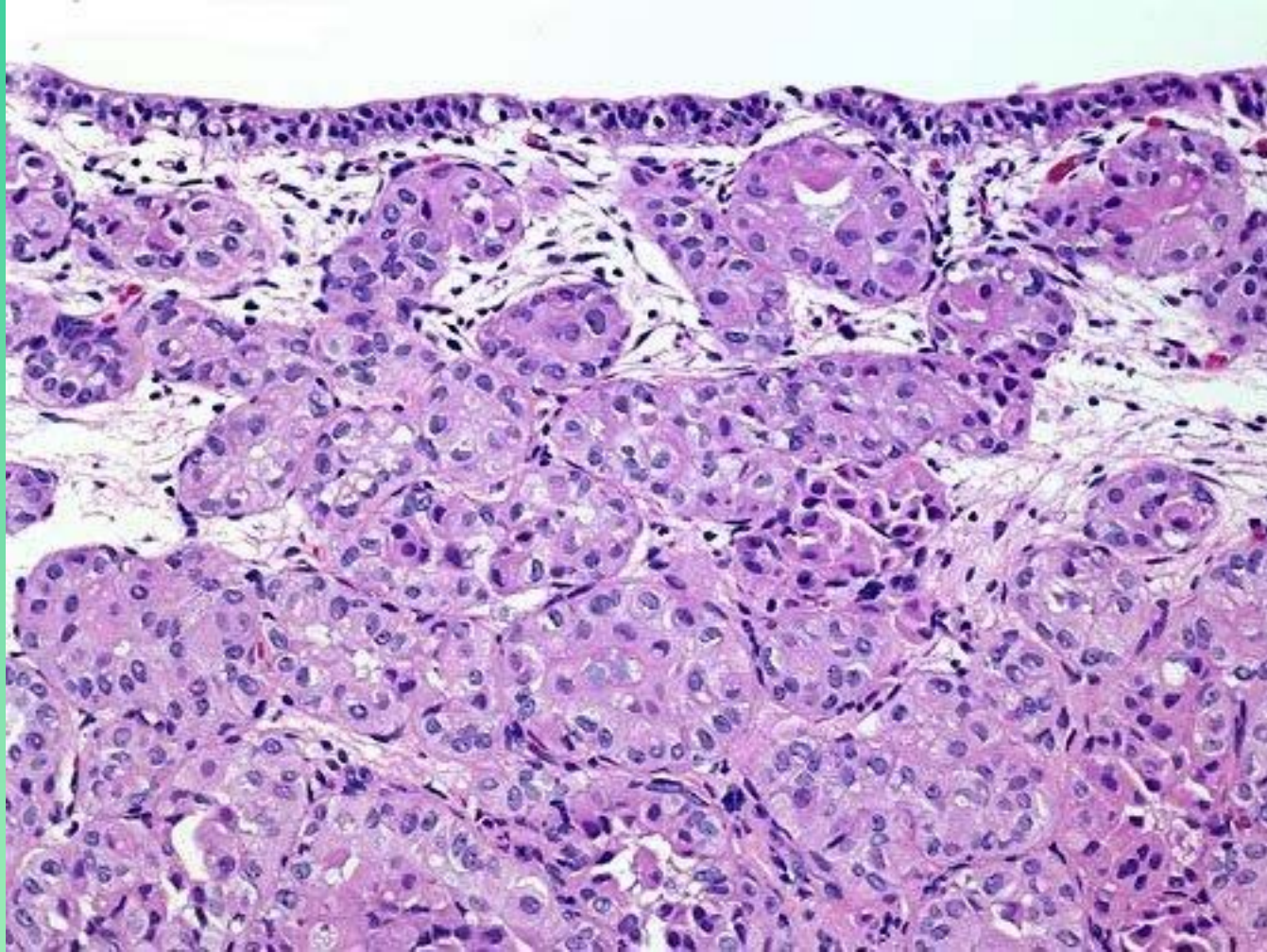
- 64 y.o. man presented with superficial bladder tumors in 2008...



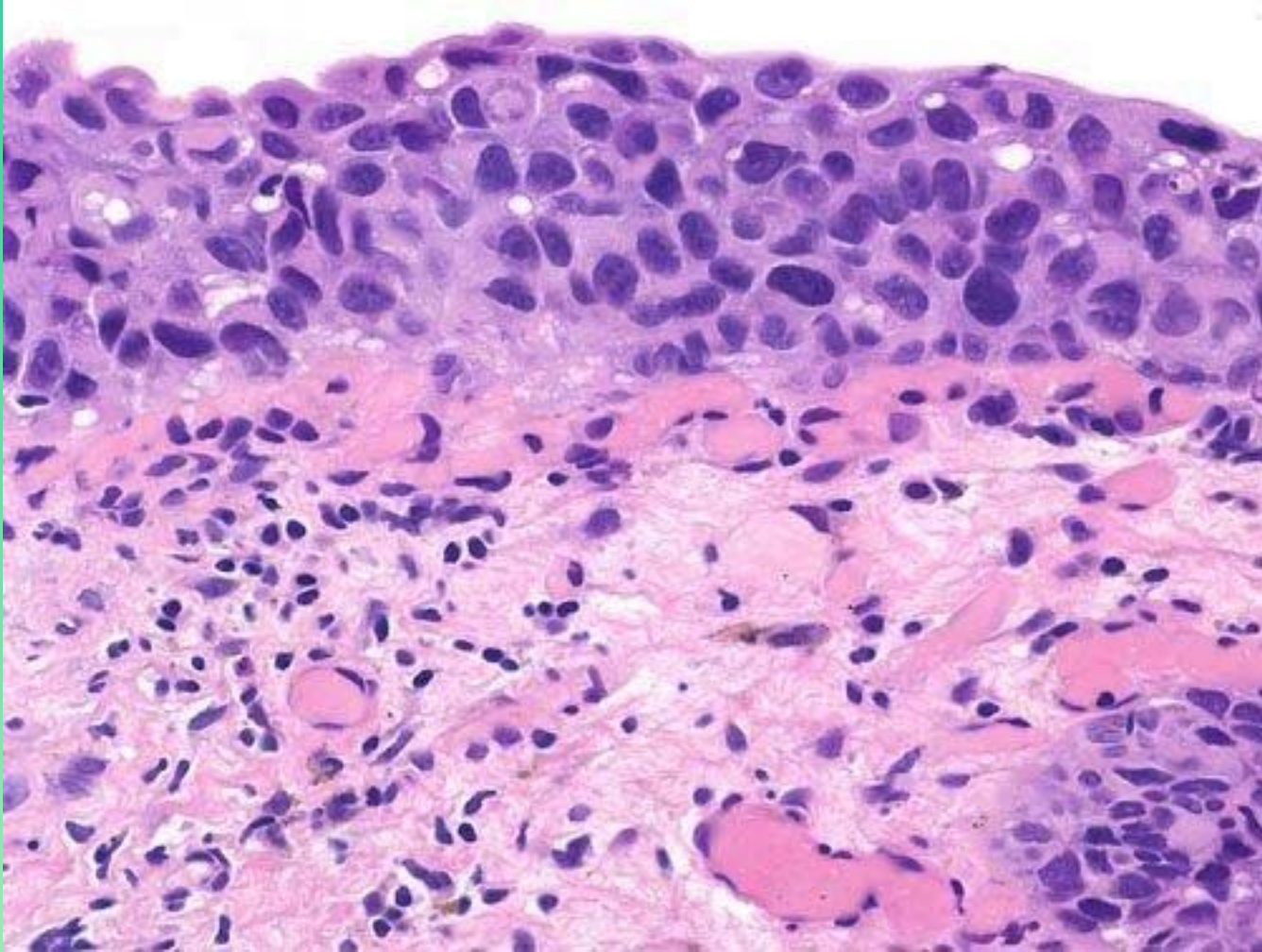
# Case Presentation

- 64 y.o. man presented with superficial bladder tumors in 2008
- Received BCG administration
- Recurred rapidly after cessation of therapy
- Decision made to perform cystectomy on that basis
- Recovered uneventfully from surgery
- Pathology....

# Invasive TCC into submucosa



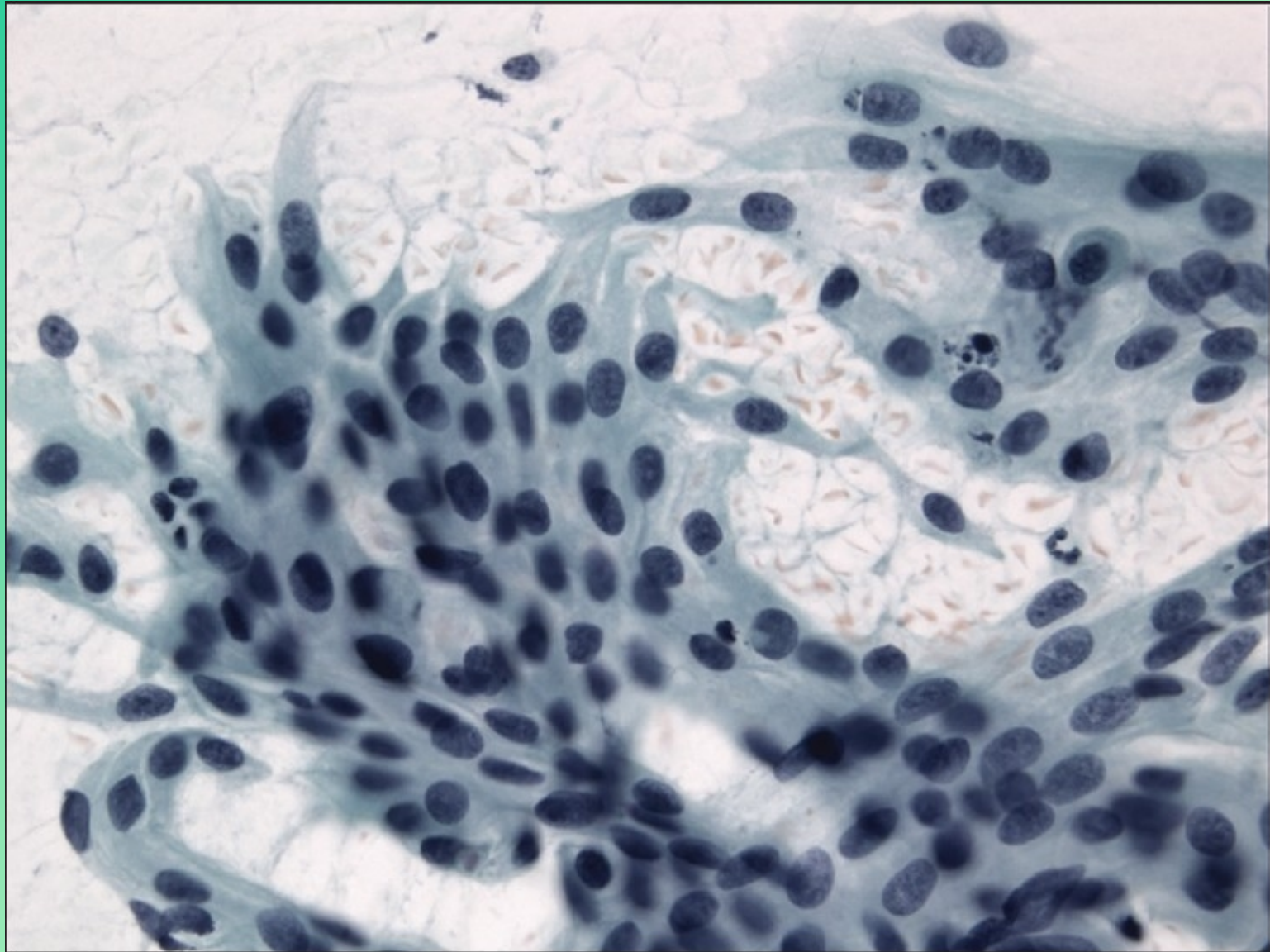
# Carcinoma in situ seen at cystectomy



# Case, continued

- About March of 2009 developed severe pain in sciatic distribution on left
- MRI spine, bone scan negative for etiology
- CT chest done.....
- On basis of history CT of abdomen and pelvis ordered...
- Fine needle aspiration of newly discovered mass performed...

# FNA of mass



# Case, continued

- Chemotherapy started with:
  - Taxotere
  - Gemcitabine
  - Cisplatin
- Much morbidity with nausea
- Developed intractable hiccoughs from Emend, relatively new anti-nausea drug at that time
- Sciatica disappeared within days of starting chemotherapy



# Case, continued

- Continued on chemotherapy at somewhat reduced doses secondary to intractable nausea and vomiting despite maximal anti-emetics
- CT scans repeated after a total of six chemotherapy treatments...
- Received four more treatments after remission status confirmed
- Treatment stopped, doing much better
- Repeat scans scheduled for early December...

# The story continues...

- Off all therapy in unmaintained remission until February, 2010 when he began to bump into things
- MRI of brain...
- Craniotomy performed with removal of solitary brain metastasis
- Quickly developed second brain lesion in cerebellum, treated with cyberknife

## More to the story....

- Soon after cyberknife he developed a recurrence of pain in the left sciatic distribution, reminiscent of original pain when he first presented with metastasis
- CT performed on June 1, 2010 and compared to the study in April
  - New large mass in vicinity of prior mass
- Chemotherapy restarted with immediate relief of pain

# The story....

- By August 2010 he had undergone six chemotherapy treatments
- CT performed....incomplete disappearance of disease
- Referred for possible stereotactic radiosurgery to only area of known systemic recurrence
- Some delay ensued because of insurance refusal to guarantee payment
- Upon beginning this treatment began to develop pain in the contralateral sciatic distribution
- Further imaging studies done...

# The story....what next?

- To summarize:
  - Two local recurrences (pelvic sidewall) after cystectomy
    - One complete remission
    - Next: partial remission
  - Two brain metastases
    - One craniotomy
    - One cyberknife, now NED in brain
  - Hematogenous metastatic spread to contralateral S-1 vertebral body with pain

# Chemo redux?

- After all radiation is finished issue of continuation of chemotherapy will come up
- Three drug combination was highly active at first exposure, less so at second exposure
- After twelve chemo treatments it is likely that most benefit will have been lost to drug resistance
- There is no standard alternative chemo
- Options include....

# Options for Resistant Disease

- Pemetrexed (Alimta)
- Oxaliplatin (Eloxatin)
- Ixabepilone (Ixempra)
- Halaven (Eribulin)
- Vinflunine

None of these drugs is FDA approved for bladder cancer; Vinflunine is the most active of the group but not available in the U.S.

- High-dose MVAC – very morbid but effective; big interest 15 years ago, not really pursued at major centers

## Bladder Cancer Staging Simplified

- T0 no primary tumor found
- Ta non-invasive papillary tumor
- Tis carcinoma in-situ
- T1 into subepithelium
- T2 into muscle
- T3 into perivesical tissue
- T4 into adjacent structures
- Nx nodes cannot be assessed
- N0 no nodal involvement
- N1 met to single LN < 2cm
- N2  $\geq 1$  LN but < 5 cm
- N3 any LN > 5 cm
- M1 Distant metastasis

Stage I: T1N0

Stage II: T2N0

Stage III: T3, early T4 N0

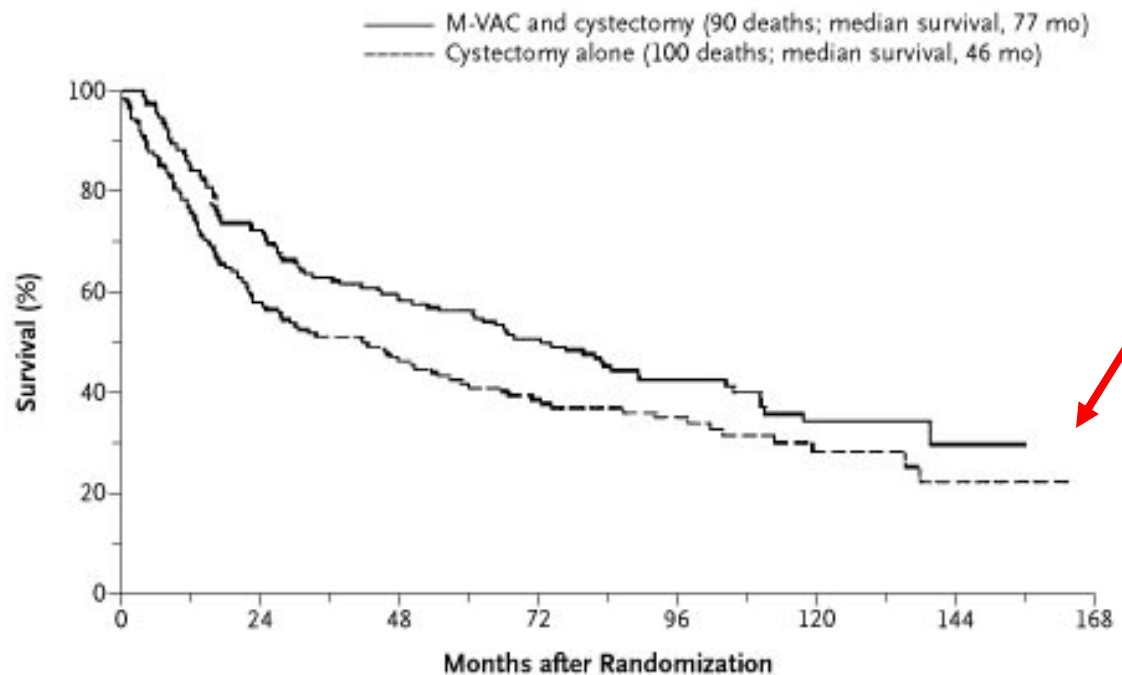
Stage IV: Late T4, any N, any M



# Overview of Treatment of Metastatic Disease

- Breakthrough came with MVAC chemotherapy in the 1980's
  - Methotrexate
  - Vinblastine
  - Adriamycin
  - Cisplatin
- Very morbid with mucositis, nausea and loss of sense of well being
- First chemo regimen that had any impact on the natural history of disease....in the neo-adjuvant setting

# Typical Results From One Study Summarized



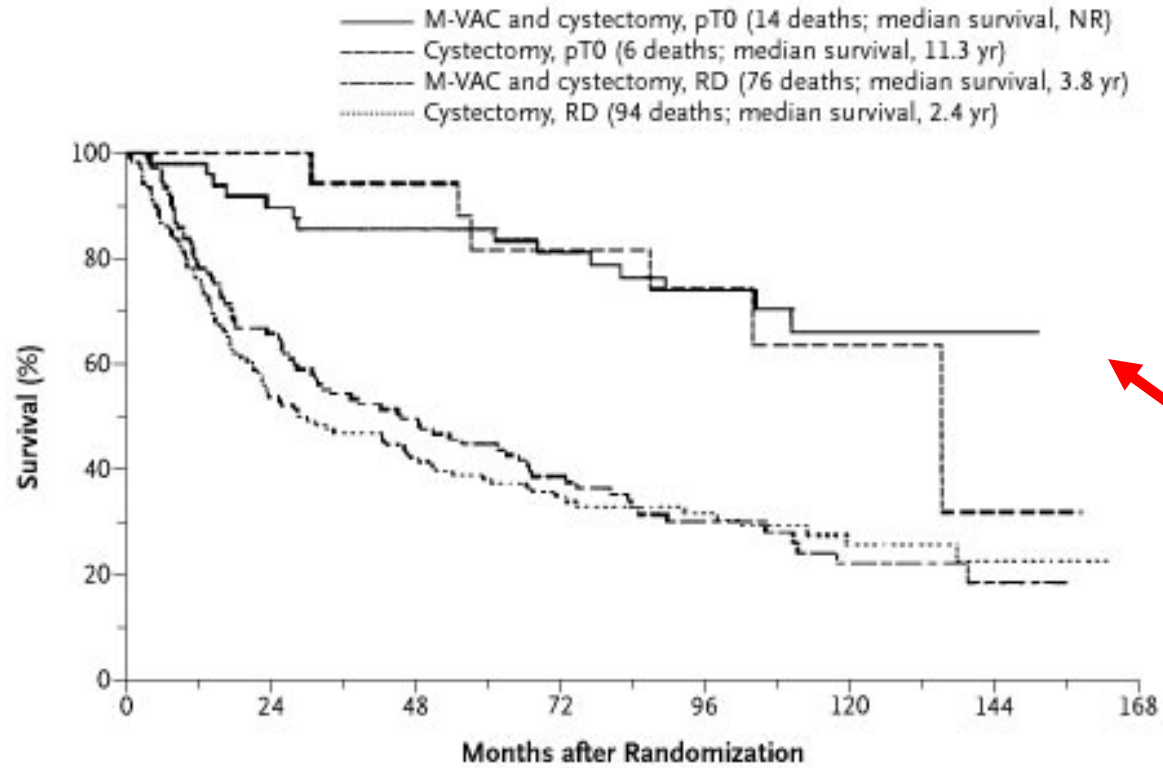
**No. at Risk**

M-VAC and cystectomy  
Cystectomy alone

153	112	92	75	46	23	6
154	88	67	50	37	18	7

Small  
difference;  
small  
numbers at  
risk

# Results further analyzed



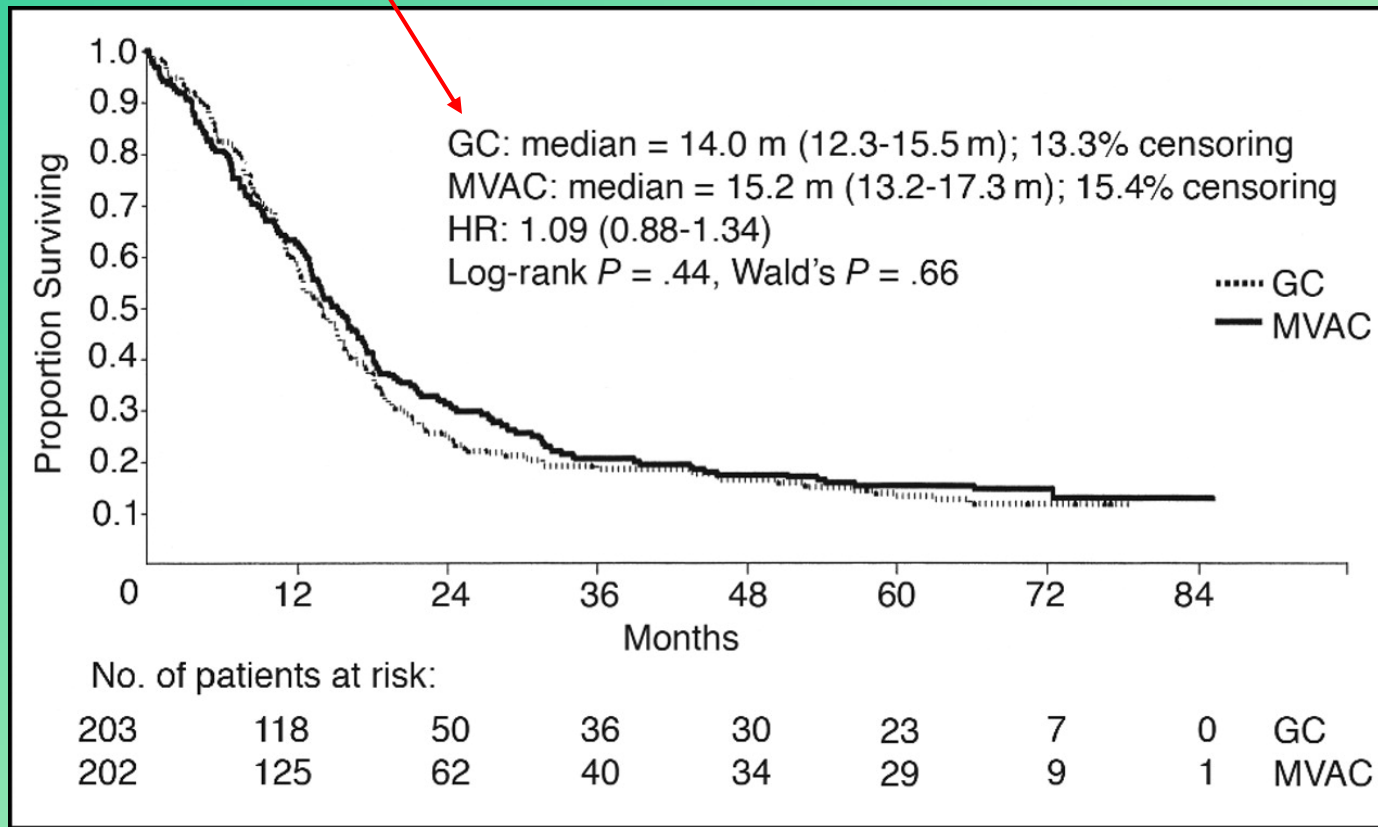
Entire benefit seen here; all patients had cystectomy

### No. at Risk

M-VAC 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

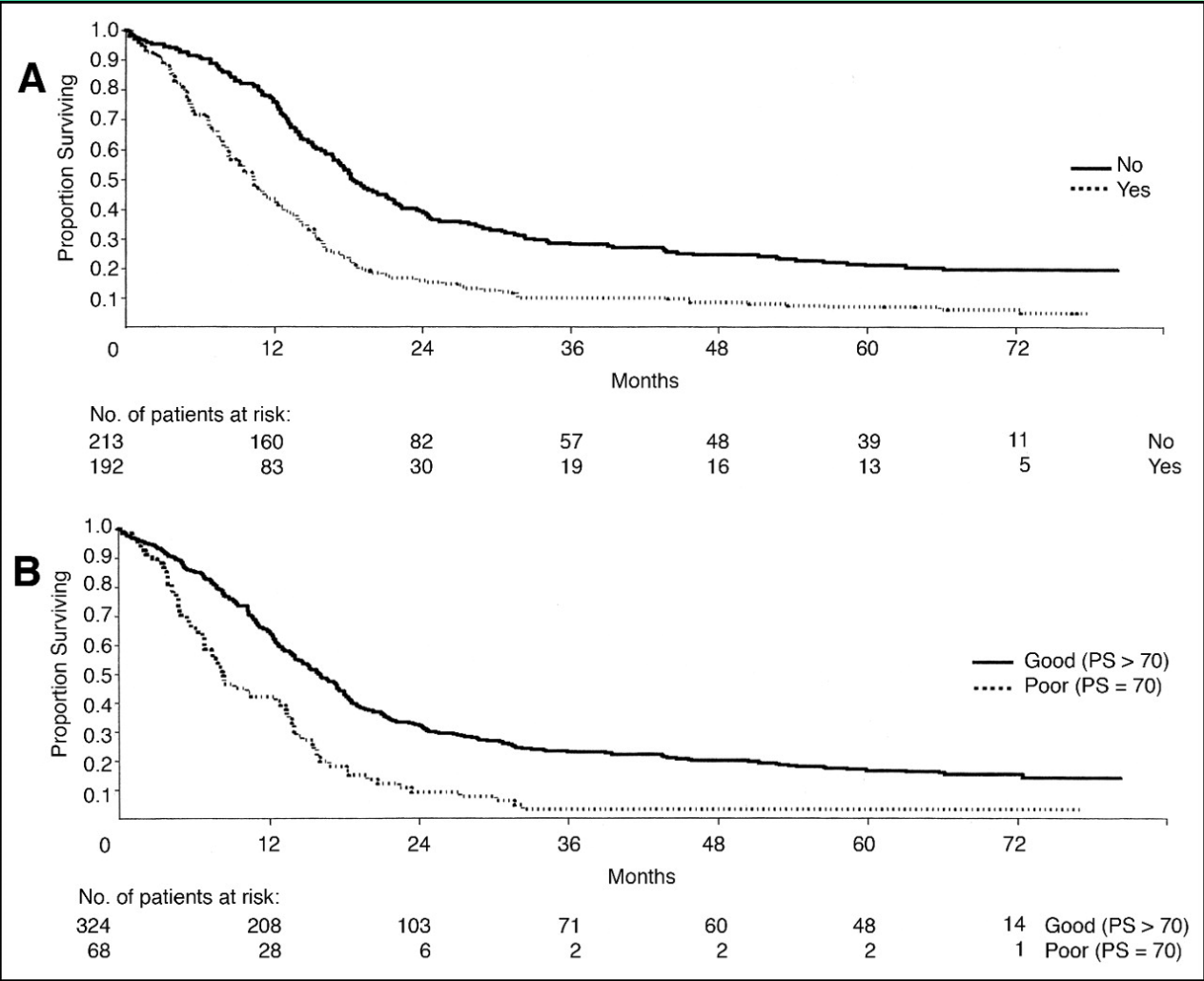
# Ability of selected chemo regimens to produce long-term survivors

## Gemcitabine + Cisplatin



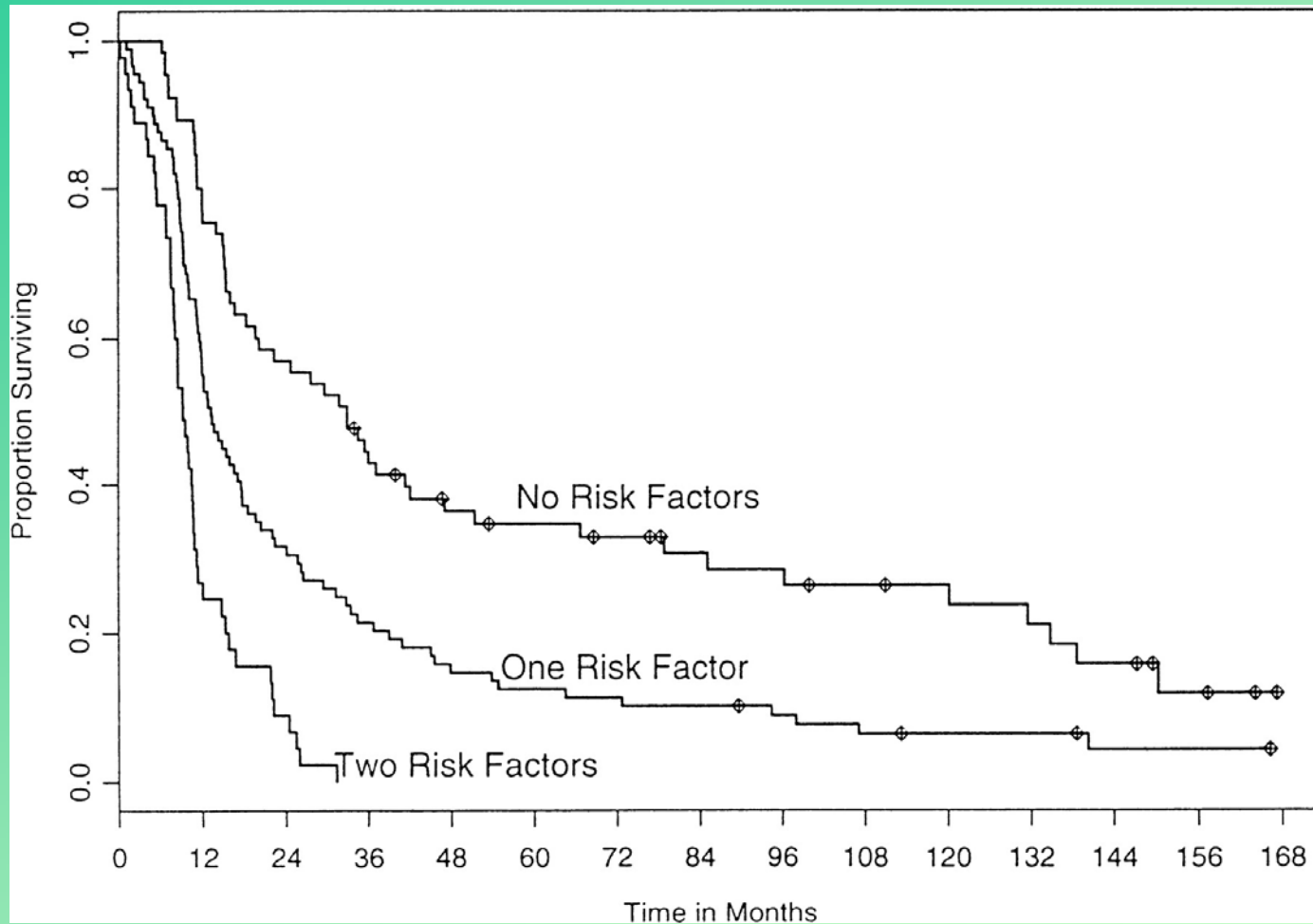
von der Maase, H. et al. J Clin Oncol; 23:4602-4608 2005

**Kaplan-Meier curves showing effect of (A) visceral metastases and (B) Karnofsky performance score (PS) on overall survival**



von der Maase, H. et al. J Clin Oncol; 23:4602-4608 2005

## Survival for all patients grouped according to number of risk factors present at baseline



Bajorin, D. F. et al. J Clin Oncol; 17:3173-3181 1999

**[Risk factors: KPS, visceral metastasis]**

# What About Our Patient

- Outlier in every aspect of his case
- Going back to the earliest part of his illness: we need a better predictor of who with early stage bladder cancer is destined to do very badly
- Such markers are present in breast cancer
- Bladder cancer is much less common and less well funded, but lessons from breast cancer will eventually spill over

# Our patient, concluded

- Demonstrates ability of modern oncology to keep people alive for extended periods of time without curing them
- Quality of life for most of that time has been excellent for this patient – not always the case, especially when there is no break in chemotherapy
- Cost of such care is astronomical
- Are we tantalizingly close to curing more of these patients??