Rising PSA after treatment:

How much does it matter, what can I do about it, and who should I ask?

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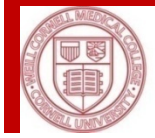

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Agenda

- What is biochemical relapse?
- What are the implications?
  - Does it matter?
- What can be done?
- Who should I ask?
- Where to go from here?

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- **What is biochemical relapse?**
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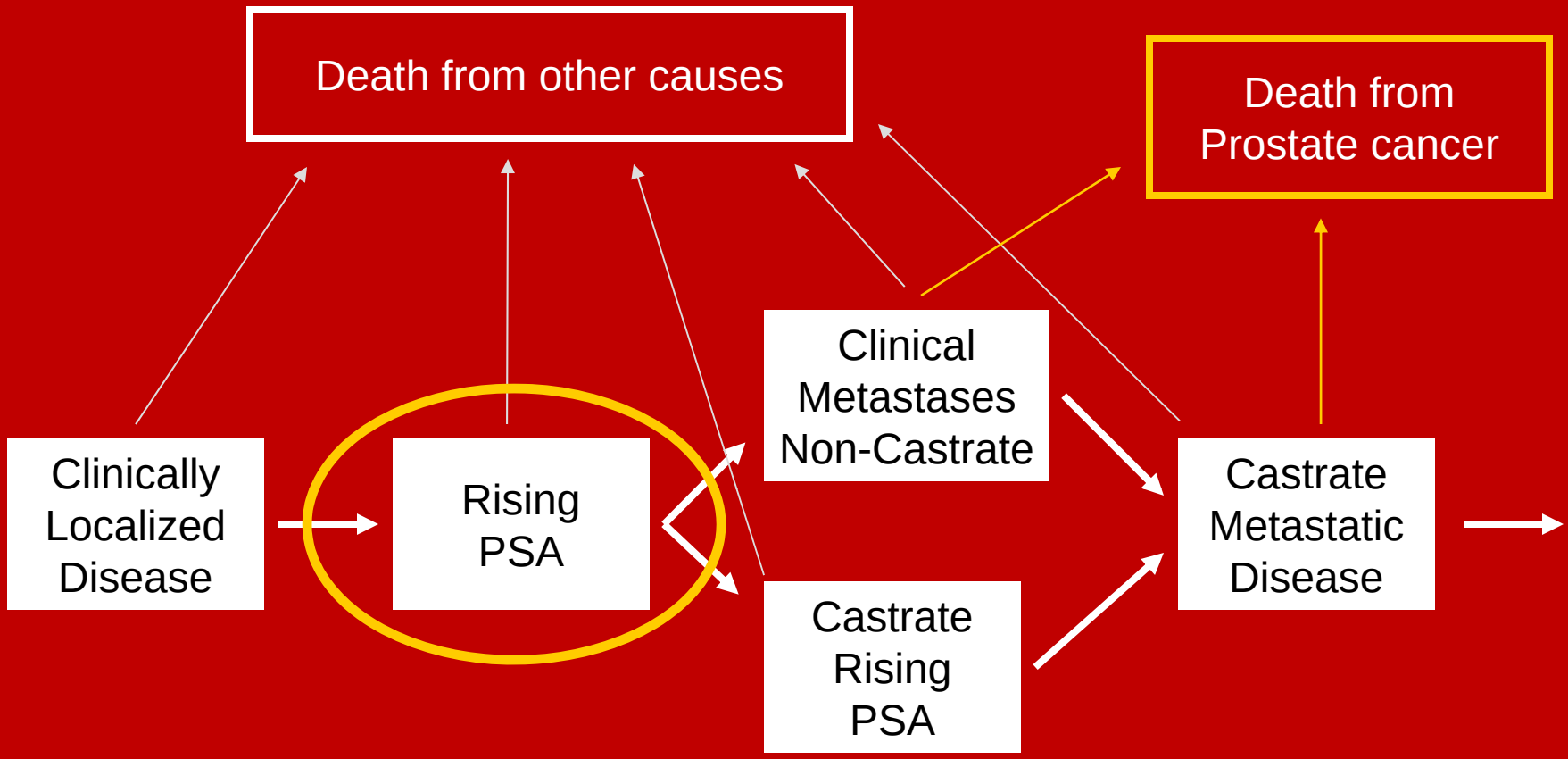
"Clinical States"



50,000 new men per year fall into this category in the U.S. alone
Estimated to be about 700,000 men currently

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Adapted from Scher et al.

Why doesn't surgery and/or radiation cure everyone?

Did my doctor miss something?

- There are 2 possibilities for biochemical "recurrence"
  - Cancer was left behind with surgery or missed with radiation
    - Possible, but rare
    - These cases may be cured ("salvage" therapy)
  - At least 1 cancer cell had already spread prior to treatment
    - "Micrometastatic" disease

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Does a rising PSA mean that I have cancer?

- Probably yes
- Residual prostate tissue after surgery may produce low, generally not rising PSA after surgery
- Residual normal prostate tissue following radiation typically produces some level of PSA which may fluctuate
- However, a steadily rising PSA after surgery or radiation essentially signifies the presence of cancer

Will a rising PSA shorten my life?

- **Not necessarily**
- The average length of life for the 2/3 of men without biochemical recurrence after local therapy is the same as the average length of life for the 1/3 of men with PSA recurrence
  - Though some choose to receive or require treatment
    - And some unfortunately develop metastatic disease and may die earlier

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- What is biochemical relapse?
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- **What can be done?**
  - **Part 1: testing**
- Who should I ask?
- Where to go from here?

Where is my PSA coming from?

Imaging

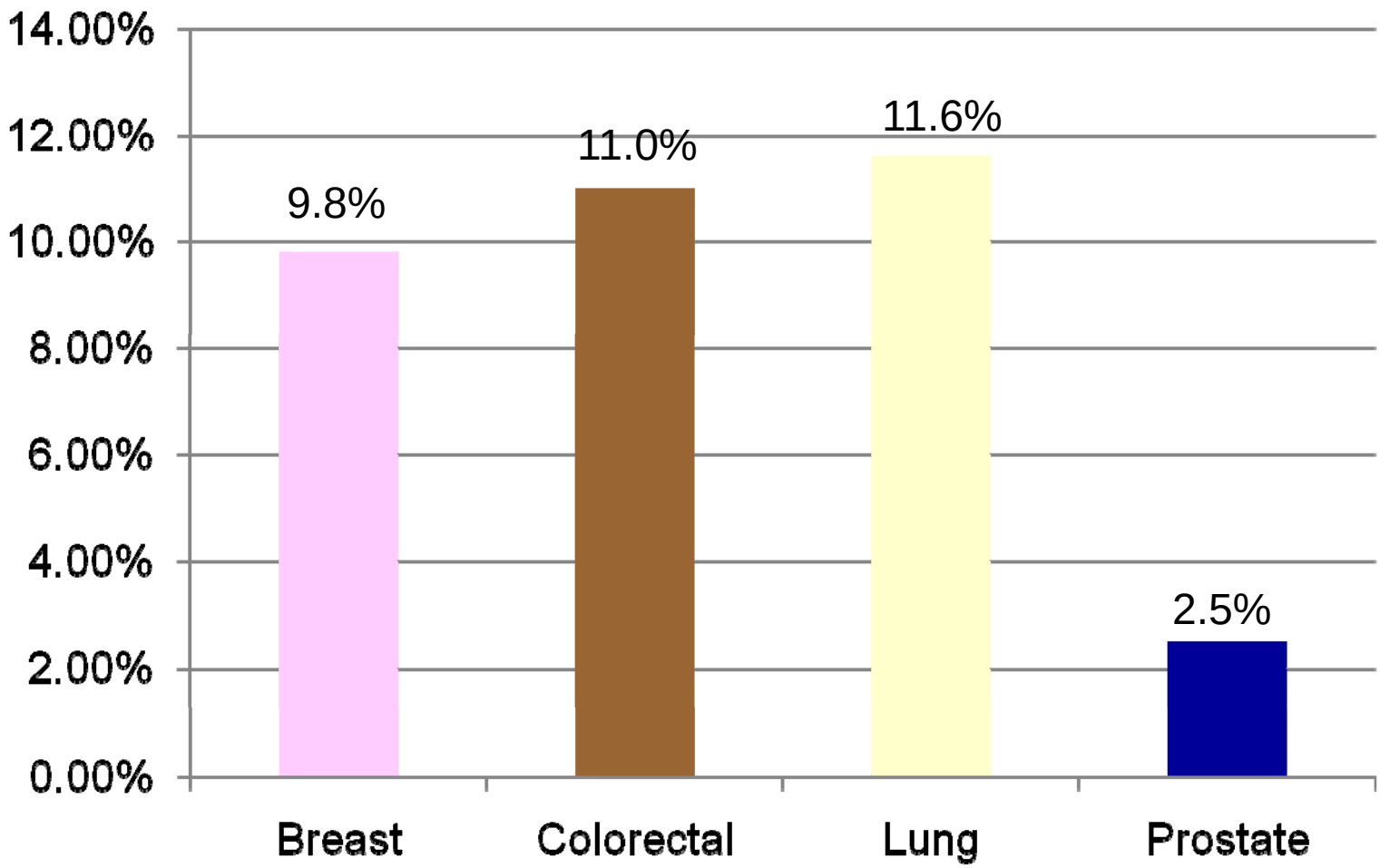
- Current imaging tools:
  - Xray
  - Ultrasound
  - CT scans
  - MRI
  - Bone scan
    - ^{99m}Tc-MDP bone scintigraphy
  - Other nuclear medicine techniques
    - FDG-PET/CT
    - NaF bone PET/CT
    - ^{11}C choline PET/CT
    - ^{111}In-capromab penditide (Prostascint®)

Problems with current imaging

- Not sensitive enough
- Not specific
- May not change treatment options

How do we make improvements in medicine?

Percent of patients participating in clinical trials



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Wassenaar et al, ASCO 2008

Patient satisfaction with care

Cancer Type	Treated with standard care	Treated on clinical trial	Statistical significance
Prostate Cancer	60.1%	69.4%	P=0.03
Colorectal Cancer	45.5%	58.9%	P=0.009
Lung Cancer	37.7%	63.6%	P=0.001

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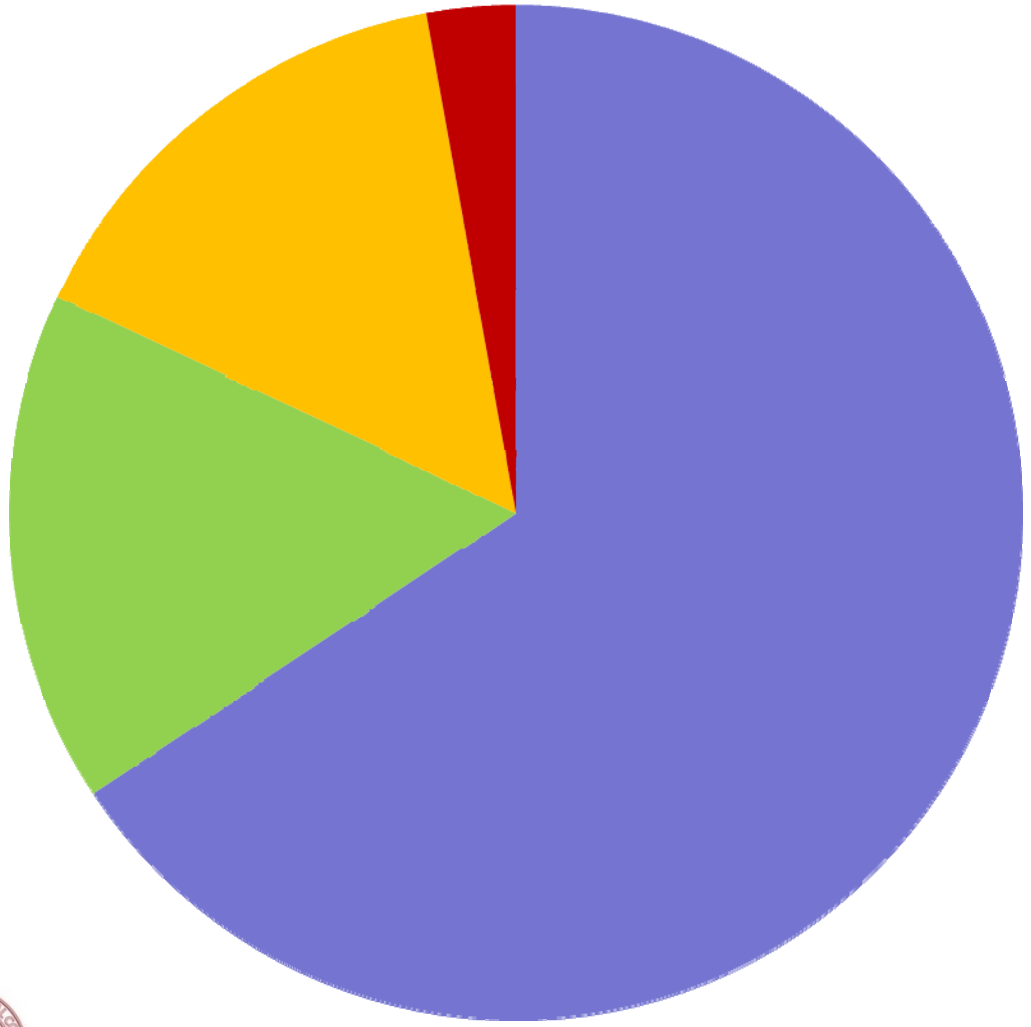
Wassenaar et al, ASCO 2008

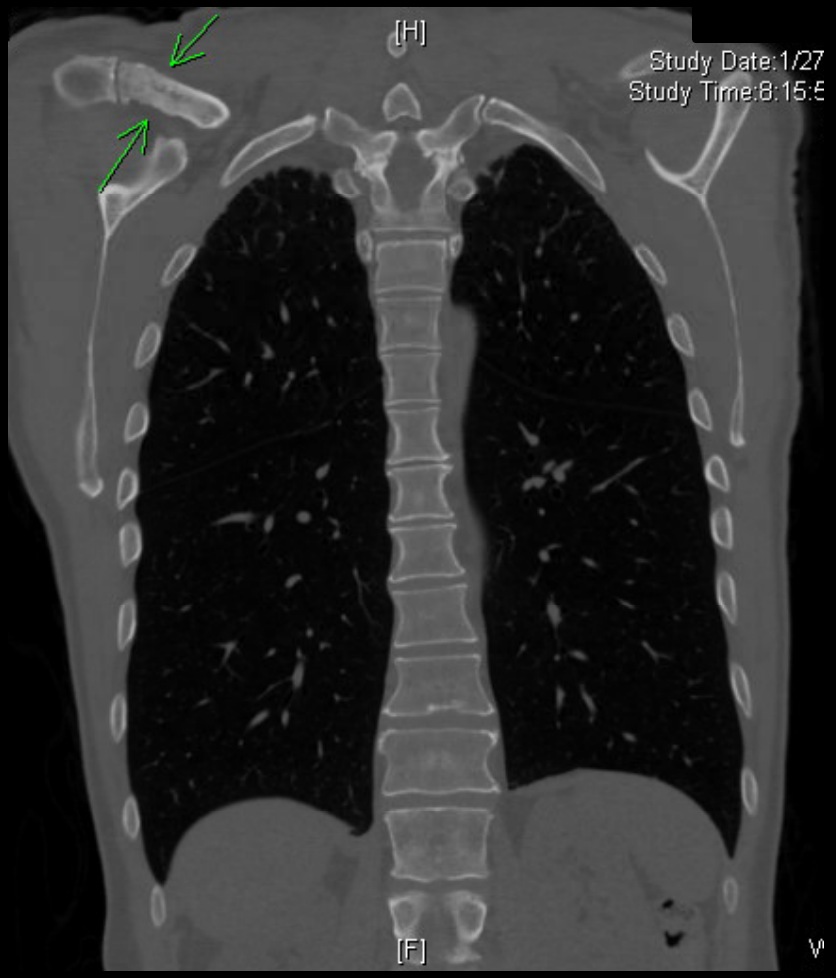
Why don’t more patients participate in clinical trials?

Primary reason for not participating in clinical trial



- Not told trial was an option (60.2%)
- Not eligible for available trial (15.0%)
- Declined participation in available trial (13.9%)
- Did not have insurance coverage for care (2.6%)

Wassenaar et al, ASCO 2008



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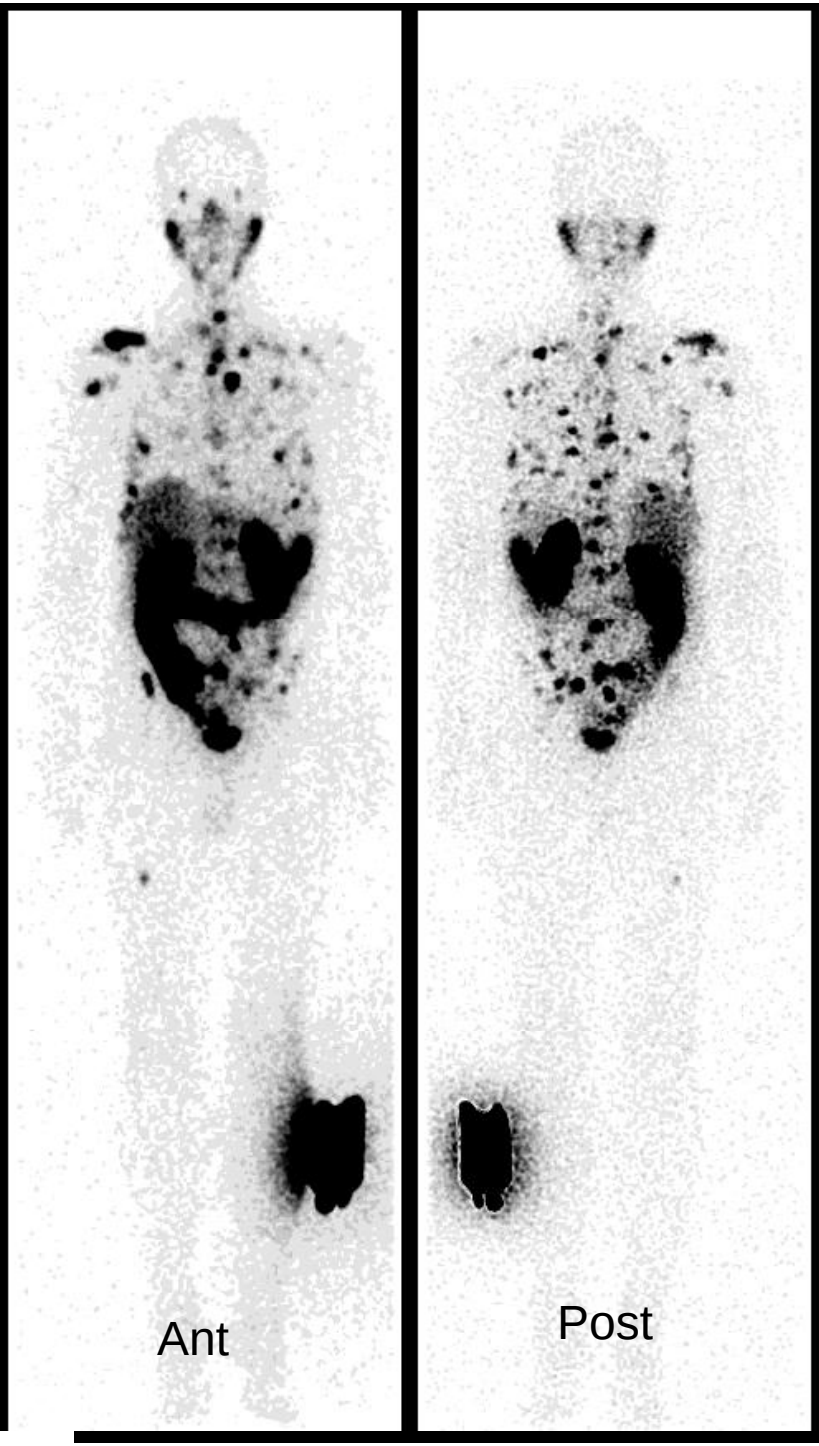

MIP ^{99m}Tc 1405

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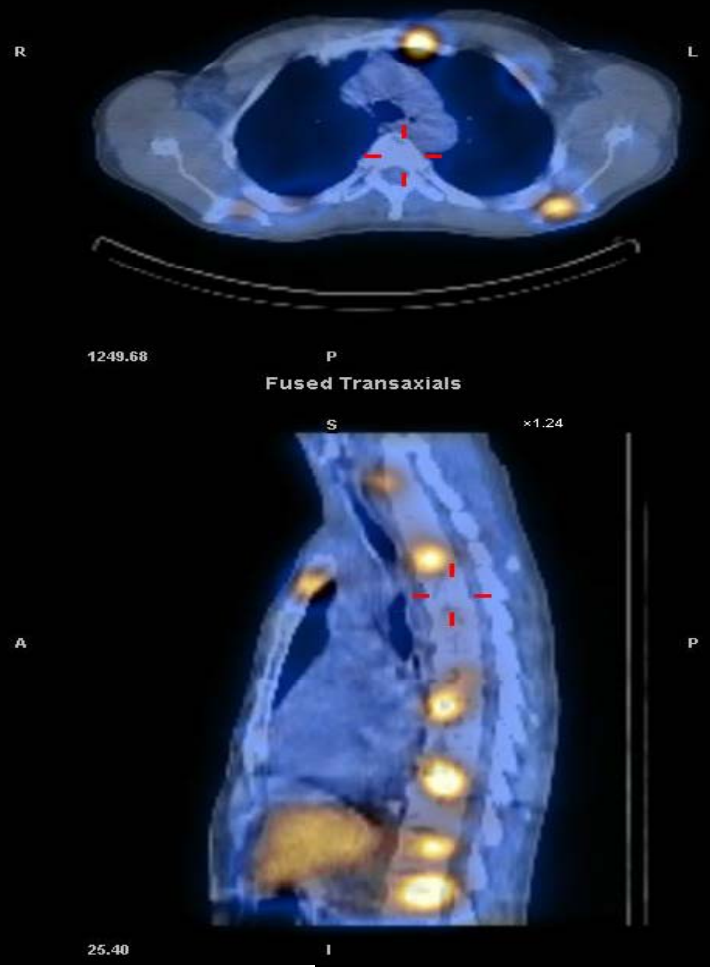

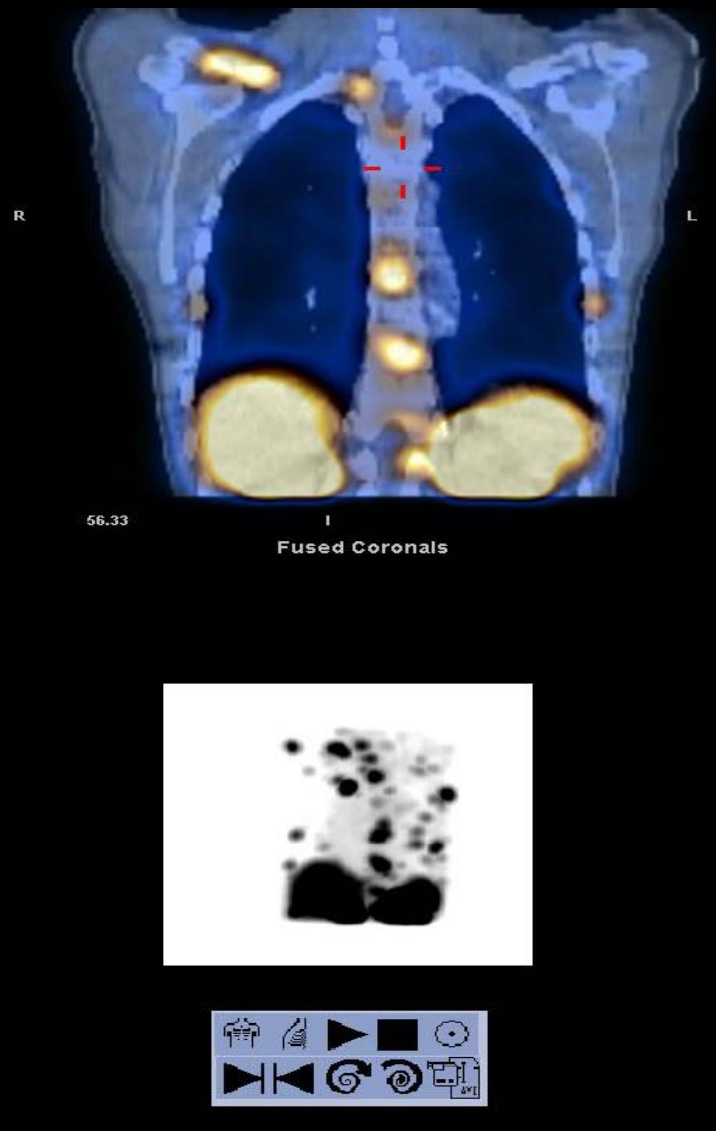

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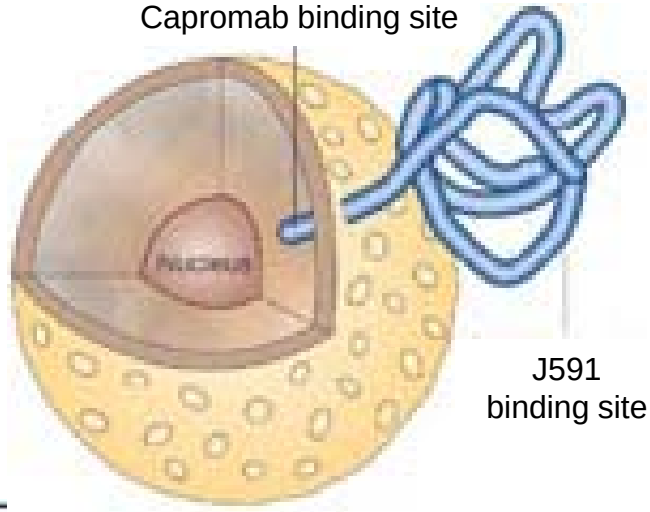
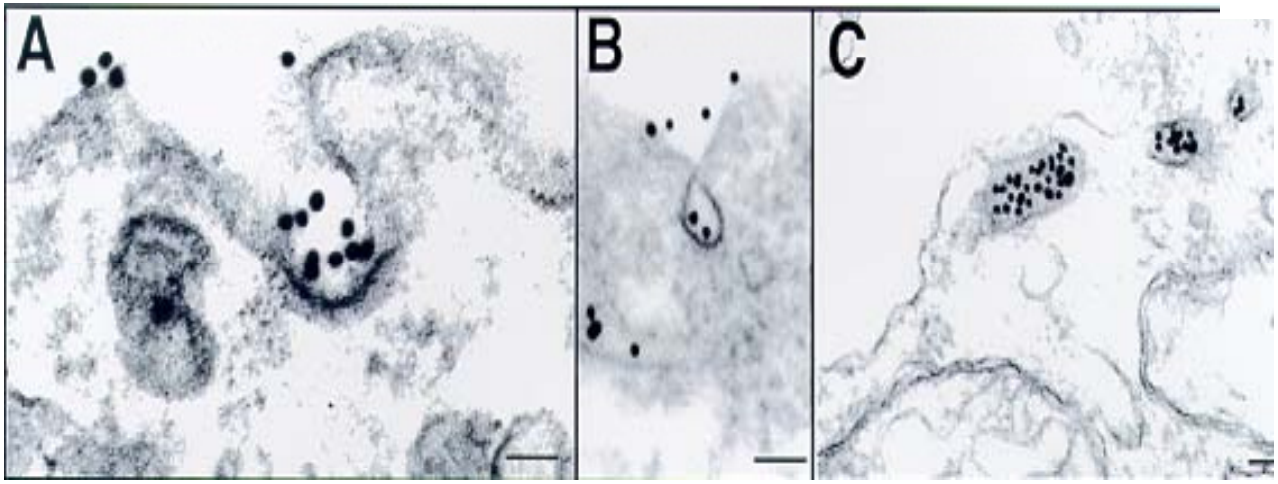
MIP ^{99m}Tc 1405 (SPECT/CT)

Second Generation Anti-PSMA Abs: **J591**

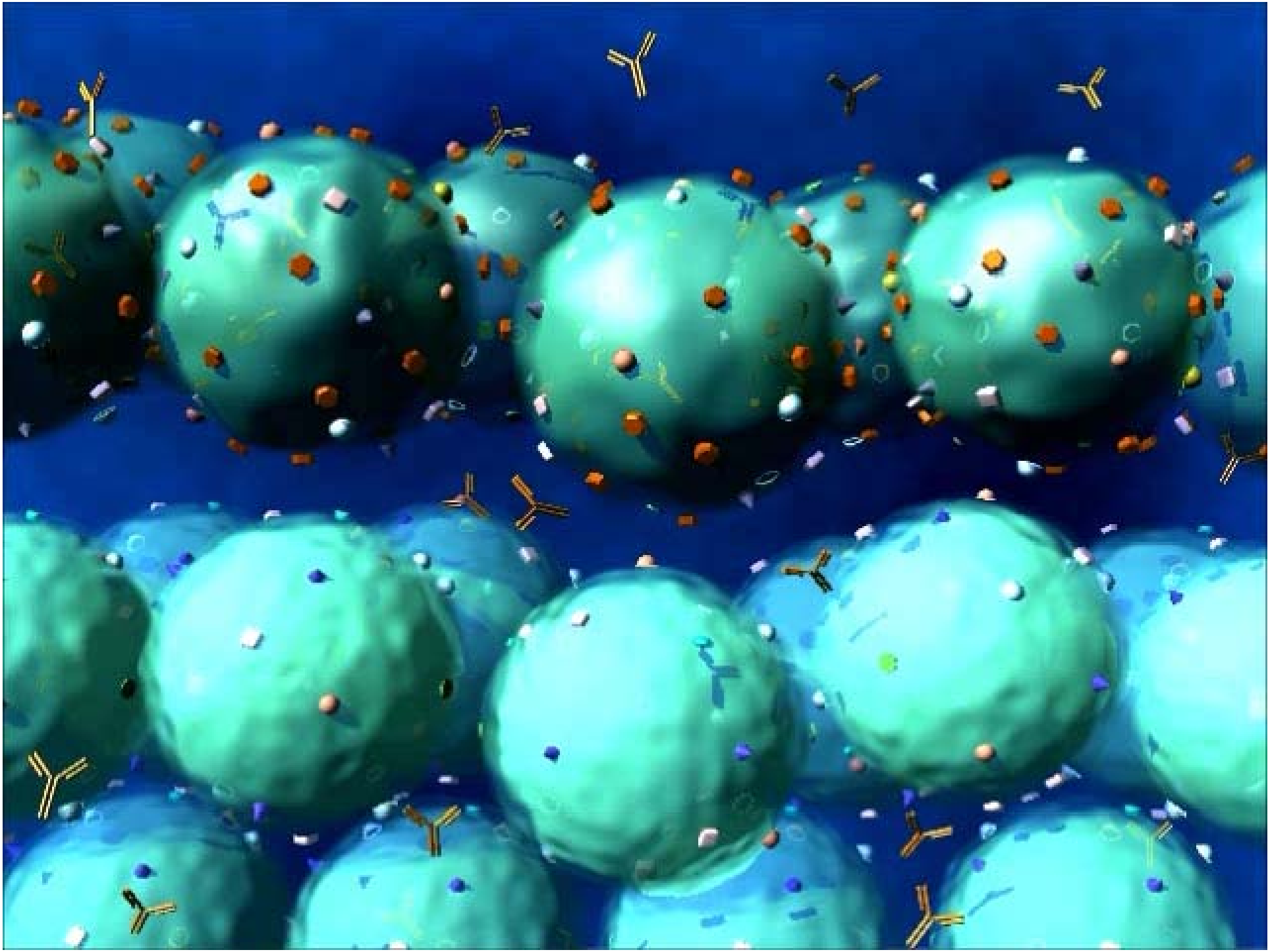
2nd generation mAbs

- Bind extracellular domain
- Bind viable PSMA^{+} cells
- Rapidly internalized





Liu H *et al*. Cancer Res 1997; 57: 3629
Liu H *et al*. Cancer Res 1998; 58: 4055



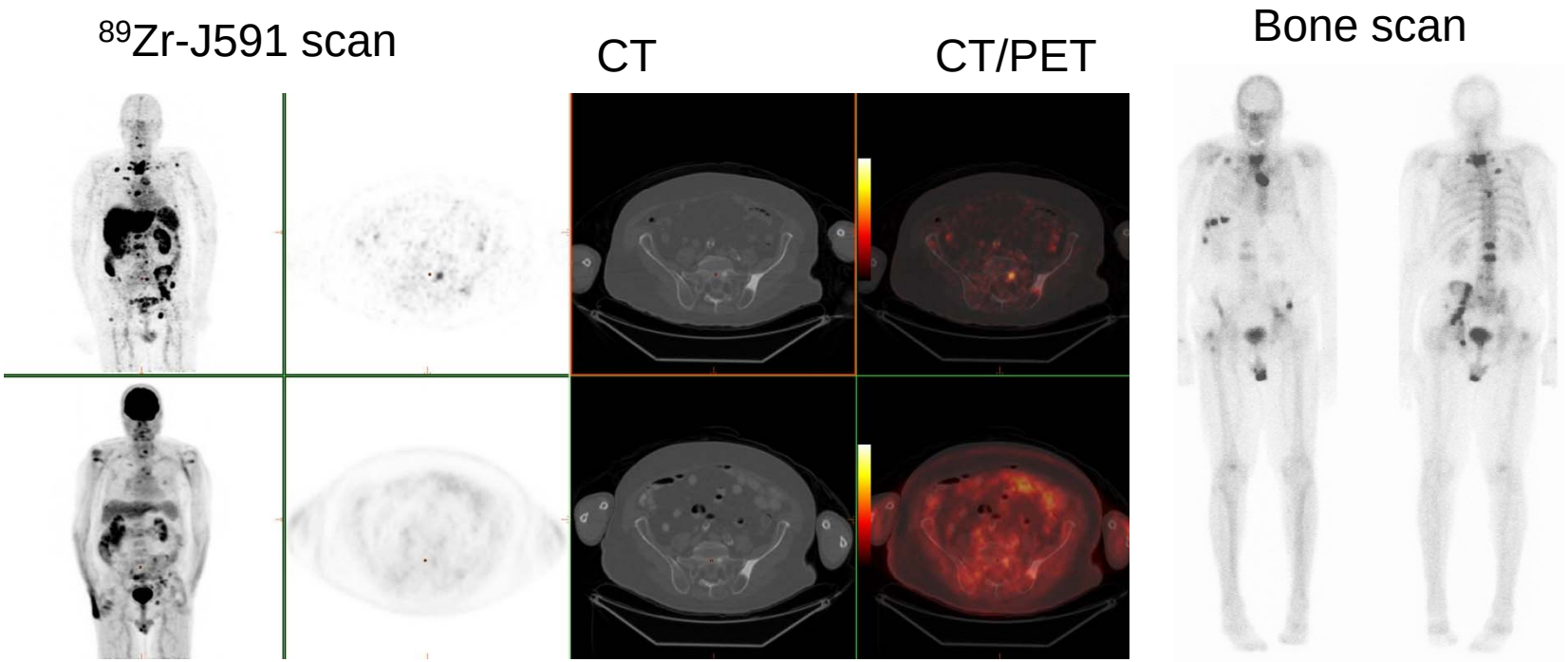
89Zr-J591 PET/CT

^{89}Zr-J591 scan

CT

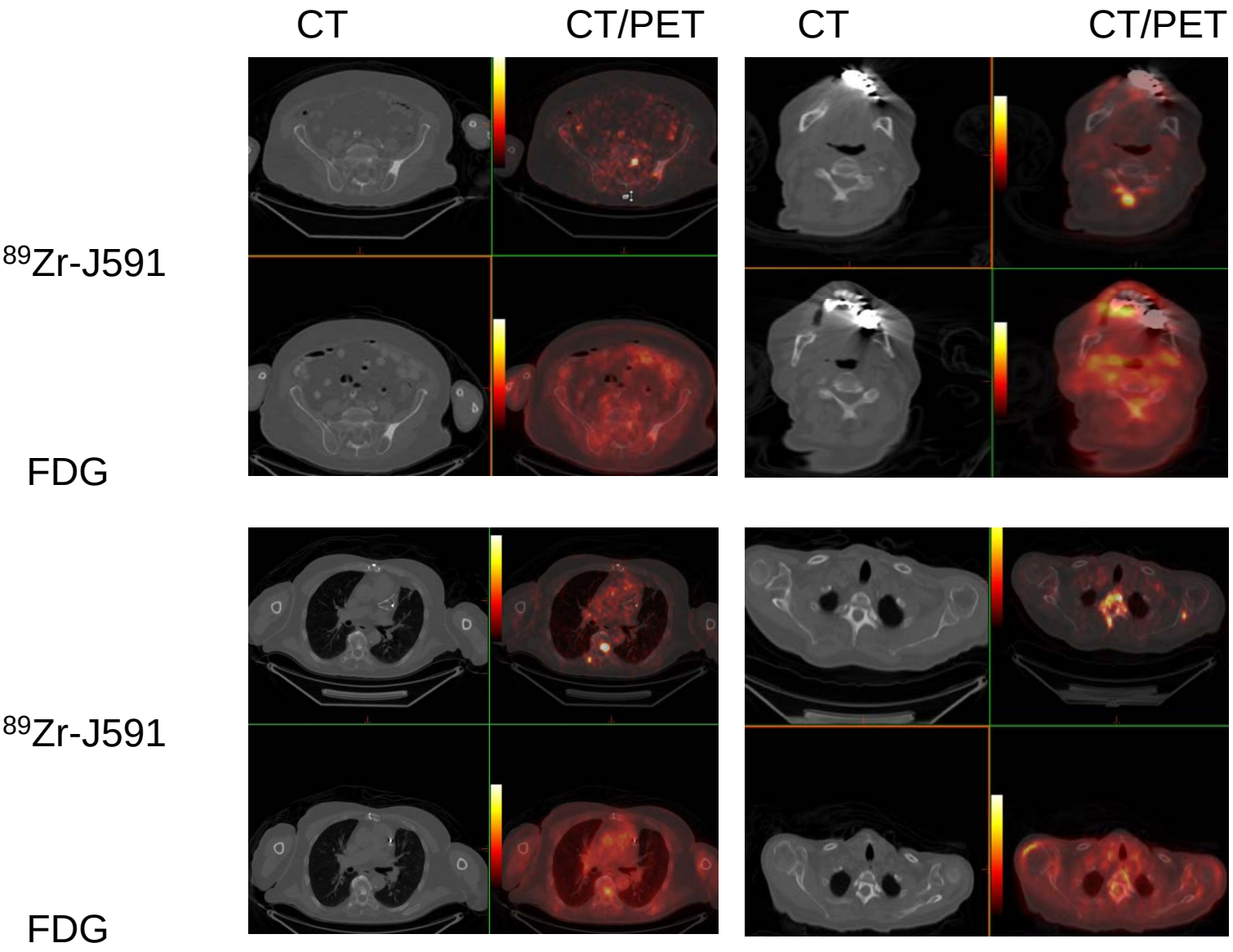
CT/PET

Bone scan



FDG scan

74 y.o. male with prostate carcinoma, PSA 8.8. Bone scan (far right) showed multiple bone lesions that were stable. FDG PET scan showed mild uptake in some but not all bone lesions. ^{89}Zr-J591 PET imaging showed more extensive uptake and involvement of the bone with uptake in number of lesions not clearly seen on bone scan and that were also not FDG avid.



^{89}Zr-J591 imaging (upper panel) Vs FDG (lower panel).
Images show lesions in sacrum and vertebrae clearly seen on ^{89}Zr-J591 study but minimal to no uptake on FDG scan.

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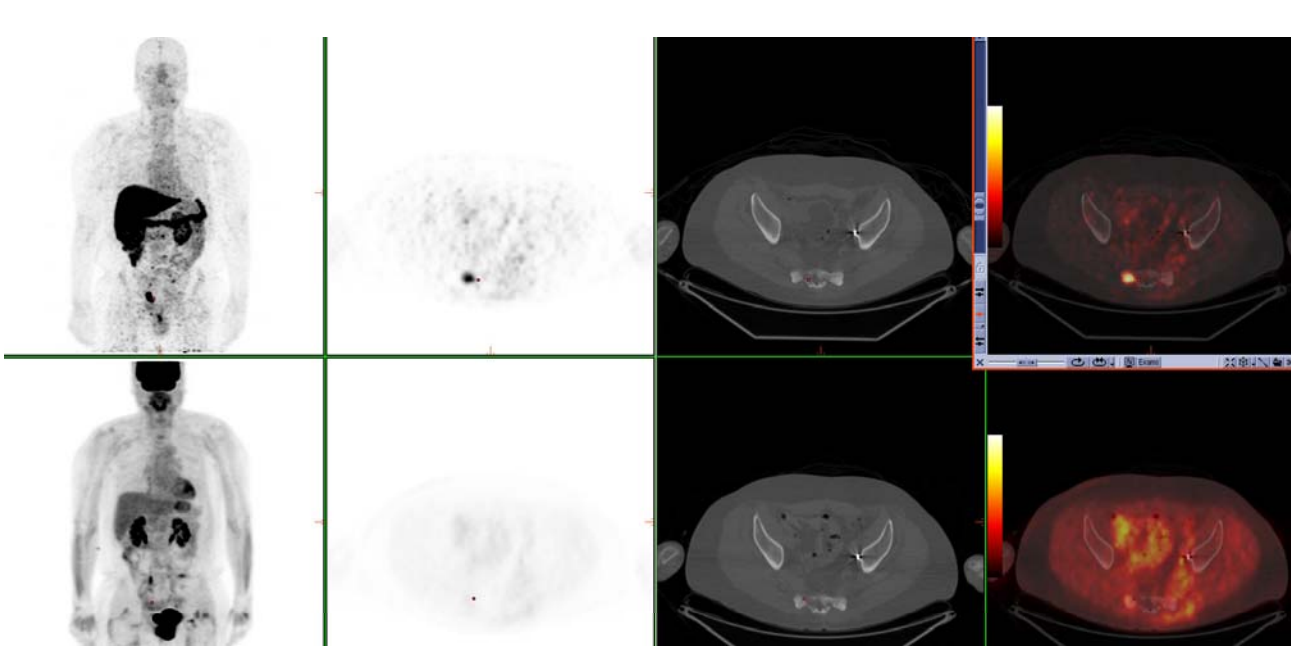
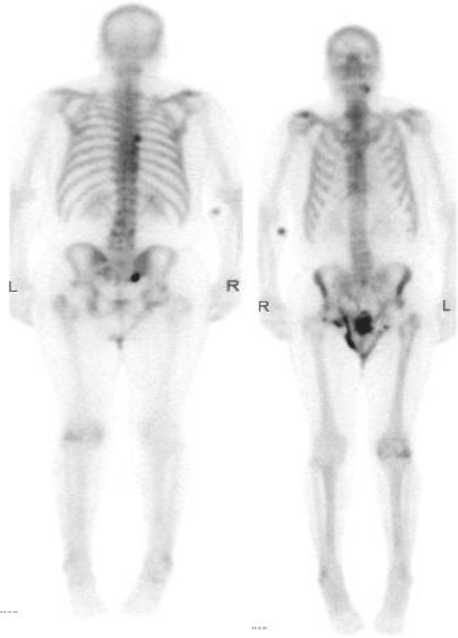
89 Zr J591 scan





FDG scan

Bone scan

66 male with prostate carcinoma; PSA 1.6. Bone scan showed sacral lesion that was stable. FDG PET scan showed mild uptake. ^{89}Zr-J591 PET imaging showed more intense uptake in the lesion and also showed involvement of the skeletal system with uptake in number of lesions not clearly seen on bone scan and that were also non-FDG avid.

Agenda

- What is biochemical relapse?
- What are the implications?
  - Does it matter?
- **What can be done?**
  - **Part 2: treatment (if necessary)**
- Who should I ask?
- Where to go from here?

Hormones and prostate cancer

- In animal experiments, Huggins and Hodges (1938) demonstrated that castration and estrogen therapy resulted in clinical quiescence of prostate cancer
- This was successfully emulated in humans (1941)
- Translational therapeutics was born
- Charles Huggins - **NOBEL PRIZE 1966**

Results of hormonal therapy for biochemical recurrence

- Universal PSA declines
- No clear improvement in survival across the board
- However, for those with unfavorable PSA kinetics, delay in time to metastatic disease and also death (but no cures currently)
  - "PSA doubling time"

New (prob better) hormonal agents are here (and more on the way)

- Abiraterone acetate (Zytiga)
- Enzalutamide (Xtandi / MDV3100)
- Orteronel (TAK700)
- ARN509
- TOK001
- …and many others

What else can I do if I want (or need) treatment?

- Nutrition
- Exercise
- Pomegranate?
- Other?

- Participate in research
  - Diagnostics
  - Therapeutics

^{177}Lu-J591 Salvage RIT

- Biochemical only relapse is common
- Radiotherapy is an effective salvage therapy for selected pts; however most pts suffer distant relapse/progression
- RIT may have greatest effect in setting of minimal disease
- J591 successfully targets known sites of disease and shows efficacy in the advanced setting

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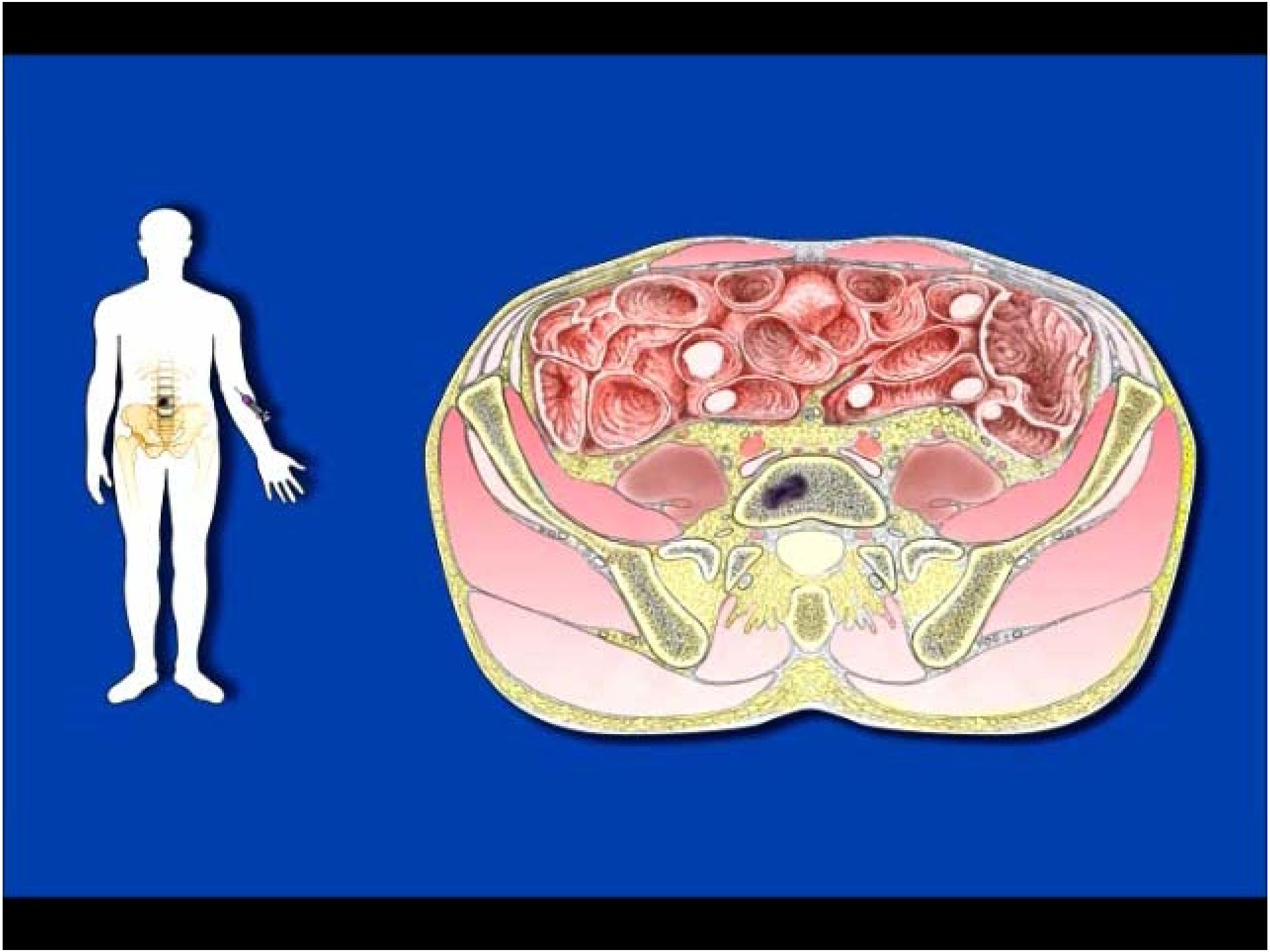
Scher JCO 2004
Freedland J Urol 2007
Pazona J Urol 2005
Buskirk J Urol 2006
Stephenson JAMA 2004, JCO 2007

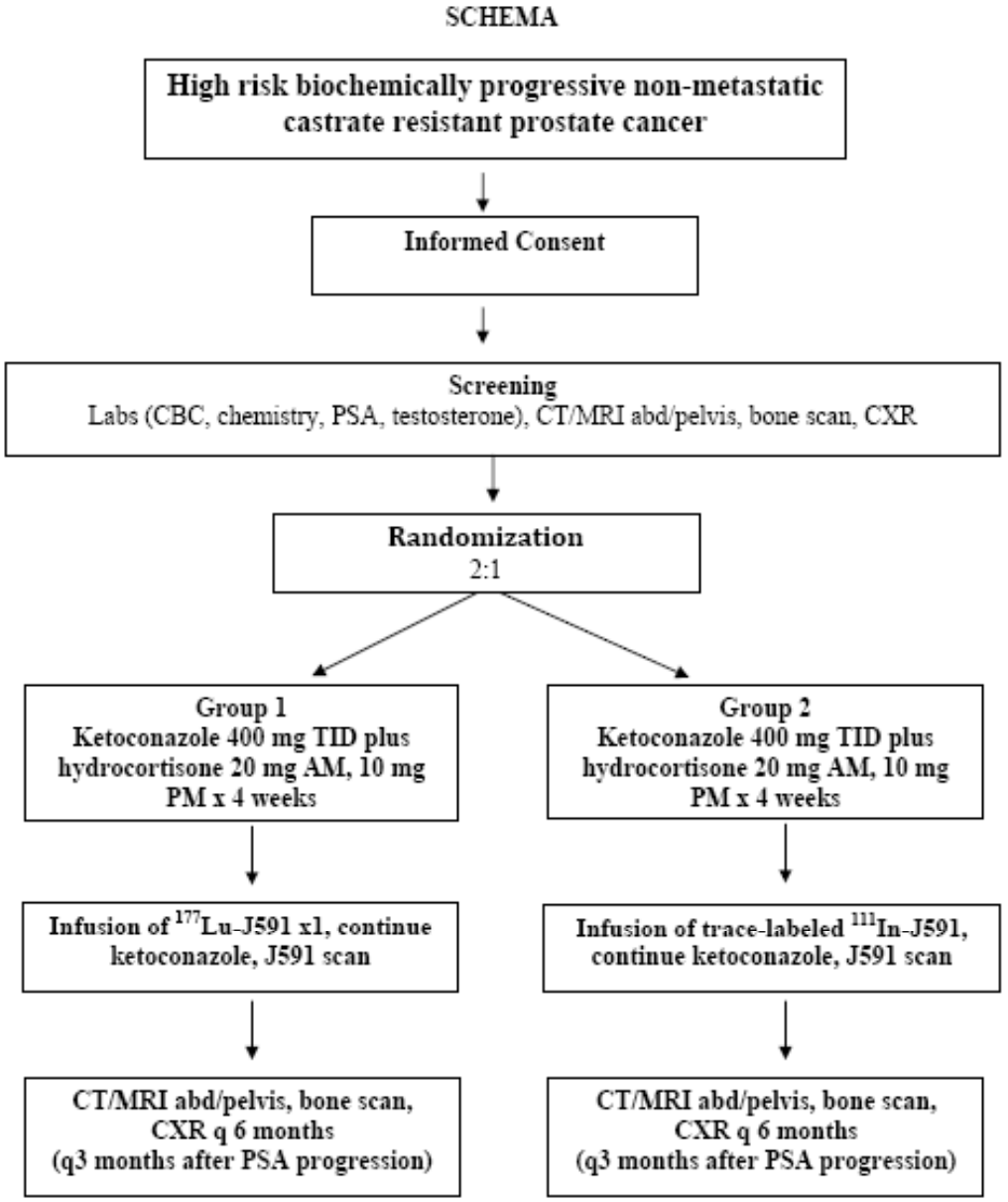
Ward J Urol 2004
Kaminski Blood 2002; JCO 2005; NEJM 2005
Press Blood 2003; JCO 2006
Leonard JCO 2005



A Randomized Phase 2 Trial of ^{177}Lu Radiolabeled Monoclonal Antibody HuJ591 (^{177}Lu-J591) and ketoconazole in Patients with High-Risk Castrate Biochemically Relapsed Prostate Cancer After Local Therapy

High risk castrate biochemically progressive entry criteria:
- PSA DT < 8 months
and/or
- absolute PSA > 20

2:1 randomization stratified by
- Investigational site
- Type of primary therapy
(Surgery vs RT)



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Tagawa et al, IMPaCT 2011

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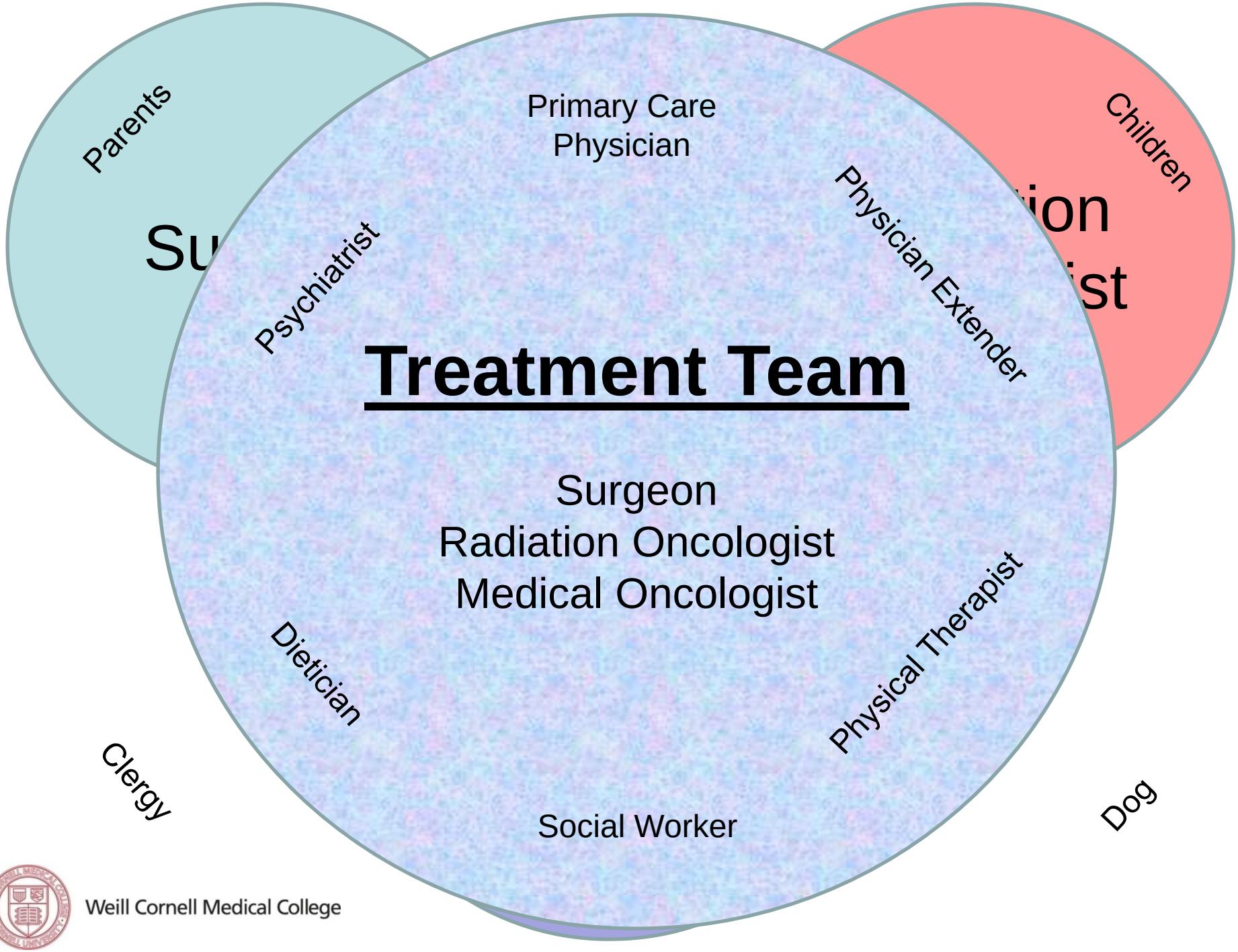

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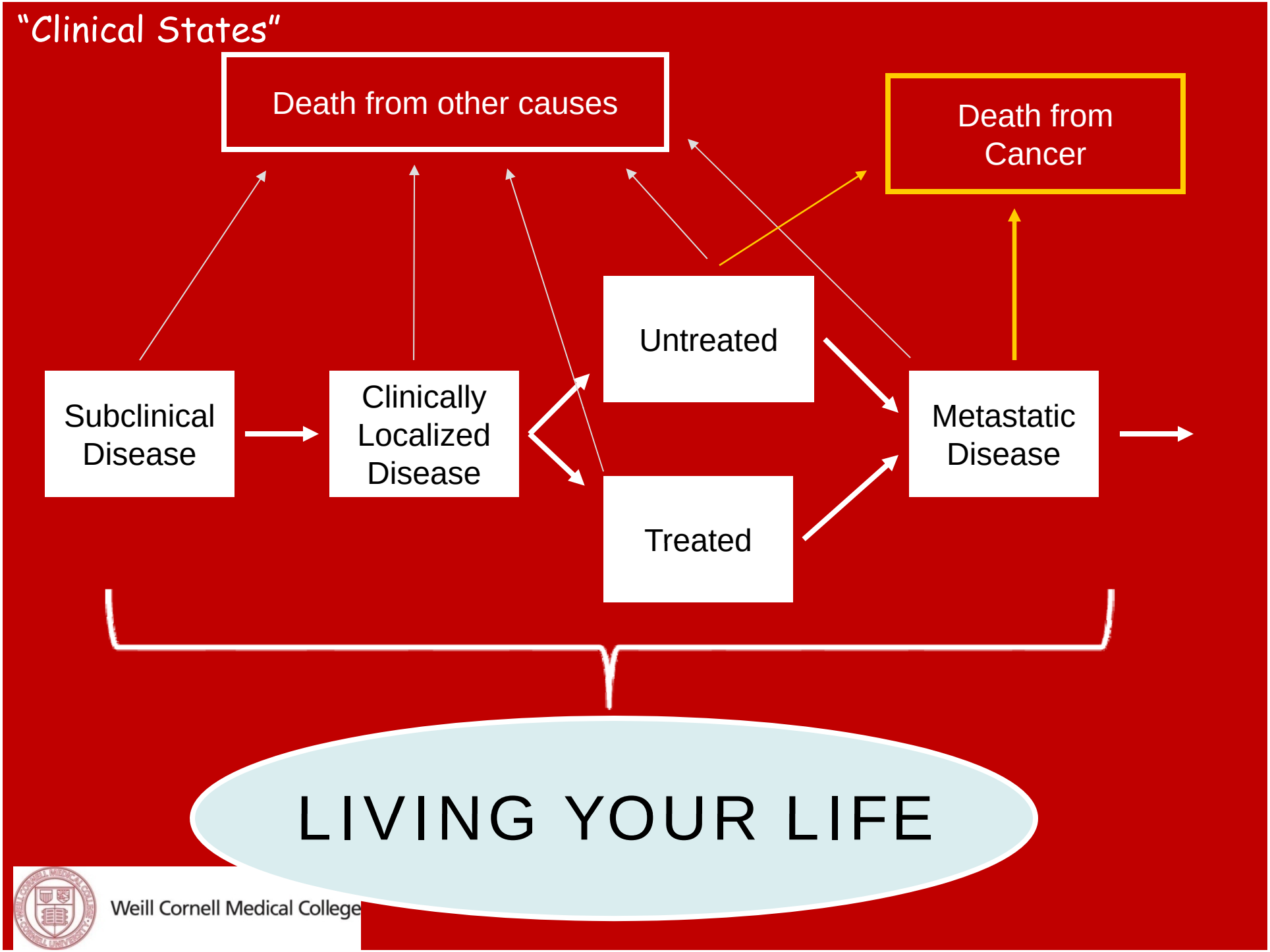
"Clinical States"
Death from other causes
Death from Cancer
Untreated
Subclinical Disease
Clinically Localized Disease
Metastatic Disease
Treated
LIVING YOUR LIFE
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How can I (we) help?

Two very important elements to make progress:

Awareness

and

Funding

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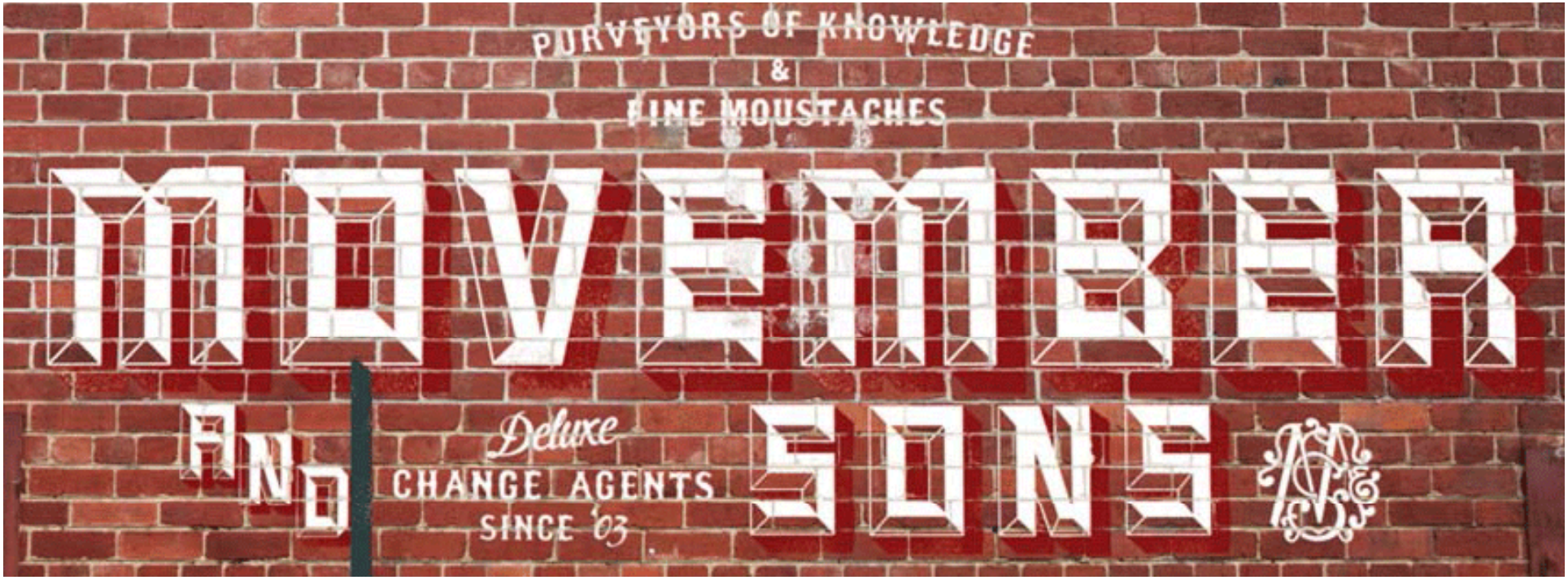
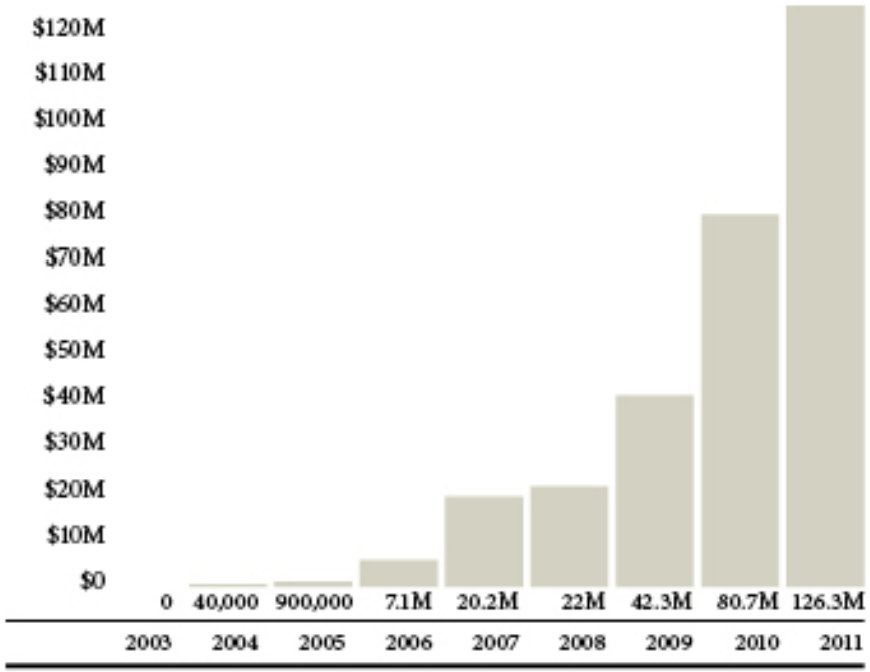


- “Mo” slang for moustache in Australia
- A conversation starter, raises awareness
- Funds raised in the U.S. go towards prostate and testicular cancer initiatives

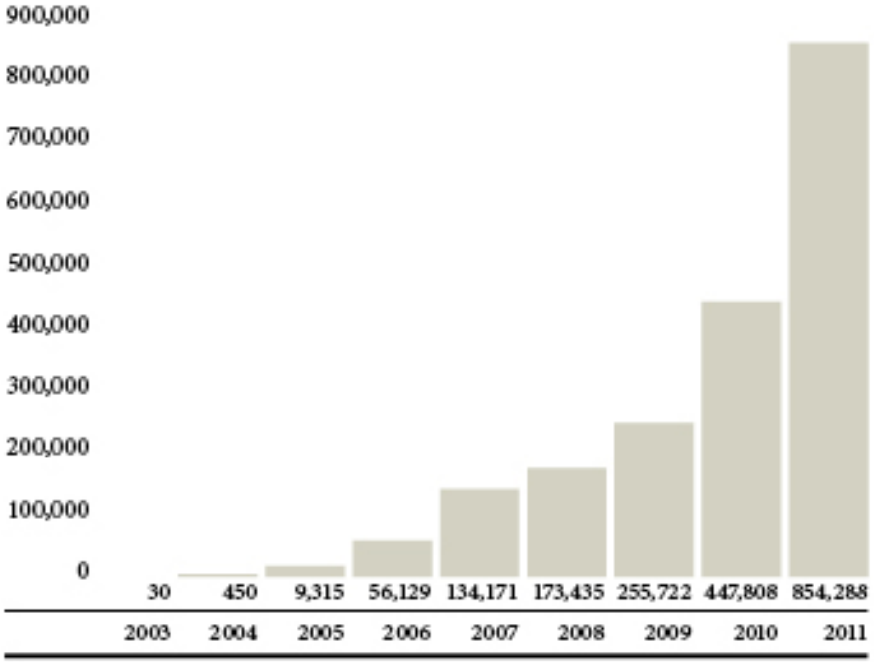
CHANGING THE FACE OF MEN'S HEALTH

MOVEMBER

GLOBAL FUNDS RAISED
$299 MILLION USD... SO FAR



GLOBAL REGISTRANTS
1.9 MILLION MO BROS & MO SISTAS... SO FAR



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