# PSA/Biochemical Recurrence of Prostate Cancer

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# PSA Recurrence- Outline/Key Questions?

- What is “early” PSA recurrence?
  - Are there PSA rises that can go untreated?
- Is “early” salvage EBRT just as good as adjuvant EBRT?
- Should ADT be added to adjuvant/salvage EBRT?
- Are PET scans accurate for early PSA recurrence?
- Are there any pivotal clinical trials now available or soon reading out to help us caring for our patients now or soon?

# Defining Biochemical Recurrence

- Following RP
  - Any detectable PSA>0.1
  - Detectable PSA value >0.4 or 0.5 ng/mL(2)
  - Detectable PSA value >0.2 ng/mL(2,3)
- Following RT

PSA value higher than absolute nadir plus 2 ng/mL (ASTRO-RTOG-Phoenix) (4)

- Relevance

A rising PSA following RP or RT may indicate disease recurrence – local or distant biochemical recurrence represents a starting point for monitoring how PSA values change over time, which can be useful for estimating the risk of metastases

ASTRO=American Society for Therapeutic Radiation and Oncology; RTOG=Radiation Therapy Oncology Group.

1. AUA PSA Best Policy Task Force. Oncology. 2000:14:267-286; 2. Moul JW. J Urol. 2000;163:1632-1642; 3. Freedland SJ, et al. Urology. 2003;61:365-369; 4. Roach M, et al. Int J Radiat Oncol Biol Phys. 2006;65:965-974; 5. Pound CR, et al. JAMA. 1999;281:1591-1597; 6. Lee WR, et al. J Clin Oncol. 1997;15:230-238; 7. Freedland SJ, et al. JAMA. 2005;294:433-439; 8. D'Amico AV, et al. J Clin Oncol. 2002;20:4567-4573

# Definition of "Early PSA Recurrence"
# (By PSA level)

- Confounding variable: Low PSA due to "benign" residual prostate: Best Data from Mayo Clinic (Toussi et al J Urol 2016)
- N=13,512 RP 1987-2010 @ Mayo Clinic
- 5041/13,512 (37.4%) had detectable PSA (0.2) –median 9.1 yr FU
- Continued PSA rise after specified "Cut-point":

  0.2: 61%

  0.3: 67%

  0.4: 74%

***-PSA above 0.4 was best predictor of progression***

# Definition of “Early PSA Recurrence” (By time from surgery)

**Assessing 10-Year Survival**

Consider PSADT, biochemical recurrence and Gleason score.

| | Survival Estimate, % (95% Confidence Interval) | | | |
|---|---|---|---|---|
| | PSA recurrence > 3 years | | PSA recurrence ≤ 3 years | |
| PSADT (months) | Gleason < 8 | Gleason ≥ 8 | Gleason < 8 | Gleason ≥ 8 |
| ≥ 15.0 | 98% (96 - 100) | 96% (93 - 98) | 93% (80 - 98) | 86% (61 - 96) |
| 9.0 - 14.9 | 95% (75 - 99) | 90% (58 - 98) | 85% (49 - 97) | 69% (30 - 92) |
| 3.0 - 8.9 | 84% (62 - 94) | 68% (37 - 89) | 55% (25 - 82) | 26% (7 - 62) |
| < 3.0 | 59% (29 - 83) | 30% (10 - 63) | 15% (3 - 53) | 1% (<1 - 55) |

Source: Freedland SJ, et al.

**Freedland et al /Johns Hopkins (follow up to Pound et al) used less than or equal to 3 years as “early” recurrence in their prognosis nomogram**

# Time to Biochemical Recurrence After RP Predicted Risk of PCSD

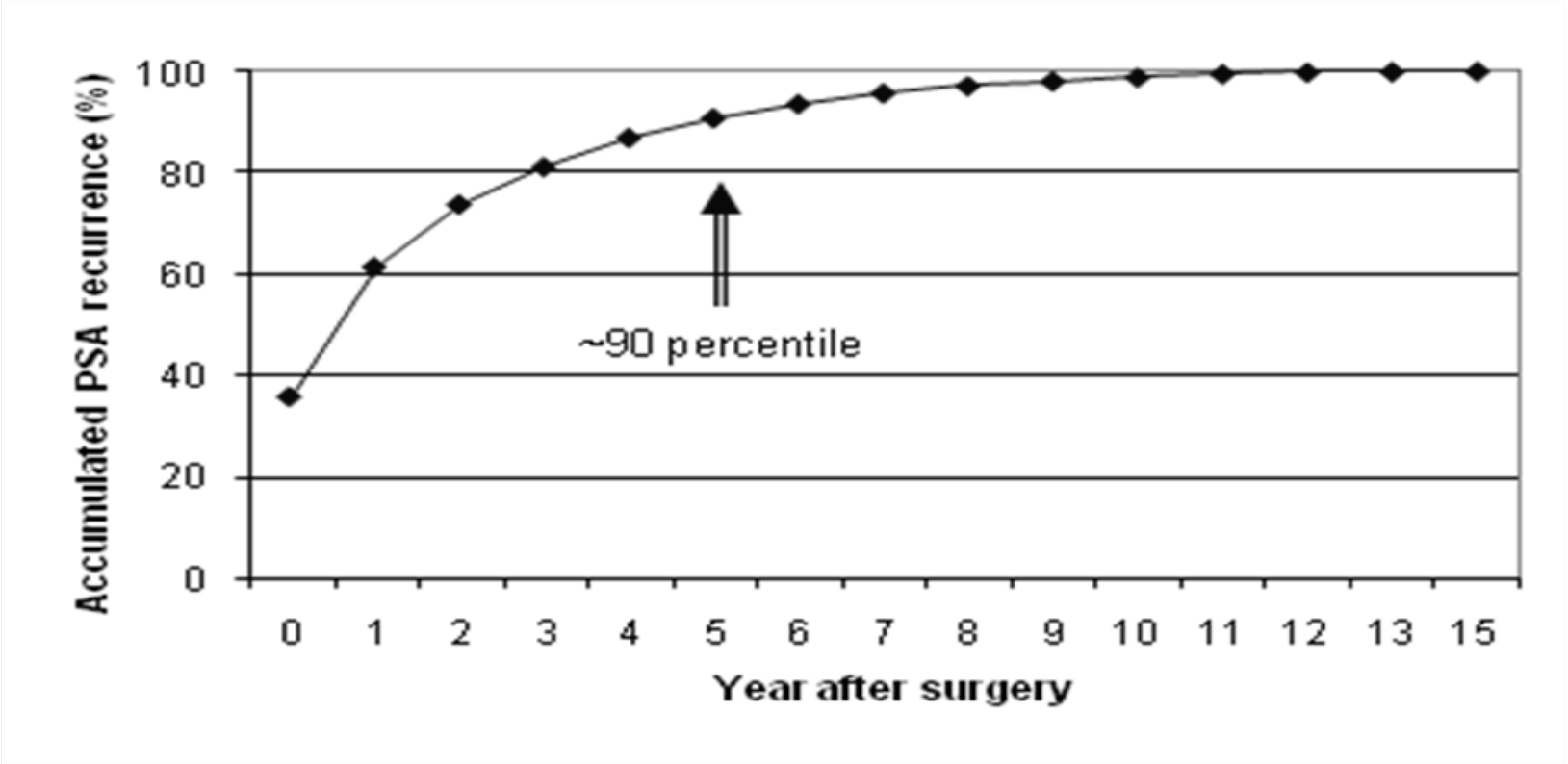
- Each year free of biochemical recurrence represented a 24% reduction in the risk of PCSD (HR=0.76, 95% CI 0.66-0.88; P<.001)
- Survival rate was significantly reduced in patients with time to biochemical Each year free of biochemical recurrence represented a 24% reduction in the risk of PCSD (HR=0.76, 95% CI 0.66-0.88; P<.001)
- Survival rate was significantly reduced in patients with time to biochemical recurrence ≤3 years vs >3 years (P<.001)

| | Time to Biochemical Recurrence† | |
|---|---|---|
| | ≤3 years | >3 years |
| 15-year actuarial survival | 41% | 87% |

Freedland SJ, et al. J Urol. 2006;176:1404-1408

# Duke Prostate Center
# N=4561 RP; 1207 PSAR (31.4%)

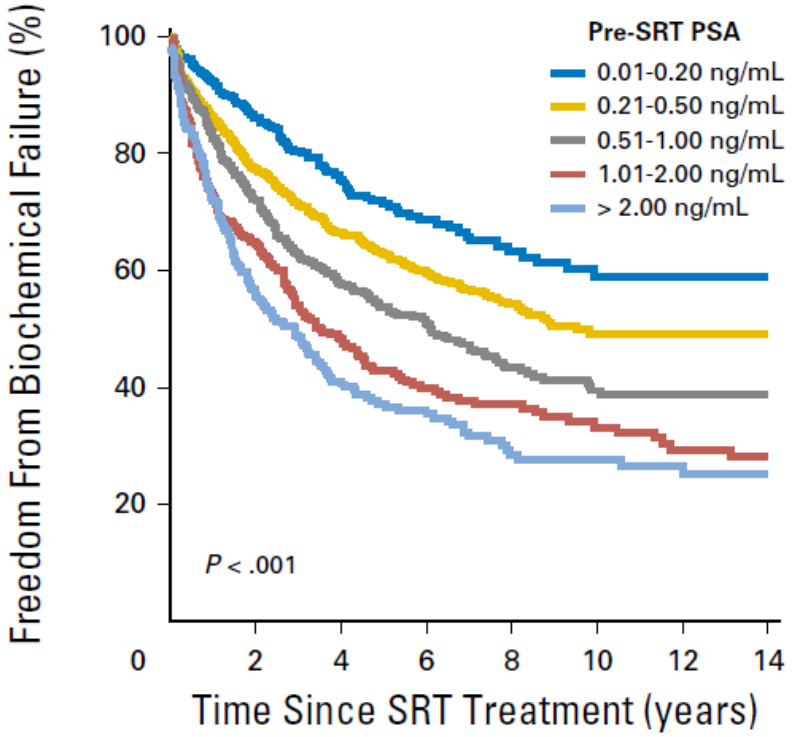
## 90% of recurrences by 5 years

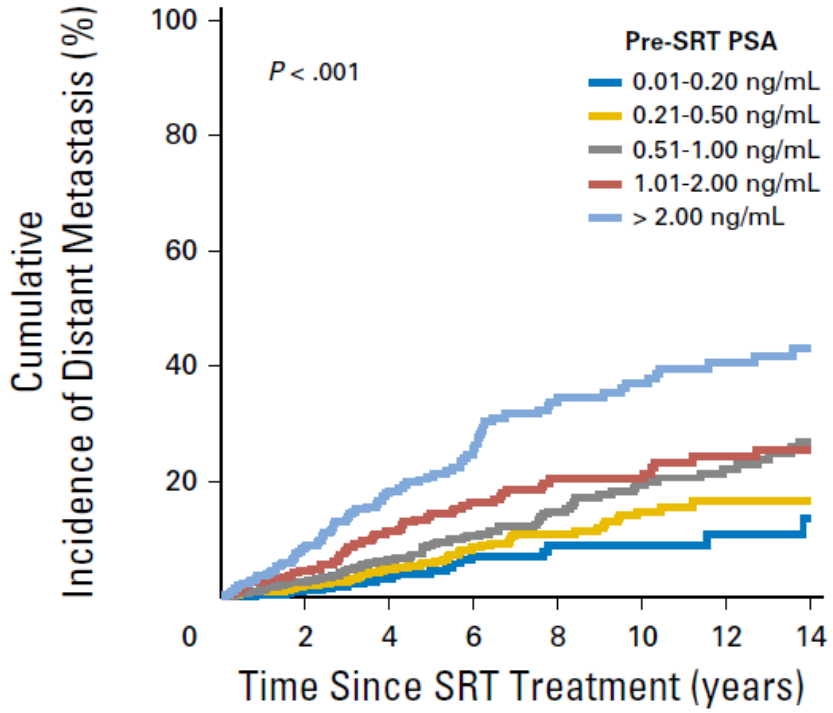



Caire et al. *Urology*74(3):643-47,Sept.2009

Tendulkar RD et al, JCO 2016

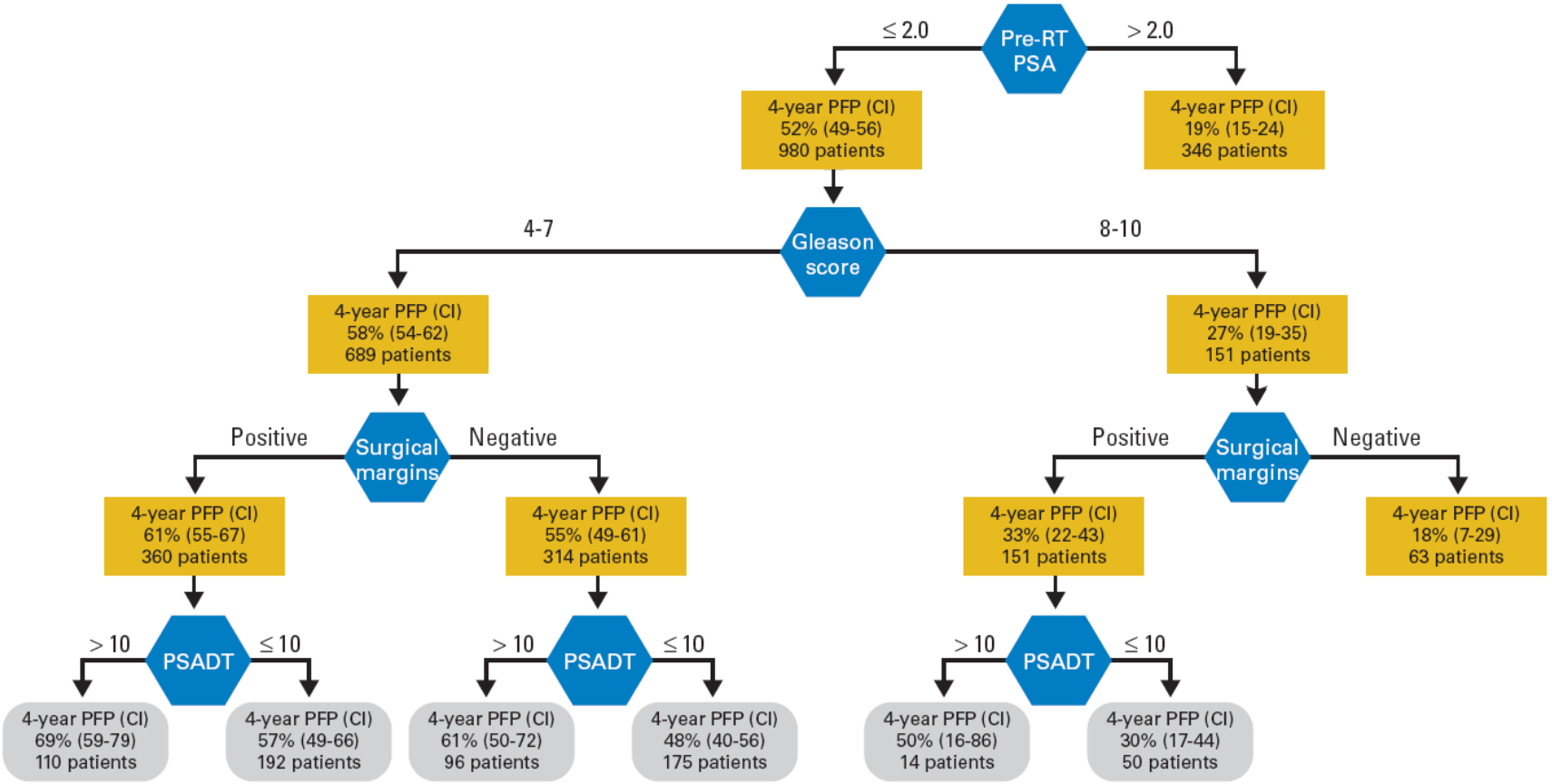
# Benefit of Salvage XRT




- 2,460 patient meta-analysis and prognostic model of node negative men with PSA recurrence after RP, treated with salvage RT
- Improved outcomes seen in those men with lower PSA levels at the time of salvage RT, as were positive margins.
- ECE/SVI and high grade disease were adversely prognostic

# PSA Response to Salvage XRT




Stephenson et al. JCO. 2007

# RTOG 96-01 Schema

**Pre-randomization Stratifications**

**Surgical margins**: positive or not
**Nadir PSA level:** < 0.5: yes or no
**Entry PSA level**: < 1.6 or 1.6 – 4.0
**Pre RP neoadjuvant STAD**: yes or no

RANDOMIZE

**Arm 1** → RT (64.8 Gy) plus AAT* (Bicalutamide 150 mg) QD**

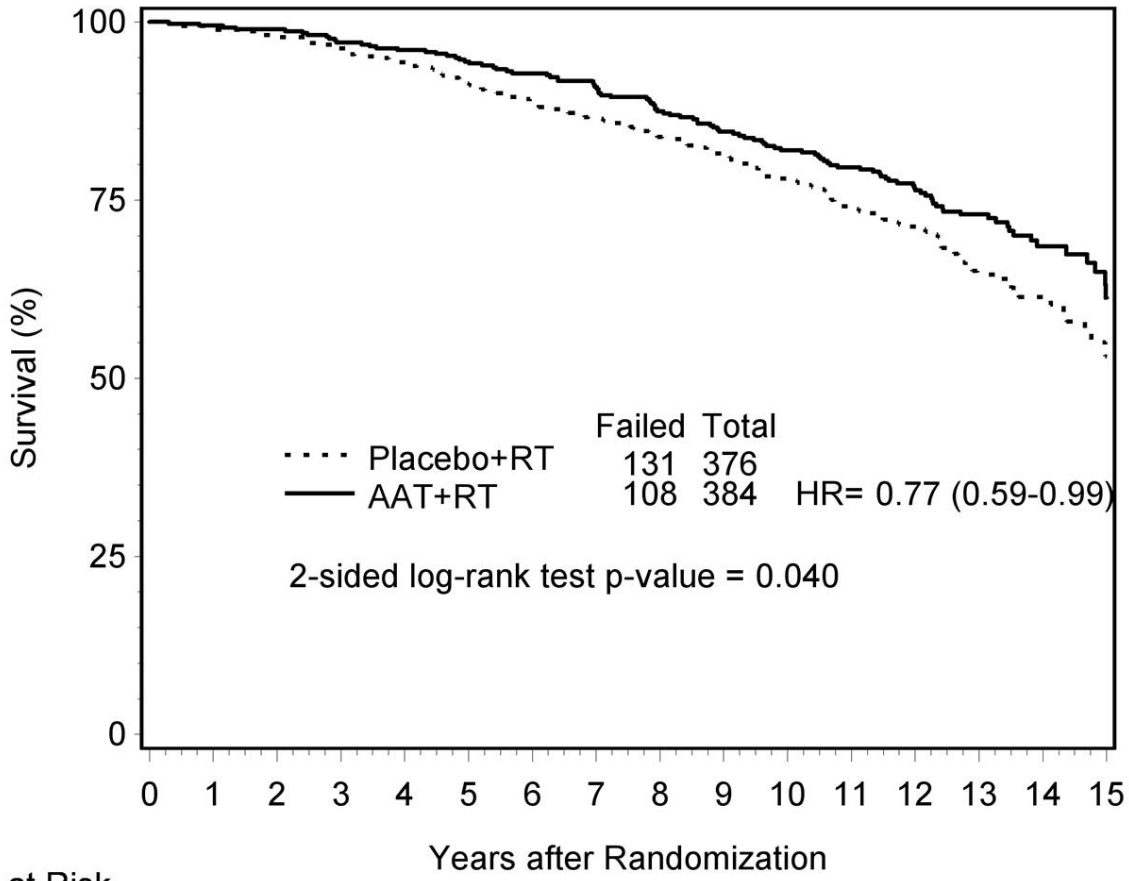
**Arm 2** → RT (64.8 Gy) plus placebo QD**

*AAT: Anti Androgen Therapy (peripheral androgen blockade)

** During and after RT for 24 months

NRG ONCOLOGY™

# Overall Survival




Patients at Risk

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Placebo+RT | 376 | 372 | 368 | 359 | 350 | 332 | 319 | 307 | 294 | 280 | 262 | 240 | 203 | 130 | 71 | 25 |
| AAT+RT | 384 | 382 | 376 | 368 | 362 | 347 | 337 | 326 | 308 | 294 | 280 | 259 | 223 | 151 | 78 | 32 |

**OS at 10 yrs: 82% vs 78%**

**p = 0.040**

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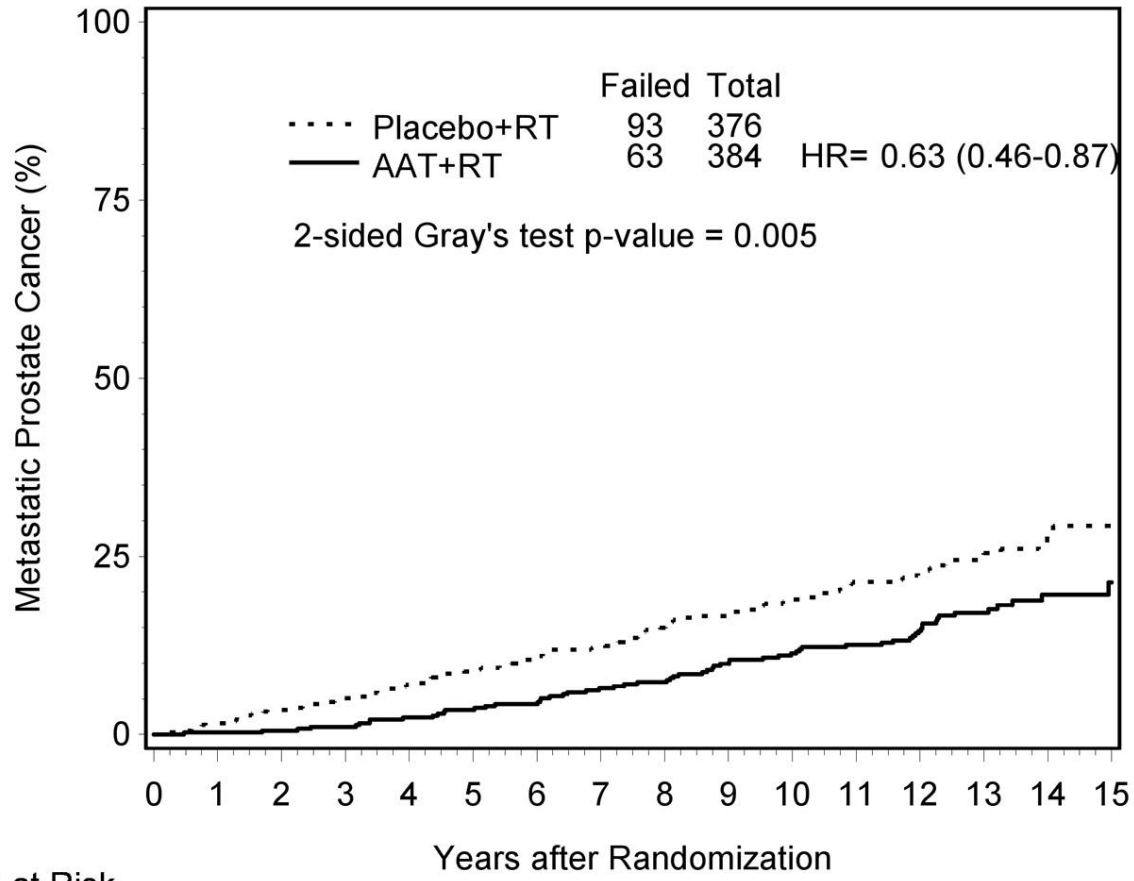
Presented By William Shipley at Genitourinary Cancers Symposium 2016, NEJM 2017

# Time to Metastatic Prostate Cancer




Patients at Risk

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Placebo+RT | 376 | 366 | 357 | 344 | 331 | 314 | 299 | 287 | 268 | 251 | 230 | 208 | 173 | 111 | 58 | 23 |
| AAT+RT | 384 | 381 | 374 | 366 | 355 | 336 | 327 | 309 | 293 | 273 | 255 | 234 | 198 | 131 | 64 | 26 |

**DM from PC at 10 yrs**

**11% vs 19%**

**p = 0.005**

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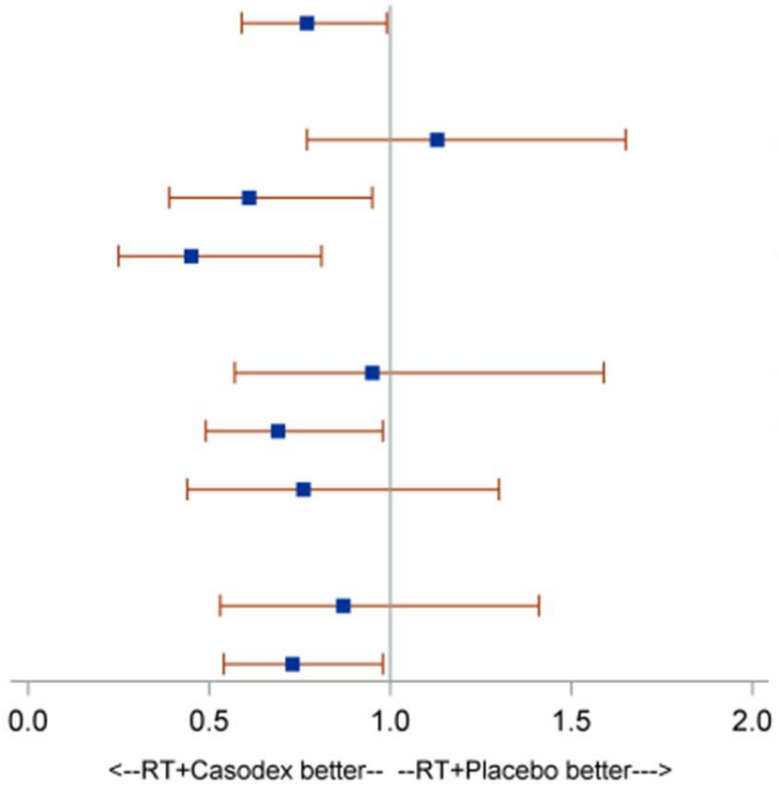
# Overall Survival: Hazard Ratios by Subgroup

| Subgroup | No.of Patients (%) | 10-Yr Overall Survival Rate | | |
|---|---|---|---|---|
| | | RT+Placebo | RT+Casodex | P-Value* |
| **Overall** | 760(100) | 78.0 | 82.0 | 0.040 |
| **Entry Level PSA (ng/ml)** | | | | |
| < 0.7 | 405( 53) | 86.1 | 82.6 | 0.526 |
| 0.7-1.5 | 237( 31) | 73.4 | 83.1 | 0.028 |
| > 1.5 | 118( 16) | 61.5 | 77.4 | 0.007 |
| **Gleason** | | | | |
| 2-6 | 214( 28) | 84.8 | 86.1 | 0.843 |
| 7 | 413( 54) | 76.4 | 83.1 | 0.039 |
| 8-10 | 131( 17) | 72.0 | 71.4 | 0.316 |
| **Surgical Margins** | | | | |
| Negative | 191( 25) | 77.8 | 78.6 | 0.559 |
| Positive | 569( 75) | 78.1 | 83.1 | 0.038 |




*2-sided log-rank test.

NRG ONCOLOGY™

Presented By William Shipley at Genitourinary Cancers Symposium 2016, NEJM 2018

# RTOG 0534 (SPPORT Trial)

| | | | |
|---|---|---|---|
| **S**<br>**T**<br>**R**<br>**A**<br>**T**<br>**I**<br>**F**<br>**Y** | **SV Involvement**<br>1. No<br>2. Yes<br><br>**Prostatectomy Gleason Score**<br>1. Gleason ≤ 7<br>2. Gleason 8-9<br><br>**Pre-Radiotherapy PSA**<br>1. PSA ≥ 0.1 and ≤ 1.0 ng/mL<br>2. PSA > 1.0 and < 2.0 ng/mL<br><br>**Pathology Stage**<br>1. pT2 and margin negative<br>2. All others | **R**<br>**A**<br>**N**<br>**D**<br>**O**<br>**M**<br>**I**<br>**Z**<br>**E** | **Arm 1: PBRT Alone**<br>PBRT 64.8-70.2 Gy<br><br>**Arm 2: PBRT + STAD**<br>PBRT 64.8-70.2 Gy + STAD for 4-6 months beginning 2 months before RT<br><br>**Arm 3: PLNRT + PBRT + STAD**<br>PLNRT to 45 Gy and PBRT to 64.8-70.2 Gy,+ STAD for 4-6 months beginning 2 months before RT |

SV = seminal vesicle; RT = radiotherapy; PBRT = prostate bed RT; PLNRT = pelvic lymph node RT; STAD = neoadjuvant and concurrent short term androgen deprivation

**FFP defined as first occurrence of:**

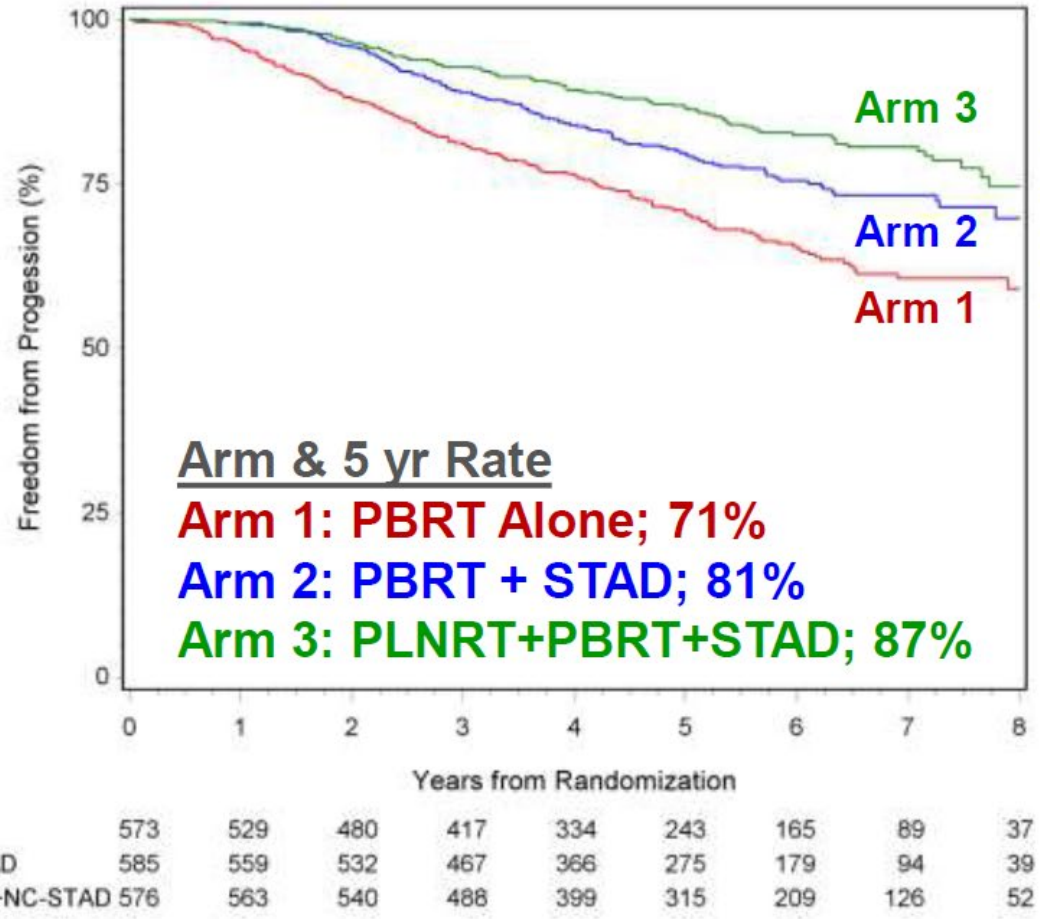
- PSA ≥ Nadir+2 ng/mL
- Clinical progression
  - Local, regional, and distant
- Death due to any cause

Primary endpoint: FFP at 5 years, anticipated 10% improvement with ADT and 20% with pelvic RT + 4-6 mo STADT plus 1st gen anti-androgen (n=1764)

Pollack A et al ASTRO 2018

# RTOG 0534 Results

## FFP: All Eligible Patients




| No. at Risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| PBRT Alone | 573 | 529 | 480 | 417 | 334 | 243 | 165 | 89 | 37 |
| PBRT+NC-STAD | 585 | 559 | 532 | 467 | 366 | 275 | 179 | 94 | 39 |
| PLNRT+PBRT+NC-STAD | 576 | 563 | 540 | 488 | 399 | 315 | 209 | 126 | 52 |

**5 yr Rate Comparison**

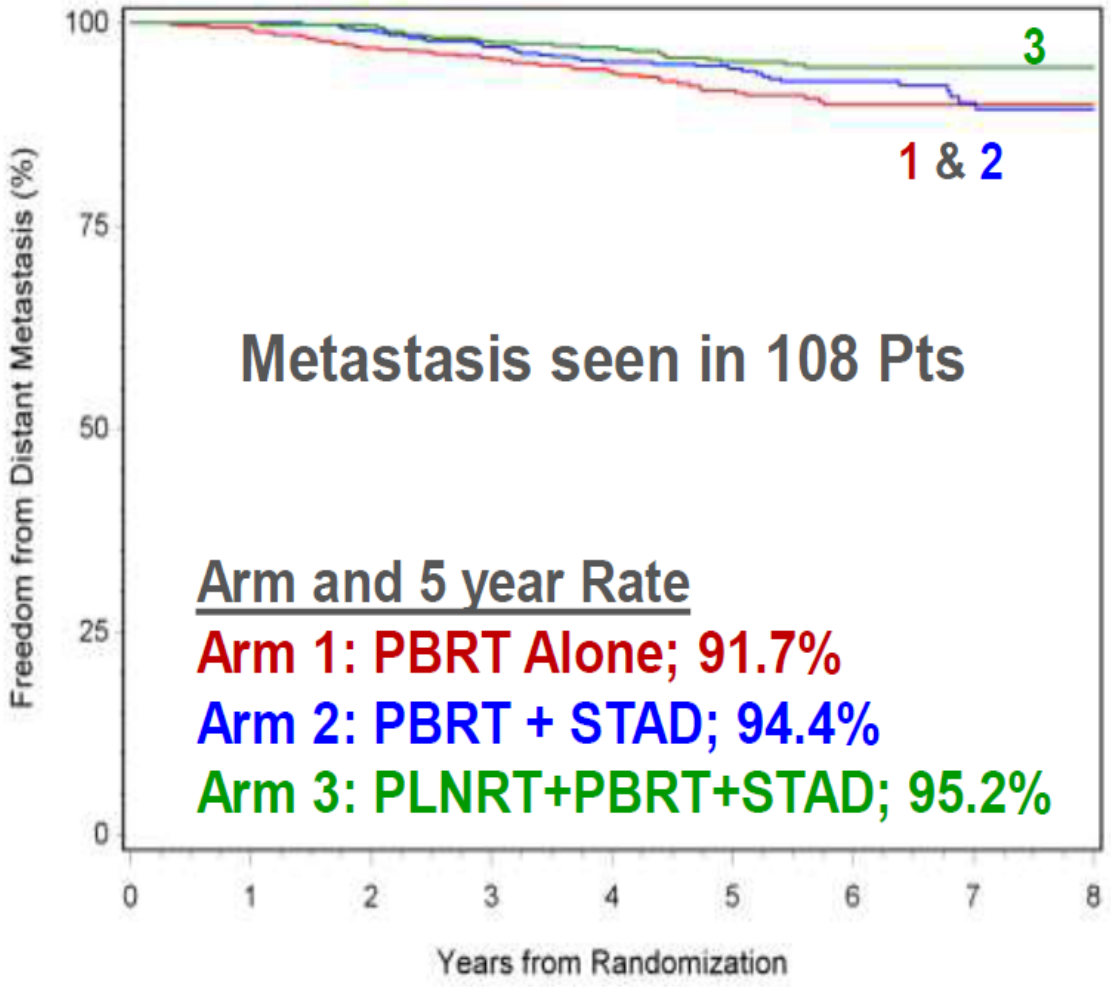
Arm 3 vs Arm 1: p<0.0001
Arm 2 vs Arm 1: p<0.0001
Arm 3 vs Arm 2: p=0.0039

**HRs and 97.5% CIs**

3 vs 1: 0.45 (0.34-0.61)
2 vs 1: 0.62 (0.47-0.82)
3 vs 2: 0.71 (0.52-0.98)

No benefits to pelvic RT if PSA<0.34 and benefits of pelvic RT overall have not yet met prespecified criteria
Benefits with ADT in all subsets

# Metastasis Free Survival




**5 yr Rate Comparison**

Arm 3 vs Arm 1: p=0.014

Arm 2 vs Arm 1: p=0.05

Arm 3 vs Arm 2: p=0.28

**HRs and 97.5% CIs**

3 vs 1: 0.52 (0.30-0.92)

2 vs 1: 0.81 (0.49-1.33)

3 vs 2: 0.64 (0.36-1.14)

- No statistically significant differences in OS

# Toxicities of Pelvic RT

Early

| | PBRT Alone (n=557) | | PBRT+STAD (n=568) | | PLNRT+PBRT+STAD (n=567) | | p-value |
|---|---|---|---|---|---|---|---|
| Type | n | % | n | % | n | % | |
| **GI** | | | | | | | |
| Grade 2+ | 11 | 2.0 | 22 | 3.9 | 39 | 6.9 | **<0.001** |
| Grade 3+ | 1 | 0.2 | 5 | 0.9 | 4 | 0.7 | 0.37 |
| **Renal/GU** | | | | | | | |
| Grade 2+ | 54 | 9.7 | 68 | 12.0 | 69 | 12.3 | 0.35 |
| Grade 3+ | 5 | 0.9 | 5 | 0.9 | 8 | 1.5 | 0.70 |
| **Blood/Bone Marrow** | | | | | | | |
| Grade 2+ | 13 | 2.3 | 10 | 1.8 | 29 | 5.1 | **0.002** |
| Grade 3+ | 3 | 0.5 | 1 | 0.2 | 15 | 2.6 | **<0.001** |

Late

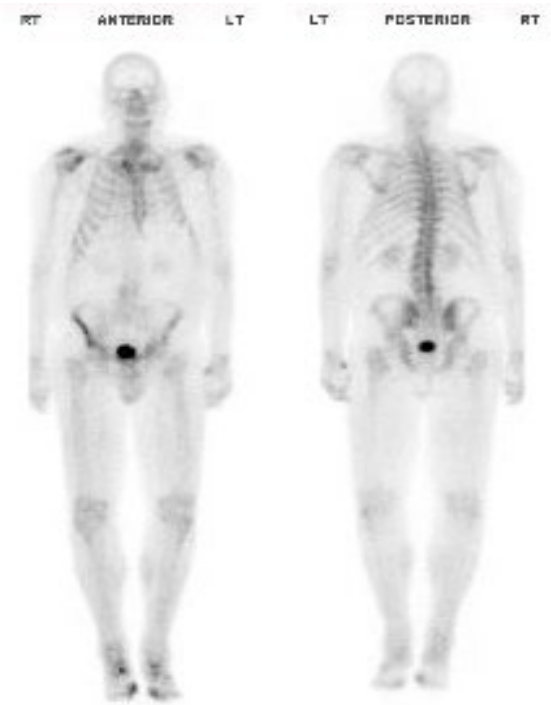
| | PBRT Alone (n=557) | | PBRT+STAD (n=571) | | PLNRT+PBRT+STAD (n=570) | | p-value |
|---|---|---|---|---|---|---|---|
| Type | n | % | n | % | n | % | |
| **GI** | | | | | | | |
| Grade 2+ | 54 | 9.7 | 50 | 8.8 | 46 | 8.1 | 0.63 |
| Grade 3+ | 4 | 0.7 | 2 | 0.4 | 6 | 1.1 | 0.34 |
| **Renal/GU** | | | | | | | |
| Grade 2+ | 188 | 33.8 | 184 | 32.2 | 197 | 34.6 | 0.70 |
| Grade 3+ | 24 | 4.4 | 28 | 4.9 | 34 | 6.0 | 0.44 |
| **Blood/Bone Marrow** | | | | | | | |
| Grade 2+ | 17 | 3.1 | 9 | 1.6 | 23 | 4.1 | **0.044** |
| Grade 3+ | 2 | 0.4 | 1 | 0.2 | 6 | 1.1 | 0.12 |

# Novel PET Tracers for Staging

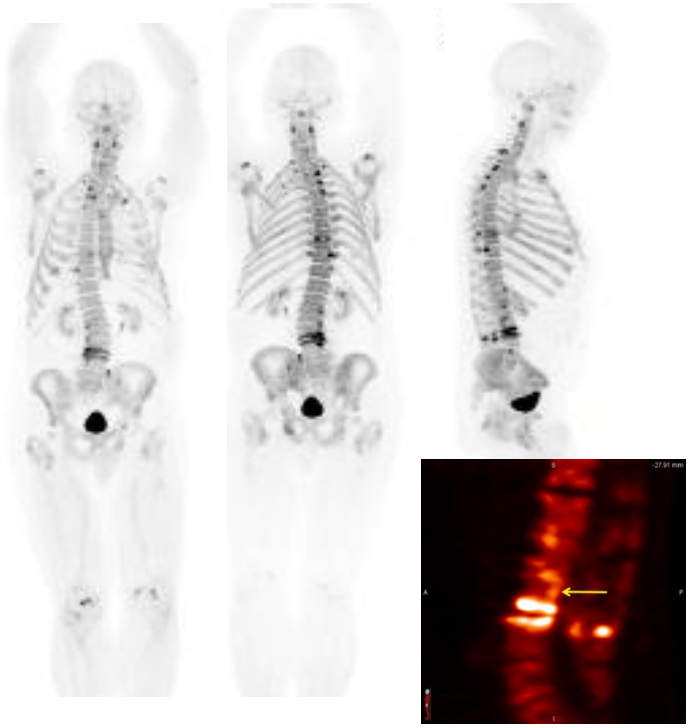
- F-18 NaF: bone imaging
- FDG:  useful for NEPC, aggressive tumors
- PSMA: useful for low PSA recurrences, but negative in NEPC
- Axumin (fluciclovine): useful for low PSA recurrences

# NaF-PET/CT has improved sensitivity for the detection of bone metastases

**$^{99m}$Tc MDP**




**$^{18}$F NaF PET CT**



Iagaru A et al. Mol Imaging Biol. 2011 Apr 9; Source: Duke patient at similar time points

# Change Patient Management

## $^{18}$F-Fluoride PET Used for Treatment Monitoring of Systemic Cancer Therapy: Results from the National Oncologic PET Registry

Bruce E. Hillner[1], Barry A. Siegel[2], Lucy Hanna[3], Fenghai Duan[3], Bruce Quinn[4], and Anthony F. Shields[5]

*[1]Department of Internal Medicine and the Massey Cancer Center, Virginia Commonwealth University, Richmond, Virginia; [2]Division of Nuclear Medicine, Mallinckrodt Institute of Radiology and the Siteman Cancer Center, Washington University School of Medicine, St. Louis, Missouri; [3]Department of Biostatistics and Center for Statistical Sciences, Brown University School of Public Health, Providence, Rhode Island; [4]Foley Hoag LLC, Boston, Massachusetts; and [5]Karmanos Cancer Institute, Wayne State University, Detroit, Michigan*

**Changed patient management in 40% patients**

Hillner B et al. J Nucl Med 2015; 56: 222-228

# NaF PET/CT registry (NOPR)

- 3,531 evaluable scan/events for prostate cancer, 1024 of which were for initial staging, 1,997 for suspected bone metastases, and 510 for suspected progression of bone metastases
- 62% of men were asymptomatic for initial staging, but 85+% were symptomatic for re-staging or for suspected bone met indications

| Treatment plan | | Initial staging ($n$ = 1,024) | Suspected FOM ($n$ = 1,997) | Suspected POM ($n$ = 510) |
|---|---|---|---|---|
| Before PET | After PET | | | |
| Nontreatment | Nontreatment | 183 (17.9) | 777 (38.9) | 122 (23.9) |
| Treatment | Treatment | 363 (35.4) | 339 (17.0) | 123 (24.1) |
| Nontreatment | Treatment | 424 (41.4) | 703 (35.2) | 239 (46.9) |
| Treatment | Nontreatment | 54 (5.3) | 178 (8.9) | 26 (5.1) |
| Rate of change in management | | 46.7% (95% CI, 43.6–49.7) | 44.1 (95% CI, 41.9–46.3) | 52.0 (95% CI, 47.6–56.3) |
| Imaging-adjusted rate* | | 12.2% (95% CI, 10.2–14.2) | 15.8 (95% CI, 14.2–17.4) | 12.4 (95% CI, 9.5–15.2) |

| | Initial staging | |
|---|---|---|
| Intended management (%) | Pre-PET | Post-PET |
| Watch | 7.6 | 14.2 |
| Image | 49.8 | 5.9 |
| Biopsy | 1.9 | 3.1 |
| Treatment | 40.7 | 76.9 |

# Post-PET/CT Changes in Management

NaF PET Findings, Post-PET Extent of Disease, and Treatments Planned

| Characteristic | Initial staging ($n$ = 1,024) | Suspected FOM ($n$ = 1,997) | Suspected POM ($n$ = 510) |
|---|---|---|---|
| NaF PET findings (%) | | | |
| Benign | 71.0 | 52.0 | 16.1 |
| Equivocal | 8.5 | 8.0 | 1.6 |
| Probable | 6.3 | 11.0 | 5.9 |
| Definite | 13.9 | 29.0 | 76.5 |
| Unifocal | 2.0 | 3.4 | 3.3 |
| Multifocal | 8.7 | 19.0 | 47.8 |
| Diffuse | 3.2 | 6.7 | 25.3 |
| Avoid diagnostic tests (%) | 69.3 | 75.2 | 79.6 |
| Avoid invasive procedures (%) | 51.3 | 58.7 | 55.9 |
| Treatment* | 76.9 | 52.2 | 71.0 |
| Local therapies | 58.6 | 10.5 | 2.4 |
| Surgery | 18.5 | 1.8† | 0.4§ |
| Radiotherapy | 52.2 | 10.5 | 3.7 |
| Directed at bone | 10.8 | 19.3 | 39.2 |
| Radiotherapy | 5.3 | 7.8 | 15.3 |
| Radiopharmaceutical therapy | 0.1‡ | 1.1 | 2.4 |
| Bisphosphonates | 6.7 | 11.5 | 27.8 |
| Systemic therapies | 38.0 | 41.6 | 61.4 |
| Hormonal | 35.4 | 32.3 | 40.8 |
| Chemotherapy | 7.9‡ | 13.5 | 29.0 |
| Immunotherapy | 2.4‡ | 6.2§ | 7.6§ |

# Limitations of Existing Data with 18-F NaF PET/CT

- Reproducibility in community sites and even between academic centers, uncertainty about which SUV metric to use (mean, max, etc)
- Variability in quality and interpretation may limit generalizability of clinical utility (Line C et al, JNM 2016)
- Numbers of patients analyzed and compared to Tc-99 bone scans is limited, but existing data suggest greater sensitivity than CT or BS 60-70% vs. >90%
- No data exist showing improved outcomes in patients who receive more sensitive bone imaging and it is unclear whether clinical management should be changed
  - i.e. perhaps local therapy SHOULD be offered to met with oligometastatic HSPC

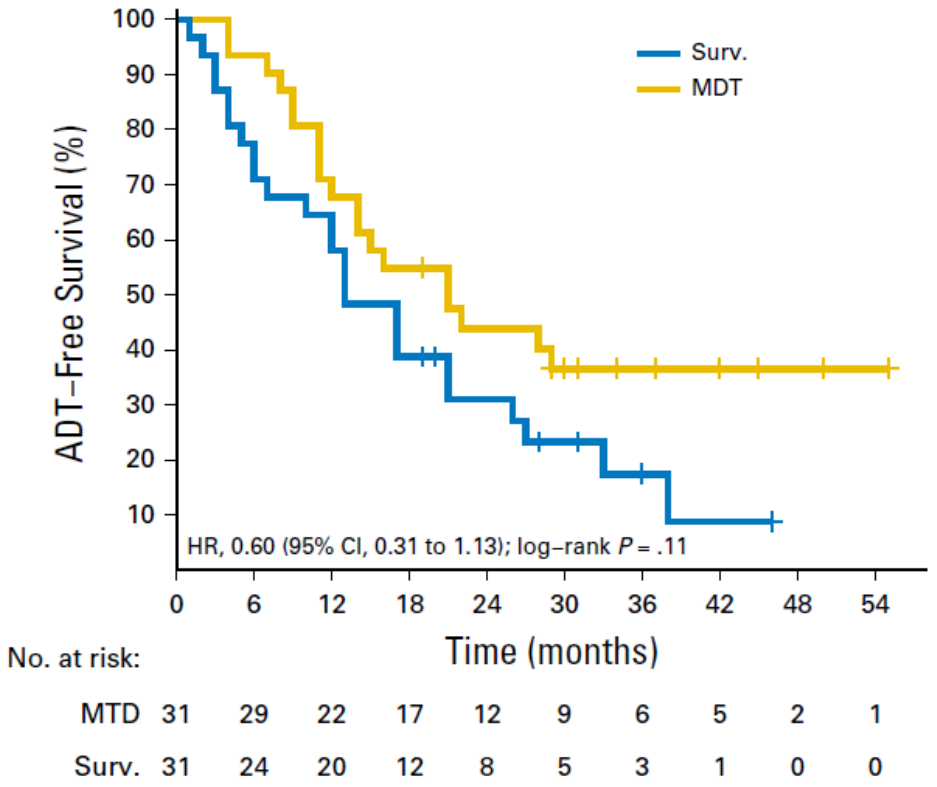
Minamimoto R JNM 2015;
Jambor I Acta Oncol 2016

# 18F-FACBC (Fluciclovine)

- Only approved in the PSA recurrent setting
- Limited sensitivity in PSA<1.0 setting, where salvage RT treatment decisions are most important!
- Unclear benefits of finding small volume nodal metastases missed on standard CT/MRI
  - Could mean early ADT which is of unclear benefits and could result in harms
  - Could mean radical nodal dissections or radiation which is of unclear benefits and could result in harms
  - Cases presented of reductions in PSA after targeted therapies, but also of missed pathologically proven nodes and further recurrences in negative nodes over time

# Radiation to PET involved sites?

- PET-directed SBRT has only limited efficacy in selected men, with perhaps 20-30% of men having sustained responses (STOMP trial)
- One randomized trial showed a modest delay in the need for ADT
- Ongoing studies are assessing broader radiation fields based on PET imaging




Ost et al JCO 2017

# Fluciclovine vs. Prostascint

| | Anti-3-[$^{18}$F]FACBC | $^{111}$In-Capromab Pendetide | p Value |
|---|---|---|---|
| Prostate/bed (91 pts): | | | |
| No. true pos | 55 | 41 | — |
| No. true neg | 12 | 17 | — |
| No. false-pos | 18 | 13 | — |
| No. false-neg | 6 | 20 | — |
| % Sensitivity (95% CI) | 90.2 (79.8, 96.3) | 67.2 (54.0, 78.7) | 0.002 |
| % Specificity (95% CI) | 40.0 (22.7, 59.4) | 56.7 (37.4, 74.5) | 0.182 |
| % Accuracy (95% CI) | 73.6 (63.3, 82.3) | 63.7 (53.0, 73.6) | <0.001 |
| % PPV (95% CI) | 75.3 (63.9, 84.7) | 75.9 (62.4, 86.5) | 0.530 |
| % NPV (95% CI) | 66.7 (41.0, 86.7) | 45.9 (29.5, 63.1) | 0.074 |
| Extraprostatic (70 pts): | | | |
| No. true pos | 22 | 4 | — |
| No. true neg | 29 | 26 | — |
| No. false-pos | 1 | 4 | — |
| No. false-neg | 18 | 36 | — |
| % Sensitivity (95% CI) | 55.0 (38.5, 70.7) | 10.0 (2.8, 23.7) | <0.001 |
| % Specificity (95% CI) | 96.7 (82.8, 99.9) | 86.7 (69.3, 96.2) | 0.248 |
| % Accuracy (95% CI) | 72.9 (60.9, 82.8) | 42.9 (31.1, 55.3) | 0.003 |
| % PPV (95% CI) | 95.7 (78.1, 99.9) | 50.0 (15.7, 84.3) | 0.001 |
| % NPV (95% CI) | 61.7 (46.4, 75.5) | 41.9 (29.5, 55.2) | 0.021 |

Higher false + rate, but lower false – rate for prostate/bed recurrence, improvement in extraprostatic staging (nodes) using histologic verification or consensus clinical review

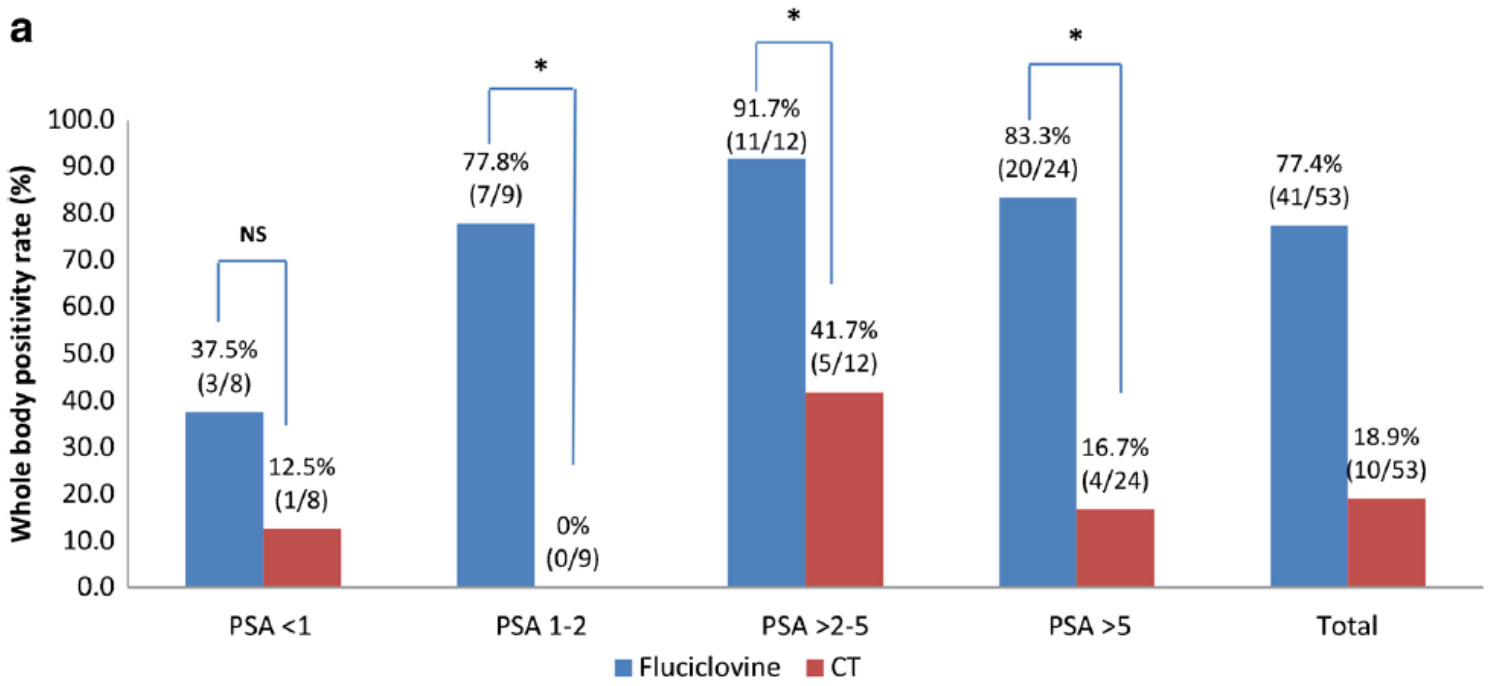
Schuster DM et al J Urol 2014

# Change in Management?

- Prospective trial (n=44 of 87 salvage RT patients) of FACBC PET/CT at Emory University
- 41% of men had RT decision changed by results (17/42), 5% due to extrapelvic metastases, 15 (36%) with broader pelvic field, 27% to narrower prostate bed only field
- Unknown if outcomes were improved in these patients because of the test
- Appears more sensitive than standard clinical CT based on small studies (n=53) using histologic verification (gold standard)
  - Se 89%, Sp 56% (PET) vs. 11%, 87% (CT) for prostate bed
  - Se 46%, Sp 100% (PET) vs 25% and 100% (CT) for extraprostatic sites
  - CT with contrast improved Se to 17-19%, Sp 82-100%

Akin-Akintayo OO et al Clin Nucl Med 2017

# FACBC vs CT: More Sensitive across PSA values

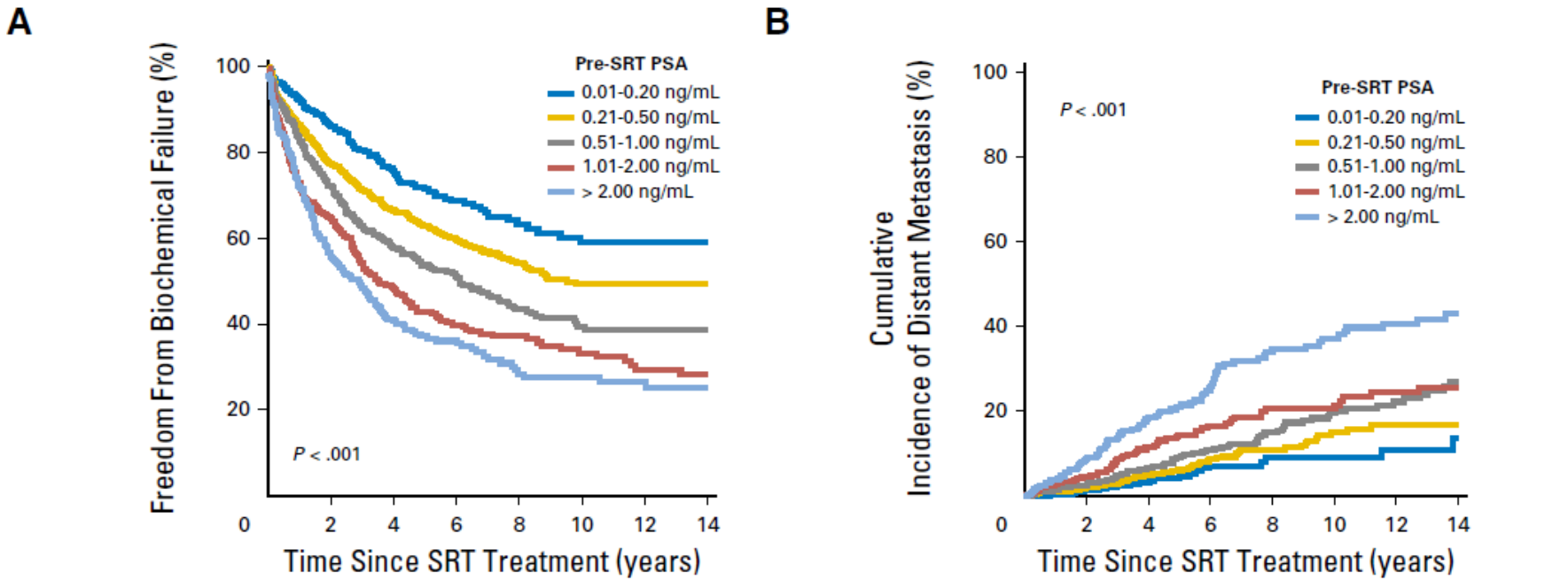



Akin-Akintayo OO et al Clin Nucl Med 2017

# Discussion

- FACBC is generally concordant with (11)C Choline but discordances have been observed in either direction for node/bone metastases
  - Nanni C et al Eur J Nucl Med Mol Imaging 2016
  - Similar Se 32-37%, Sp 40 vs 67% (favoring FACBC) with greater PPV even with low PSA values
  - Both tracers tend to be insensitive at low PSA values when decisions around salvage RT after RP are made
- FACBC PET/CT could be considered along with 11C Choline as an alternative to CT imaging post-local therapy for re-staging given the poor performance of CT
  - Cost-effectiveness has not been demonstrated
  - Clinical utility has not been demonstrated

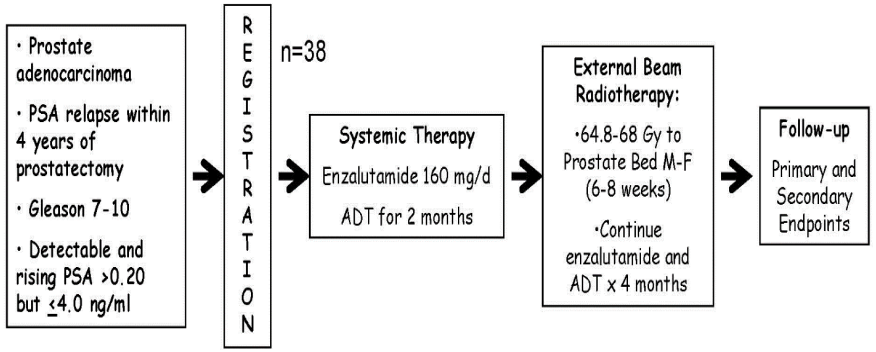
# Early salvage RT is critical especially at PSA values where novel PET tracers have not demonstrated sensitivity!



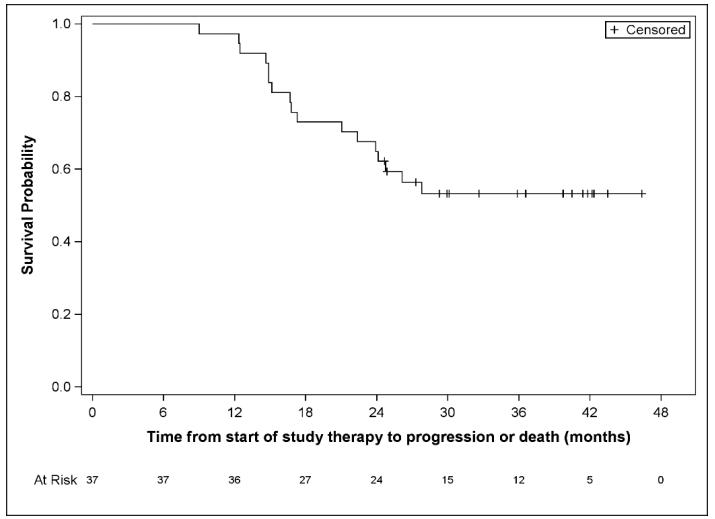

Tendulkar RD et al JCO 2016

# Novel AR Inhibition with Salvage RT

Duke STREAM Phase 2 Trial




| Baseline Characteristics | Value, % (n=38) |
|---|---|
| Age, median years (range) | 64 (range 39-76) |
| Race: white/black/other (%) | 90/8/2 |
| Gleason Sum 8-10 (%) | 47% |
| Karnofsky Score ≥90 (%) | 97% |
| N1 disease at RP (%) | 21% |
| Median PSA ng/ml at study entry (range) | 0.40 (0.19-4.19) |
| pT stage: T2 | 21% |
| T3a | 40% |
| T3b | 32% |
| T4 | 5% |
| Positive margins (%) | 47% |
| Time since RP, year (Range) | 1.1 (0.2, 6.9) |




- Primary endpoint of 2 year PFS was 65%, exceeding historic data in a similar population of men treated with RT/docetaxel alone by 15%
- No new safety signals and 37 men were able to complete salvage RT
- Toxicities included HTN, fatigue and recovery of baseline QOL by 12 mo
- Has led to ongoing phase 2 and 3 trials (STARTAR and NRG GU006)

Armstrong AJ et al GU Symposium 2019 abstract 29

# My approach to salvage therapy

- Enrollment in clinical trials is needed to address critical questions
  - 6-24 months of ADT or bicalutamide is reasonable to reduce risk of PSA recurrence, metastases, and death
- Adjuvant RT should be deferred until incontinence resolves (3-6 months post RP)
- Outside of trial, I discuss risks/benefits of early vs deferred radiation (adjuvant vs. early salvage) and follow men closely with PSA every 3 months post-op for several years, restage upon recurrence
- Consider novel PET imaging but value of PET-directed RT remains investigational
- For N+ men, ADT is reasonable but controversial whether to do immediately or based on PSA trigger


Thank you!
Duke Cancer Institute