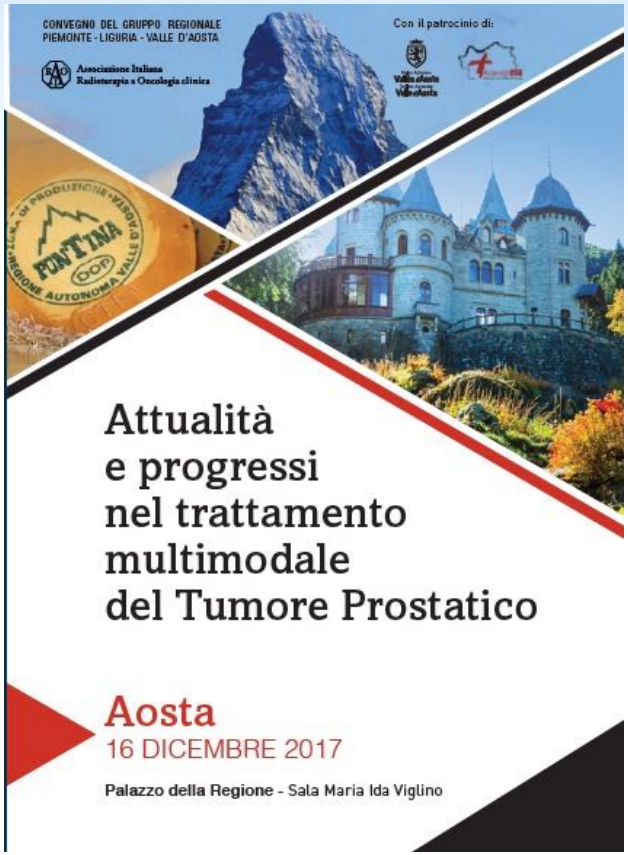


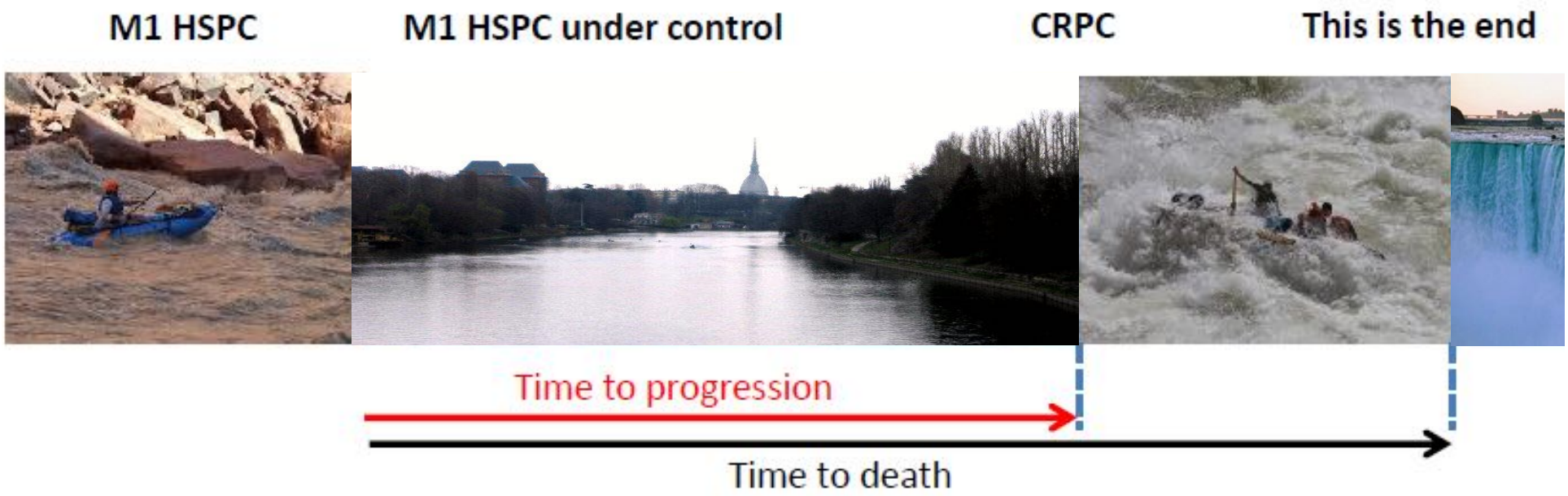

# Nuove prospettive della terapia della malattia sensibile alla castrazione

**Marcello Tucci**
**SCDU Oncologia Medica**
**Azienda Ospedaliero Universitaria San Luigi di Orbassano**
**Università degli studi di Torino**

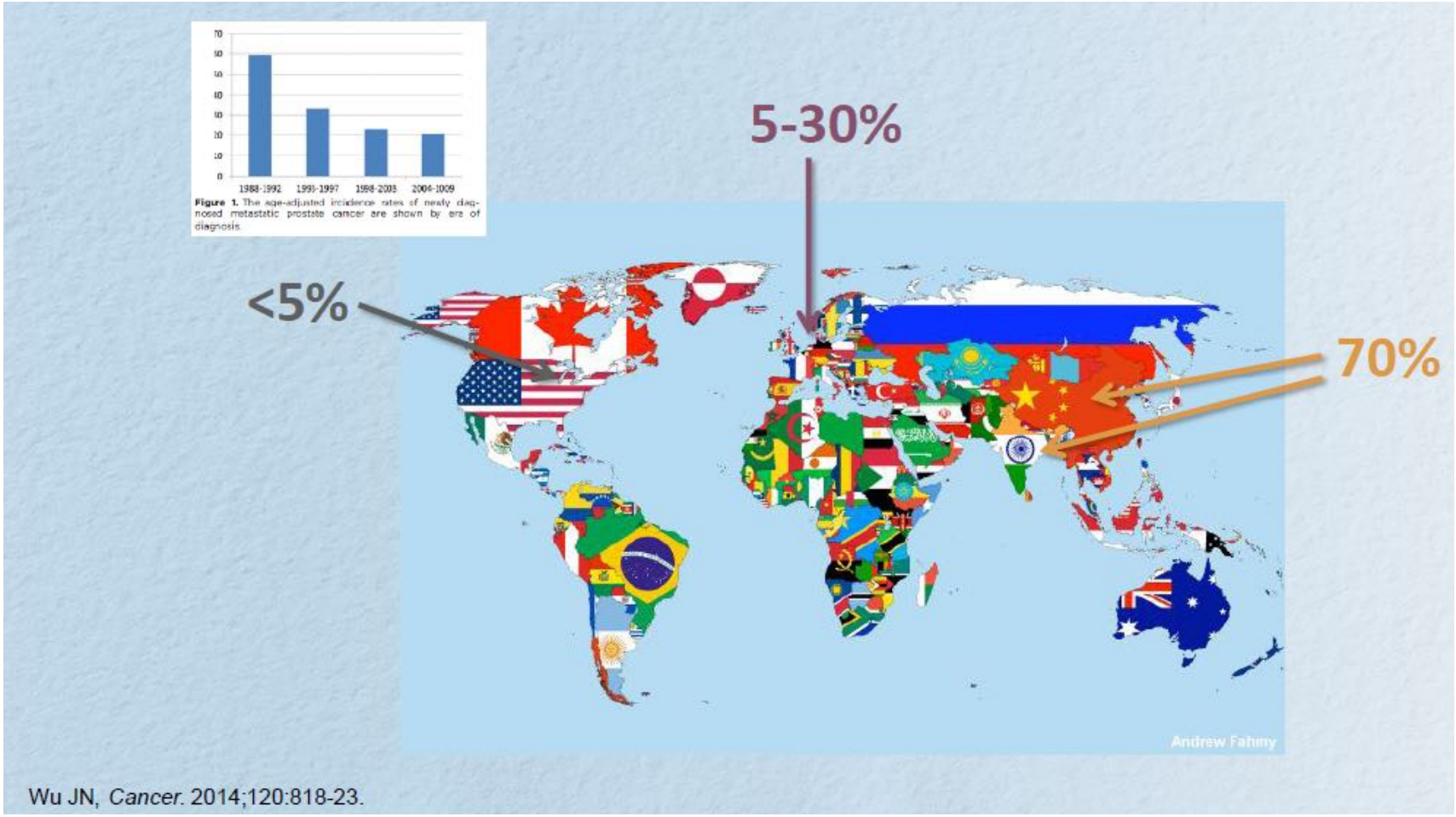
# The natural history of metastatic, hormone-naive prostate cancer

# The natural history of metastatic, hormone-naive prostate cancer

## THE HOPE

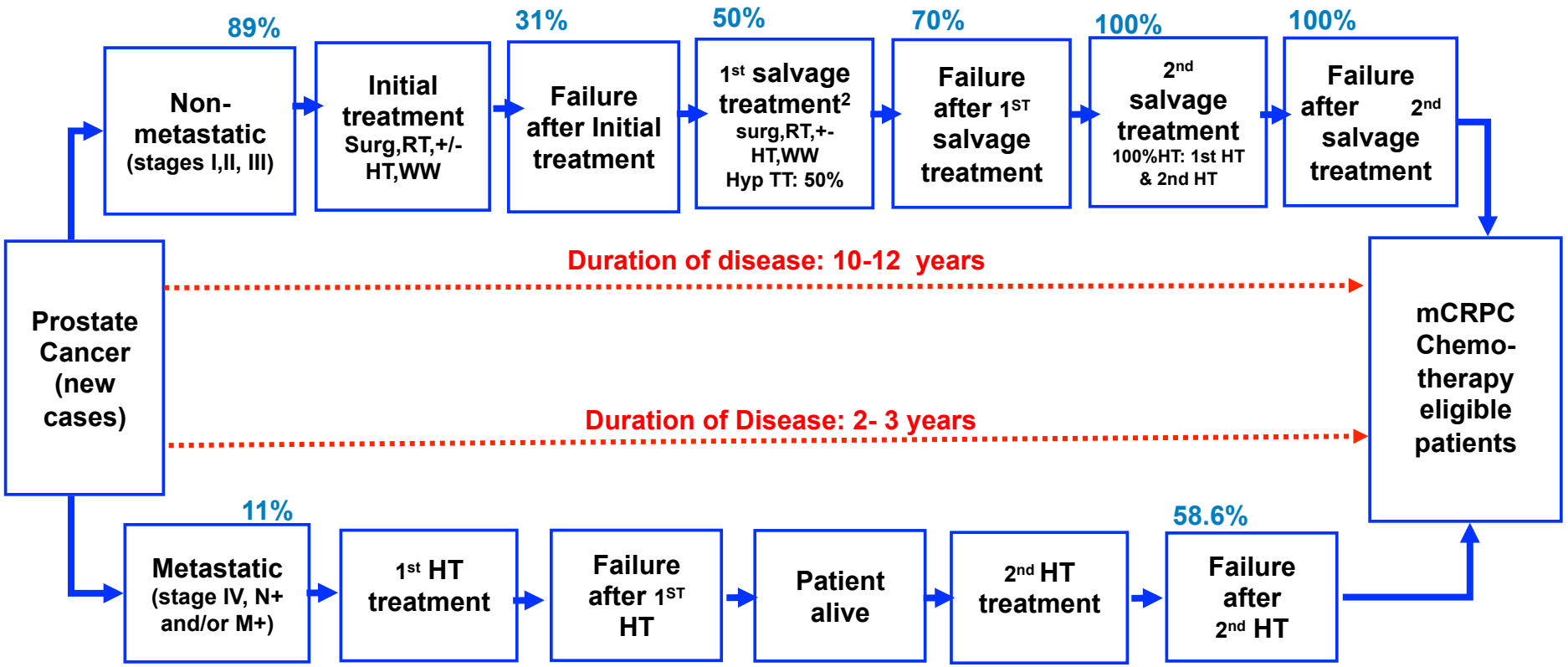


# Incidence of *de novo* metastatic PC




Wu JN, *Cancer*. 2014;120:818-23.

# Prostate cancer patients flow




***Source**: GHOMA / Analytic Epidemiology*

# *De novo* metastatic prostate cancer: have we made progresses?

## No Improvement Noted in Overall or Cause-Specific Survival for Men Presenting With Metastatic Prostate Cancer Over a 20-Year Period

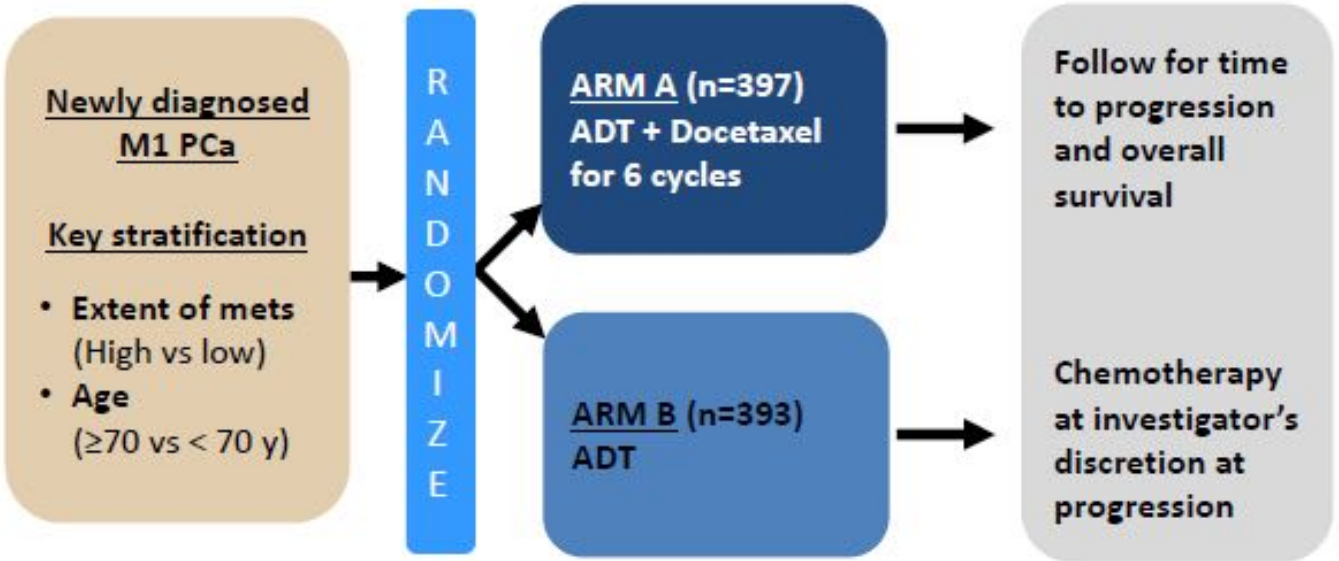
Jennifer N. Wu, MD[1]; Kari M. Fish, MPH[2]; Christopher P. Evans, MD[1]; Ralph W. deVere White, MD[1]; and Marc A. Dall'Era, MD[1]

| | | | | | |
|---|---|---|---|---|---|
| Flutamide | 697 | 424 | 178 | 32 | 0 |
| Placebo | 685 | 408 | 152 | 32 | 0 |

Vogelzang NJ, Urology 1995; 46: 220-226
Eisenberger, N Engl J Med 1998, 339: 1036-42

Hussain M, N Engl J Med 2013; 368: 1314-25
Wu JN, Cancer 2014; 120: 818-23

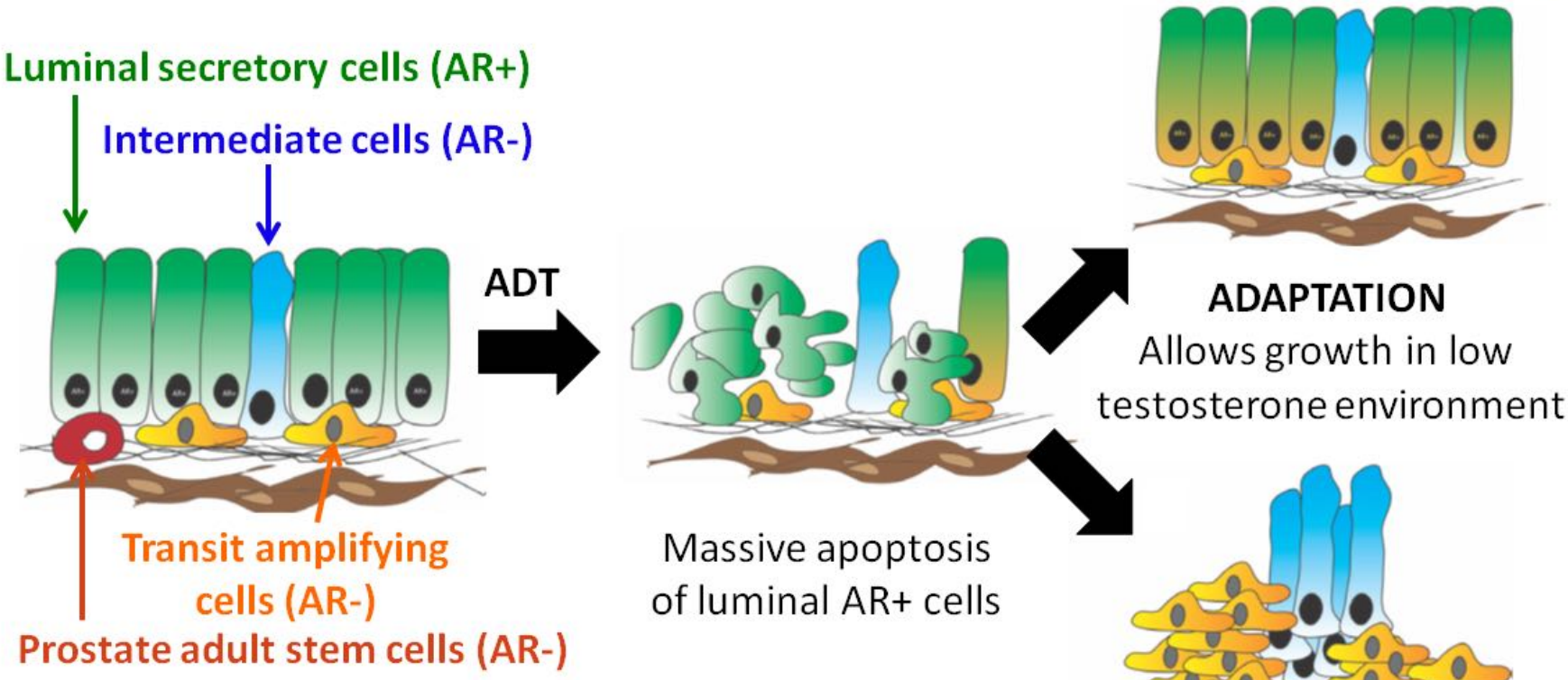
# E3805 – CHAARTED study




- Open-label, multicenter, phase III trial conducted in US
- Standard dexamethasone premedication **but no daily prednisone**

Sweeney C et al. J Clin Oncol 2014;32(June 20 suppl):abstract LBA2. ADT: androgen deprivation therapy; Mets: Metastases; PS: Performance Status; SRE: Skeletal Related Events; CAB: Complete Androgen Blockade; docétaxel (75mg/m2 every 21 days)

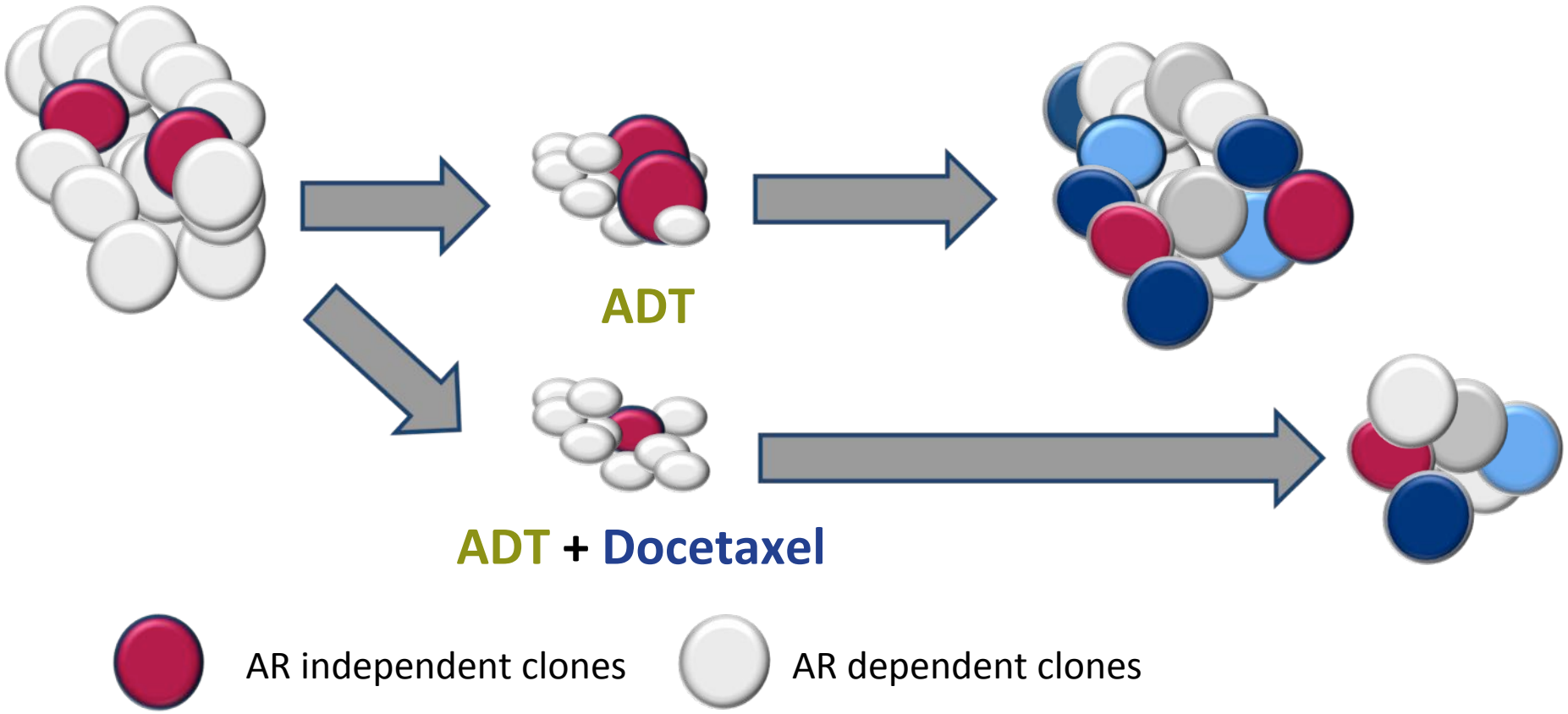
# PCa progression in low testosterone environment: 2 leading theories




**In most patients, both theories coexist: ADT response in some mets may be associated with radiological/clinical progression of other mets**

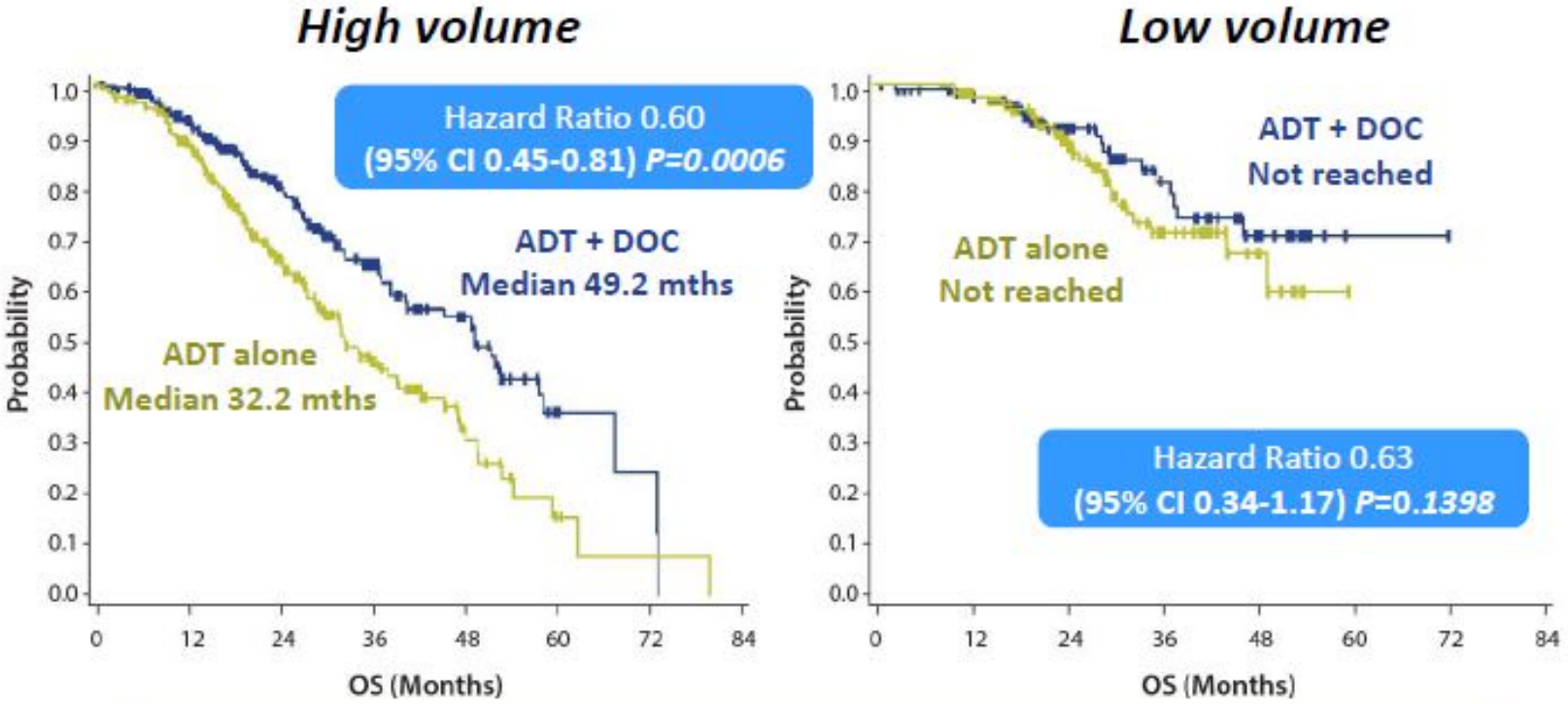
Tombal. B. Eur J Cancer 2011;47:S179-188
ADT: Androgen Deprivation Therapy; AR: androgen receptor; mets: metastases

# The CHAARTED hypothesis




Sweeney C et al. J Clin Oncol 2014;32(June 20 suppl):abstract LBA2
ADT: Androgen Deprivation Therapy; AR: androgen receptor

# Overall survival by extent of metastatic disease at start of ADT




**17-month benefit in median OS (from 32.2 to 49.2 months) for high volume disease**

Sweeney C et al. J Clin Oncol 2014;32(June 20 suppl):abstract LBA2
ADT: androgen deprivation therapy; DOC: docétaxel 75mg/m²

# CHAARTED Key eligibility criteria

- **High volume metastatic disease:**
  - visceral metastases

  and/or
  - 4 or more bone metastases (with at least 1 beyond pelvis and vertebral column)

- At study initiation, only patients with high volume disease were to be accrued
  - Study amendment to allow patients with low volume to be enrolled, with stratification on disease volume

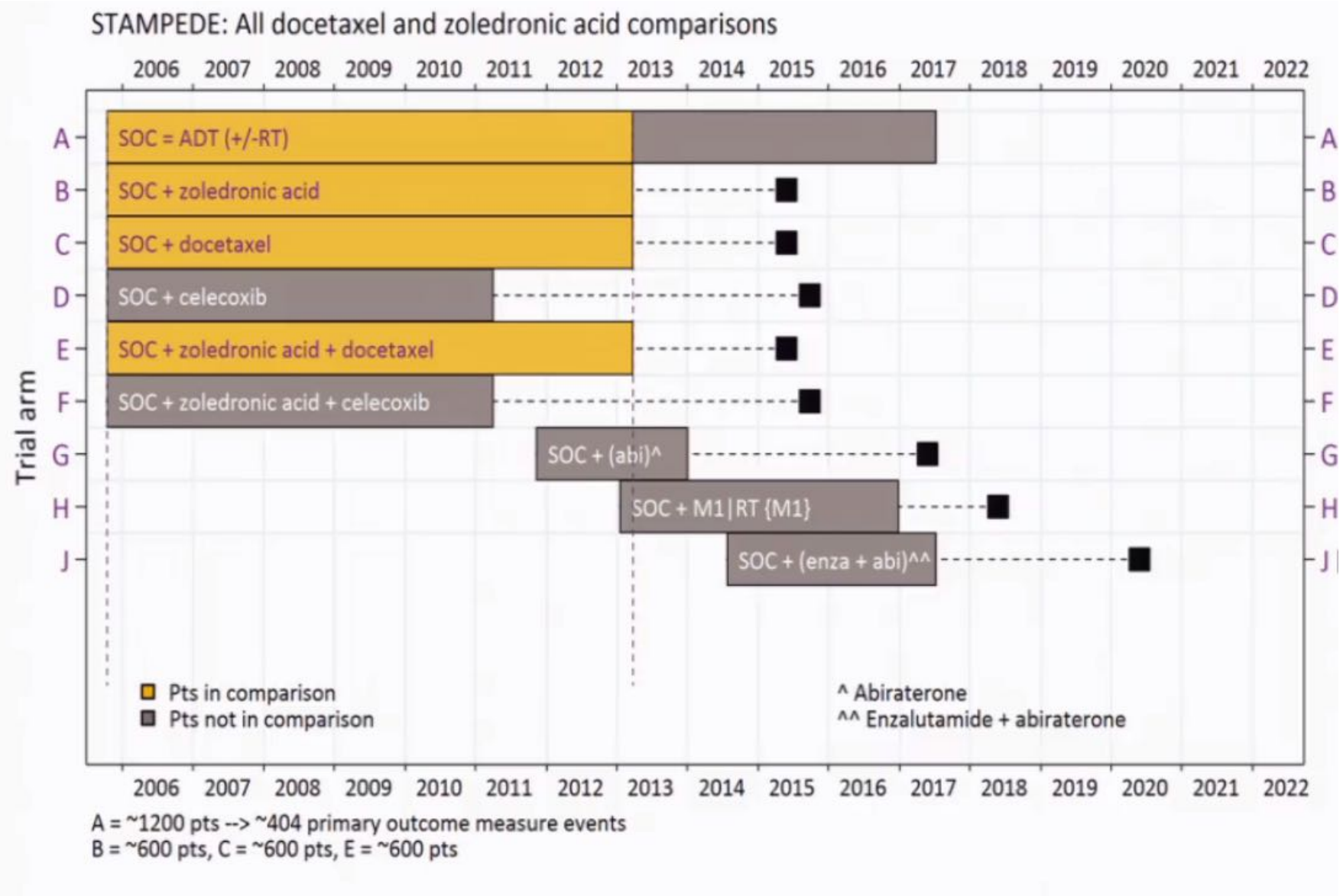
**Is high volume disease definition based on robust data?**

Sweeney C et al. J Clin Oncol 2014;32(June 20 suppl):abstract LBA2. *ADT: androgen deprivation therapy;*

# High volume disease is prognostic in metastatic hormone sensitive prostate cancer

| Clinical Status | Trials (name) | Patients number | Definition of disease spread | mOS (minimal vs severe) |
|---|---|---|---|---|
| SWOG: S8894[1] | Orchidectomy ± Flutamide | 1387 | Appendicular skeletal, visceral met or both | 51 vs 27 mths |
| SWOG: S8494[2] | Leuprolide ± Flutamide | 603 | Absence of mets in ribs, long bones, skull, soft tissues other than LN | 39 vs 26 mths |
| SWOG-9346[3] | Intermittent vs continuous ADT | 3040 | Ribs, long bones, or visceral mets | Continuous tt 6.9 vs 4.4 yrs |
| MD Anderson[4] | ADT ± KAVE | 306 | 3 or more bone mets or visceral mets | 7.8 vs 3.75 yrs |

1. Eisenberg M et al. N Engl J Med 1988;339:1036-42; 2. Crawford E et al. N Engl J Med 1989;321:419-24;
3. Hussain M et al. N Engl J Med 2013;368:1314-25; 4. Millikan E et al. J Clin Oncol 2008;26:5936-42




James ND et al. The Lancet, published online Dec 2015.

# Patients characteristics

Accrual: 2962 patients

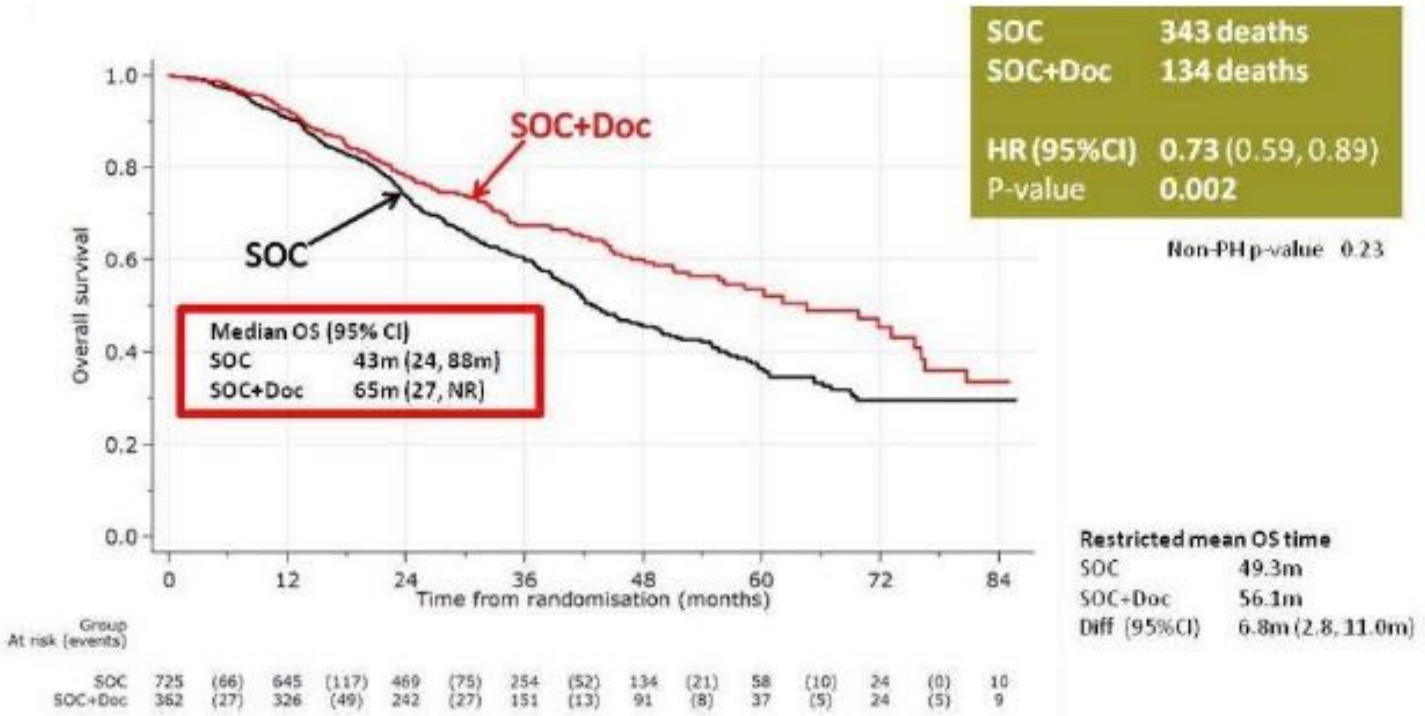
- 1184 Standard of care (SOC)
- 593 SOC + zoledronic acid
- 592 SOC + docetaxel
- 593 SOC + docetaxel + zoledronic acid

-Metastatic patients: 61% of patients

-62% of 2797 newly diagnosed patients had metastatic disease at study entry

James ND et al. The Lancet, published online Dec 2015.

# STAMPEDE – OS in M1 Patients Docetaxel




Phase III randomized trial in 2962 men with M0/M1 in 4 groups with zometa with hormone-naïve Pca; Primary endpoint: overall survival

*OS: overall survival*

James, ND et al. Lancet. 2016;387:1163-77.

EUROPEAN UROLOGY 69 (2016) 563–573

available at www.sciencedirect.com
journal homepage: www.europeanurology.com


European Association of Urology

Platinum Priority – Review – Prostate Cancer

*Editorial by Guru Sonpavde and Joaquim Bellmunt on pp. 574–575 of this issue*

# Addition of Docetaxel to Androgen Deprivation Therapy for Patients with Hormone-sensitive Metastatic Prostate Cancer: A Systematic Review and Meta-analysis

*Marcello Tucci*[a], *Valentina Bertaglia*[a], *Francesca Vignani*[a], *Consuelo Buttigliero*[a], *Cristian Fiori*[b], *Francesco Porpiglia*[b], *Giorgio Vittorio Scagliotti*[a], *Massimo Di Maio*[a,*]

[a] *Division of Medical Oncology, Department of Oncology, University of Turin, San Luigi Gonzaga Hospital, Orbassano, Turin, Italy;* [b] *Division of Urology, Department of Oncology, University of Turin, San Luigi Gonzaga Hospital, Orbassano, Turin, Italy*

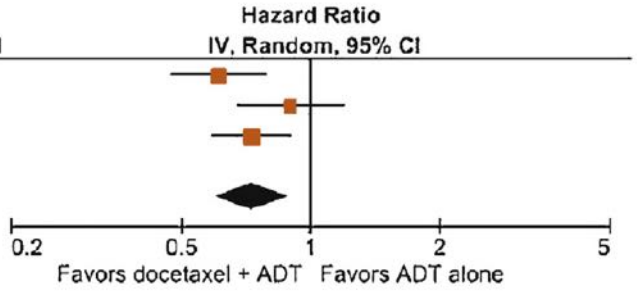
**Tucci M et al, Eur Urol 2016; 69: 563 - 573**

# Addition of docetaxel to ADT: a meta-analysis

## OVERALL SURVIVAL: Only metastatic patients

| Study or Subgroup | log[Hazard Ratio] | SE | Docetaxel + ADT Total | ADT alone Total | Weight | Hazard Ratio IV, Random, 95% CI |
|---|---|---|---|---|---|---|
| CHAARTED | -0.4943 | 0.133 | 397 | 393 | 32.1% | 0.61 [0.47, 0.79] |
| GETUG-AFU 15 | -0.1054 | 0.1468 | 192 | 193 | 28.8% | 0.90 [0.67, 1.20] |
| STAMPEDE Docetaxel | -0.3147 | 0.1086 | 362 | 725 | 39.1% | 0.73 [0.59, 0.90] |
| **Total (95% CI)** | | | **951** | **1311** | **100.0%** | **0.73 [0.60, 0.90]** |

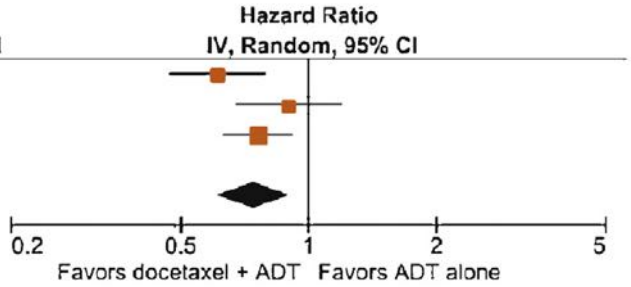
Heterogeneity: Tau² = 0.02; Chi² = 3.86, df = 2 (P = 0.15); I² = 48%
Test for overall effect: Z = 3.03 (P = 0.002)




## OVERALL SURVIVAL: All randomized patients

| Study or Subgroup | log[Hazard Ratio] | SE | Docetaxel + ADT Total | ADT alone Total | Weight | Hazard Ratio IV, Random, 95% CI |
|---|---|---|---|---|---|---|
| CHAARTED | -0.4943 | 0.133 | 397 | 393 | 30.8% | 0.61 [0.47, 0.79] |
| GETUG-AFU 15 | -0.1054 | 0.1468 | 192 | 193 | 27.5% | 0.90 [0.67, 1.20] |
| STAMPEDE Docetaxel | -0.2744 | 0.0957 | 592 | 1184 | 41.7% | 0.76 [0.63, 0.92] |
| **Total (95% CI)** | | | **1181** | **1770** | **100.0%** | **0.74 [0.61, 0.91]** |

Heterogeneity: Tau² = 0.01; Chi² = 3.96, df = 2 (P = 0.14); I² = 49%
Test for overall effect: Z = 2.95 (P = 0.003)




**Tucci M et al, Eur Urol 2016; 69: 563 - 573**

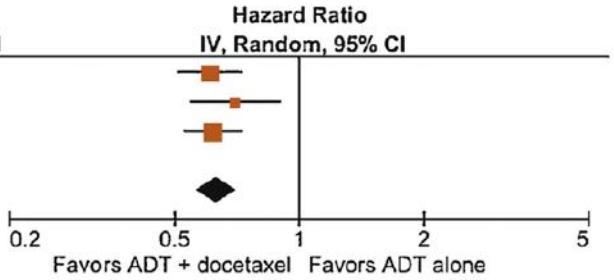
# Addition of docetaxel to ADT: a meta-analysis

## PROGRESSION-FREE SURVIVAL: Only metastatic patients

**A**

| Study or Subgroup | log[Hazard Ratio] | SE | Docetaxel + ADT Total | ADT alone Total | Weight | Hazard Ratio IV, Random, 95% CI |
|---|---|---|---|---|---|---|
| CHAARTED | -0.4943 | 0.0914 | 397 | 393 | 36.9% | 0.61 [0.51, 0.73] |
| GETUG-AFU 15 | -0.3567 | 0.1282 | 192 | 193 | 18.7% | 0.70 [0.54, 0.90] |
| STAMPEDE Docetaxel | -0.478 | 0.0833 | 362 | 725 | 44.4% | 0.62 [0.53, 0.73] |
| **Total (95% CI)** | | | **951** | **1311** | **100.0%** | **0.63 [0.57, 0.70]** |

Heterogeneity: Tau² = 0.00; Chi² = 0.84, df = 2 (P = 0.66); I² = 0%
Test for overall effect: Z = 8.31 (P < 0.00001)

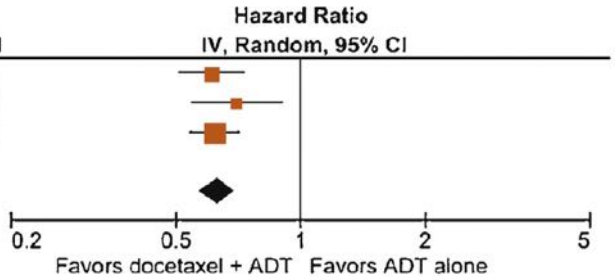



## PROGRESSION-FREE SURVIVAL: All randomized patients

**B**

| Study or Subgroup | log[Hazard Ratio] | SE | Docetaxel + ADT Total | ADT alone Total | Weight | Hazard Ratio IV, Random, 95% CI |
|---|---|---|---|---|---|---|
| CHAARTED | -0.4943 | 0.0914 | 397 | 393 | 31.4% | 0.61 [0.51, 0.73] |
| GETUG-AFU 15 | -0.3567 | 0.1282 | 192 | 193 | 15.9% | 0.70 [0.54, 0.90] |
| STAMPEDE Docetaxel | -0.478 | 0.0705 | 592 | 1184 | 52.7% | 0.62 [0.54, 0.71] |
| **Total (95% CI)** | | | **1181** | **1770** | **100.0%** | **0.63 [0.57, 0.70]** |

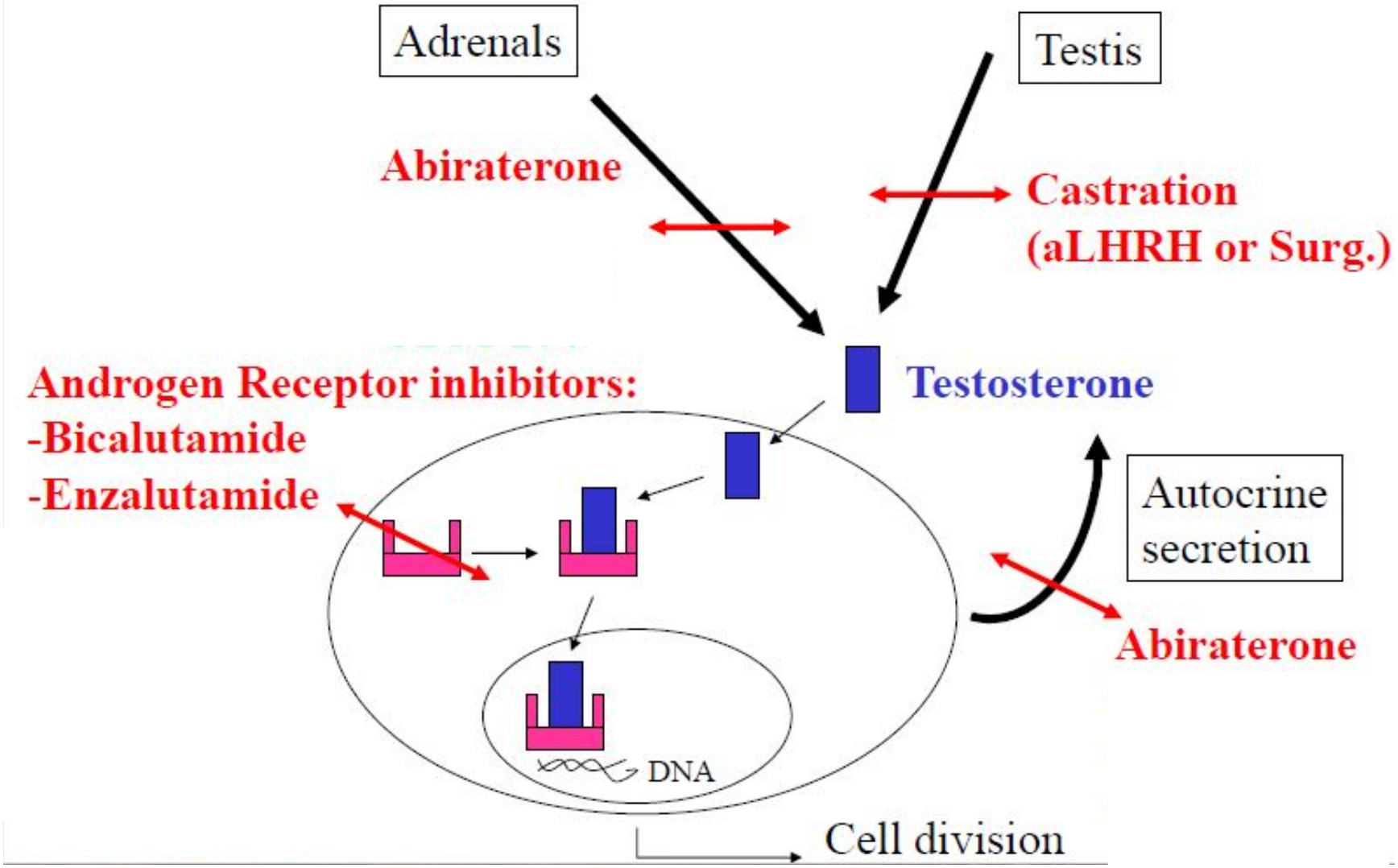
Heterogeneity: Tau² = 0.00; Chi² = 0.85, df = 2 (P = 0.65); I² = 0%
Test for overall effect: Z = 9.06 (P < 0.00001)

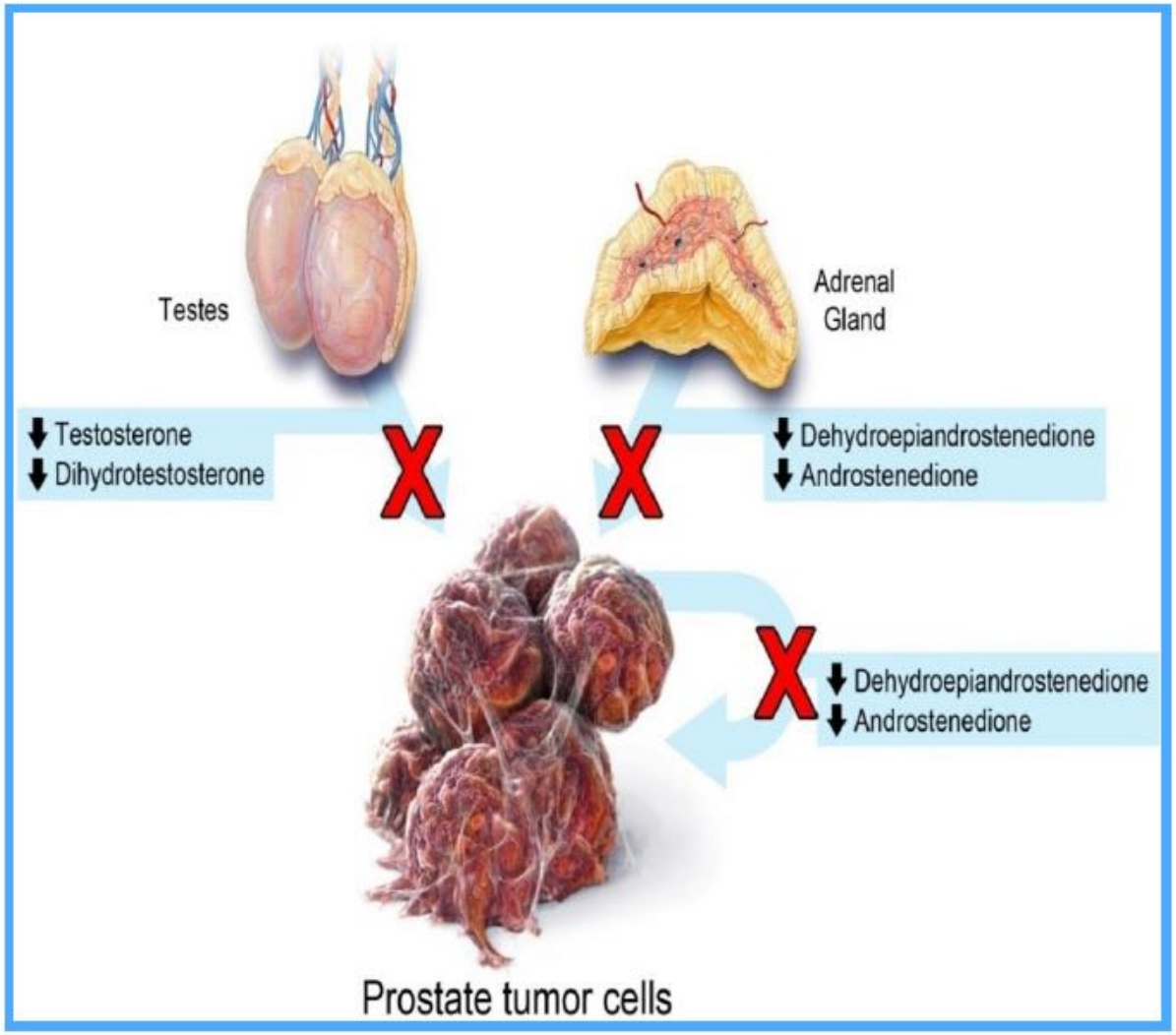



Tucci M et al, Eur Urol 2016; 69: 563 - 573

| |
|---|
| **QUESITO GRADE**:<br>Nei pazienti con malattia metastatica (M1) ormono-sensibile, "high volume" alla diagnosi secondo i criteri CHAARTED, che non abbiano controindicazioni alla chemioterapia, è raccomandabile l'associazione del Docetaxel up-front alla terapia androgeno-soppressiva? |
| **RACCOMANDAZIONE**:<br>Nei pazienti con malattia metastatica (M1) ormono-sensibile, "high volume" alla diagnosi secondo i criteri CHAARTED, l'associazione up-front di Docetaxel (6 cicli) alla terapia androgeno-soppressiva dovrebbe essere presa in considerazione. |
| Forza della raccomandazione: **POSITIVA FORTE** |

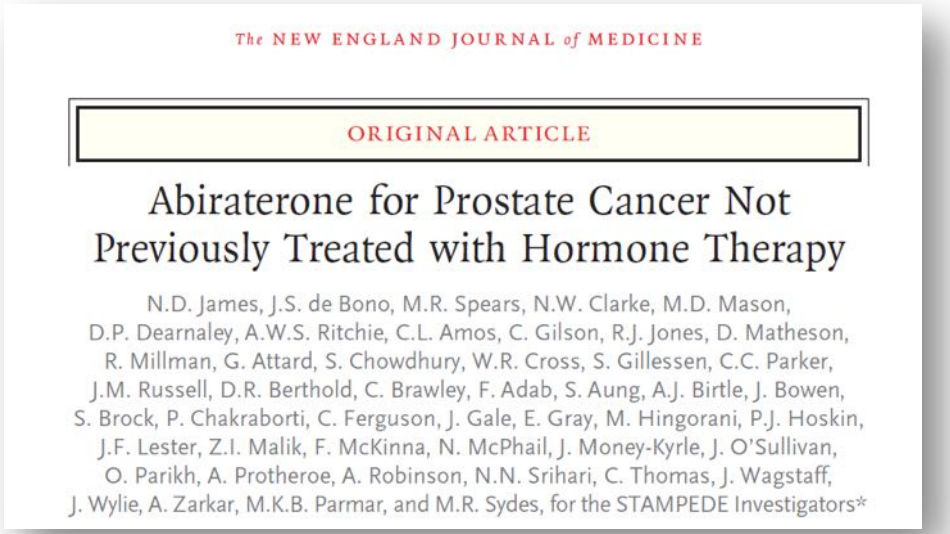
# Targeting the AR pathway






# Abiraterone Inhibits Androgen Biosynthesis Through CYP17

## *STAMPEDE*
## *N Engl J Med*. 2017 June 3
**[Epub ahead of print]**



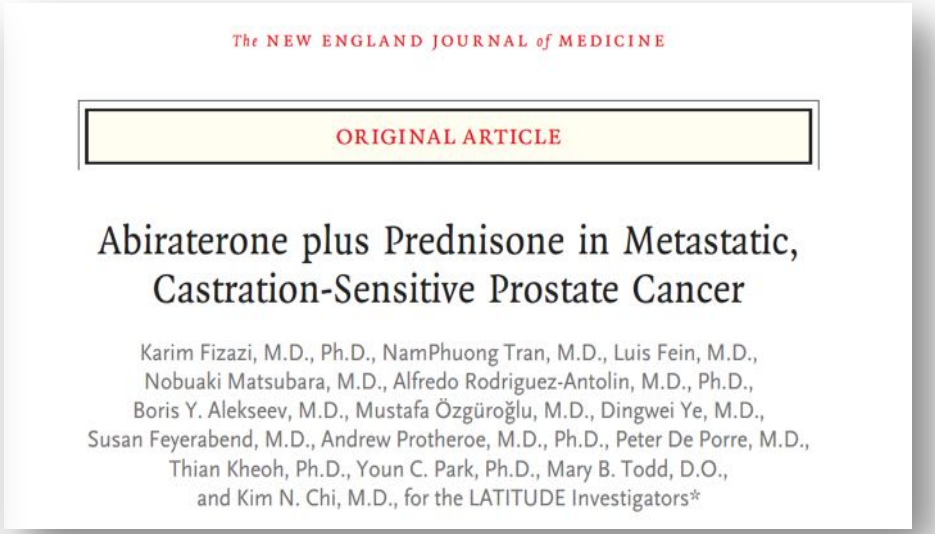
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy

N.D. James, J.S. de Bono, M.R. Spears, N.W. Clarke, M.D. Mason, D.P. Dearnaley, A.W.S. Ritchie, C.L. Amos, C. Gilson, R.J. Jones, D. Matheson, R. Millman, G. Attard, S. Chowdhury, W.R. Cross, S. Gillessen, C.C. Parker, J.M. Russell, D.R. Berthold, C. Brawley, F. Adab, S. Aung, A.J. Birtle, J. Bowen, S. Brock, P. Chakraborti, C. Ferguson, J. Gale, E. Gray, M. Hingorani, P.J. Hoskin, J.F. Lester, Z.I. Malik, F. McKinna, N. McPhail, J. Money-Kyrle, J. O'Sullivan, O. Parikh, A. Protheroe, A. Robinson, N.N. Srihari, C. Thomas, J. Wagstaff, J. Wylie, A. Zarkar, M.K.B. Parmar, and M.R. Sydes, for the STAMPEDE Investigators*

## *LATITUDE*
## *N Engl J Med*. 2017 June 4
**[Epub ahead of print]**



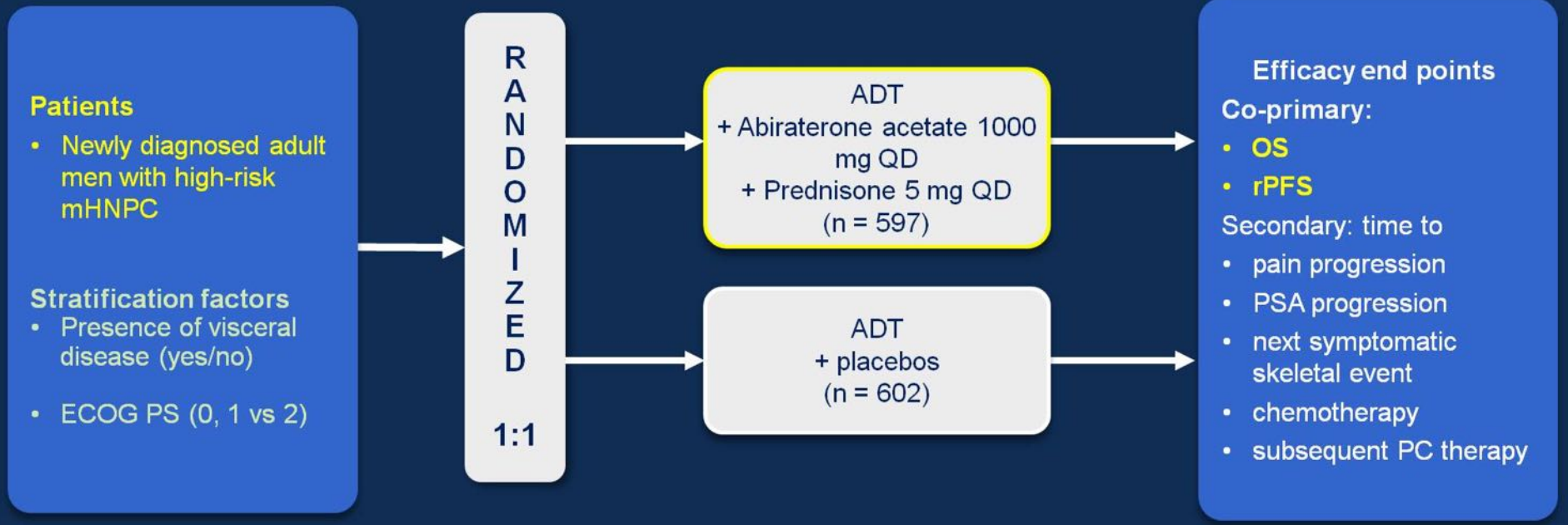
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

Karim Fizazi, M.D., Ph.D., NamPhuong Tran, M.D., Luis Fein, M.D., Nobuaki Matsubara, M.D., Alfredo Rodriguez-Antolin, M.D., Ph.D., Boris Y. Alekseev, M.D., Mustafa Özgüroğlu, M.D., Dingwei Ye, M.D., Susan Feyerabend, M.D., Andrew Protheroe, M.D., Ph.D., Peter De Porre, M.D., Thian Kheoh, Ph.D., Youn C. Park, Ph.D., Mary B. Todd, D.O., and Kim N. Chi, M.D., for the LATITUDE Investigators*

# Overall study design of LATITUDE




- **Conducted at 235 sites in 34 countries in Europe, Asia-Pacific, Latin America, and Canada**
- **Designed and fully enrolled prior to publication of CHAARTED/STAMPEDE results**

# Objective

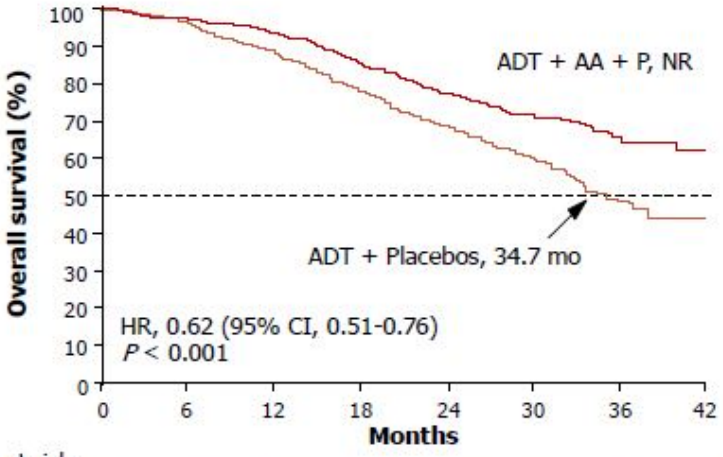
To evaluate the addition of AA + P to ADT on clinical benefit in men with newly diagnosed, high-risk, mCNPC

**High-risk defined as meeting at least 2 of 3 high-risk criteria:**

- Gleason score of ≥ 8
- Presence of ≥ 3 lesions on bone scan
- Presence of measurable visceral lesion

# LATITUDE: Co-primary End Points

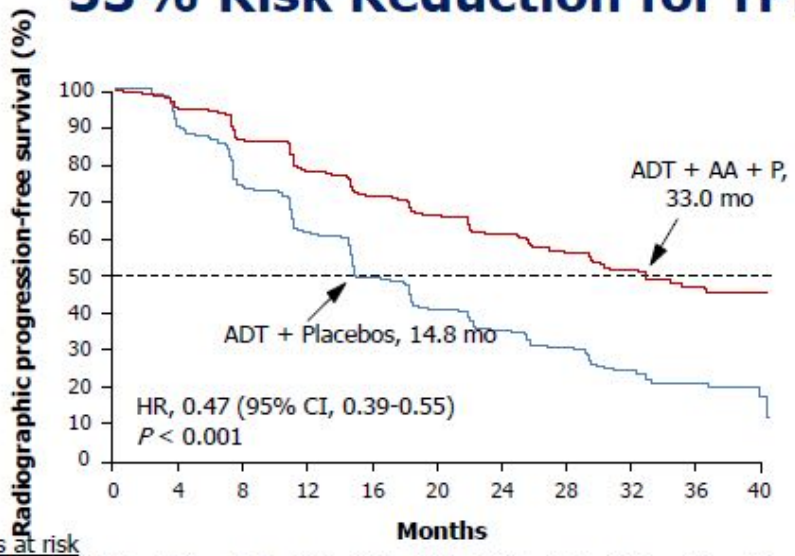
## 38% Risk Reduction for Death




Patients at risk

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| ADT + AA + P | 597 | 565 | 529 | 479 | 388 | 233 | 93 | 9 |
| ADT + Placebos | 602 | 564 | 504 | 432 | 332 | 172 | 57 | 2 |

## 53% Risk Reduction for rPFS



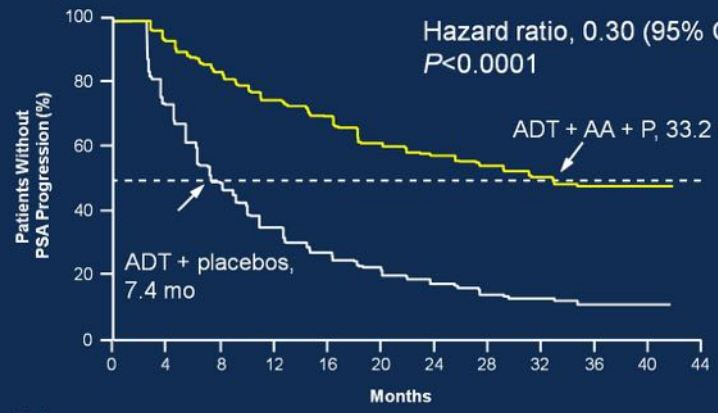

Patients at risk

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ADT + AA + P | 597 | 533 | 464 | 400 | 353 | 316 | 251 | 177 | 102 | 51 | 21 |
| ADT + Placebos | 602 | 488 | 367 | 289 | 214 | 168 | 127 | 81 | 41 | 17 | 7 |



Fizazi K, et al. N Engl J Med. 2017;377:352-360. CI, confidence interval; HR, hazard ratio; NR, not reached.

## Statistically significant 70% risk reduction of time to PSA progression

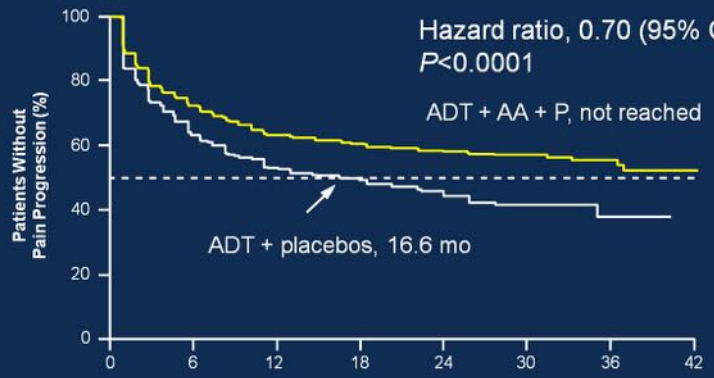



No. at risk

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ADT + AA + P | 597 | 520 | 447 | 379 | 340 | 285 | 227 | 162 | 95 | 48 | 18 | 0 |
| ADT + placebos | 602 | 393 | 250 | 172 | 129 | 102 | 65 | 33 | 19 | 8 | 5 | 0 |




## Statistically significant 30% risk reduction of time to pain progression




No. at risk

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| ADT + AA + P | 597 | 395 | 297 | 247 | 181 | 96 | 39 | 2 |
| ADT + placebos | 602 | 332 | 211 | 137 | 82 | 36 | 7 | 0 |




Presented By Karim Fizazi at 2017 ASCO Annual Meeting

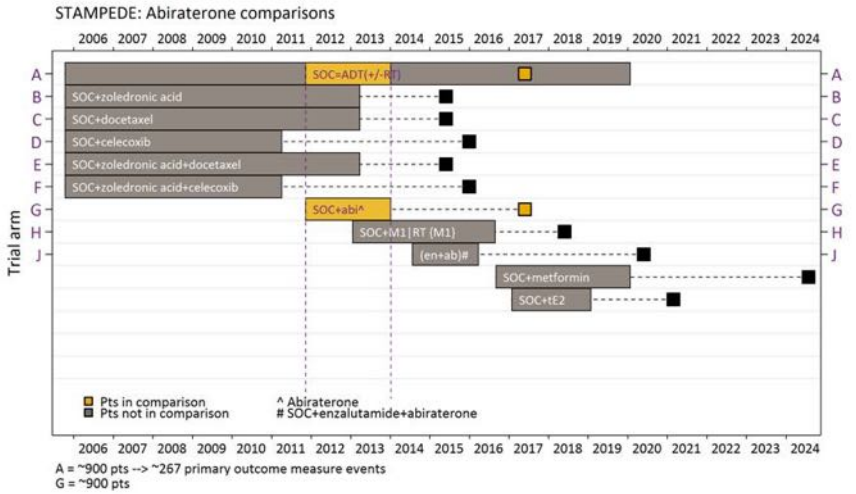
# Accrual

## Comparison

Open: Nov-2011

Closed: Jan-2014

Accrual: 1917



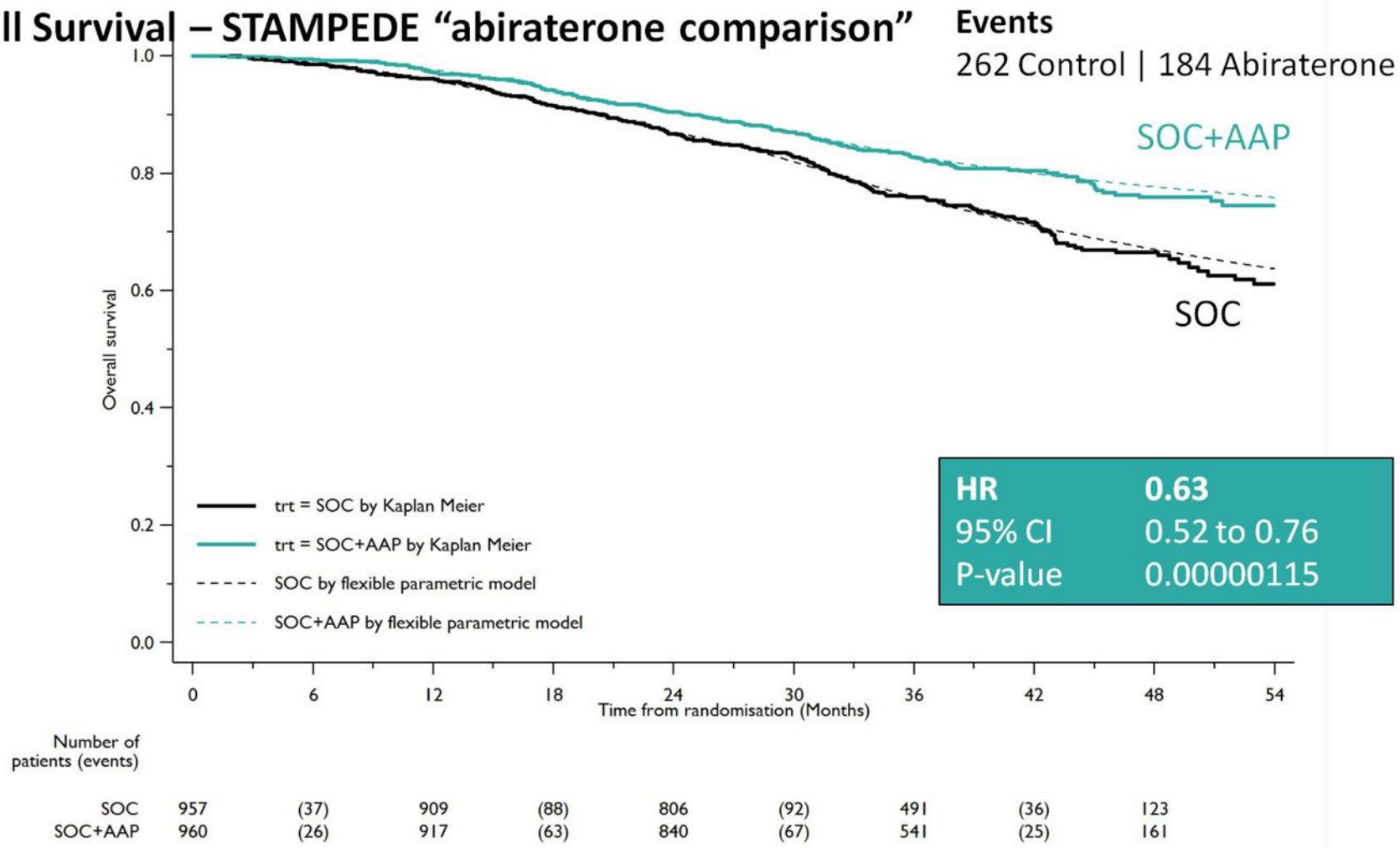

## Number of patients

957 **A** Standard-of-care* (SOC)

960 **G** SOC + abiraterone acetate + prednisolone (SOC+AAP)

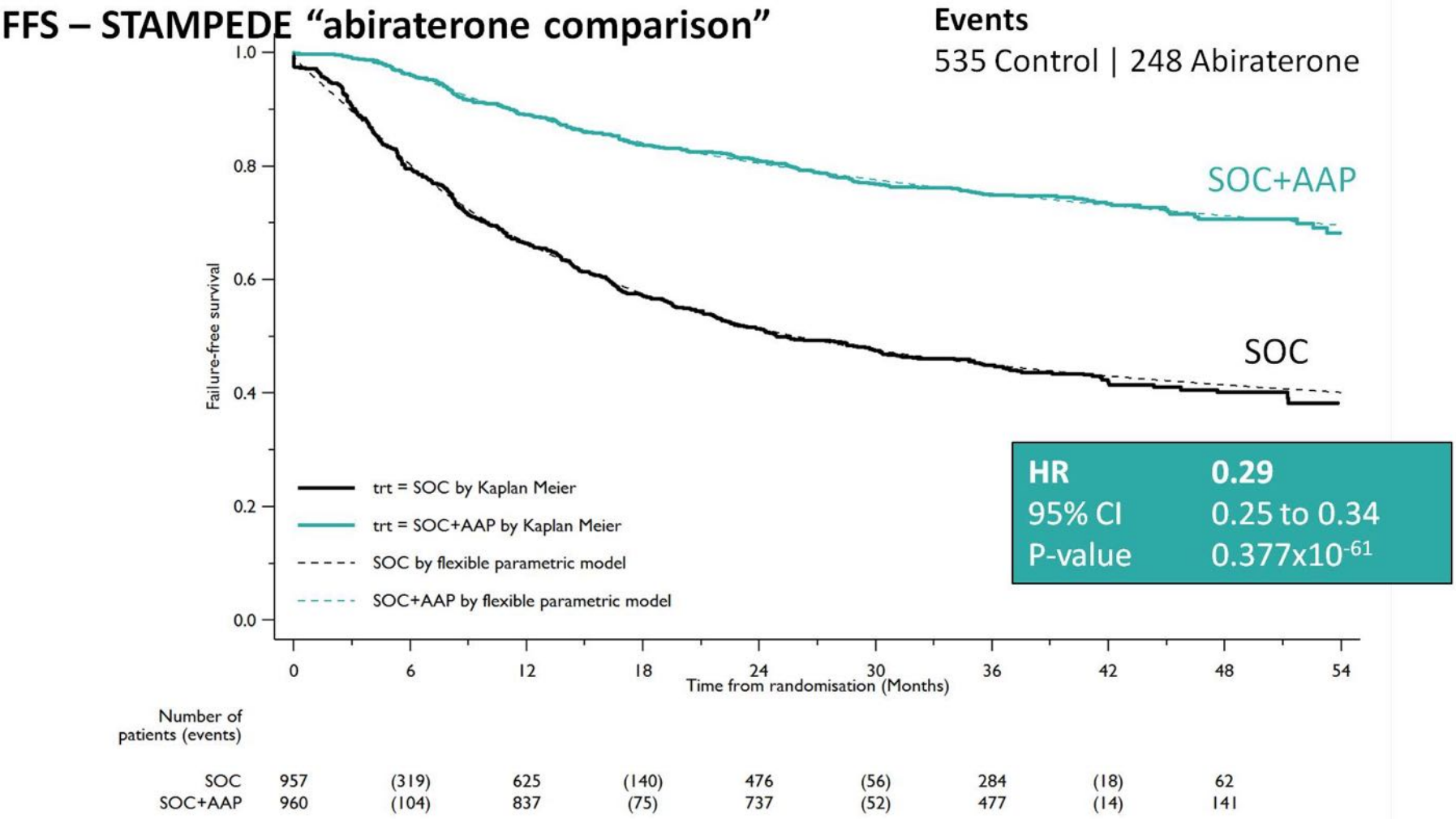
*SOC = ADT ± RT

# Overall Survival – STAMPEDE "abiraterone comparison"



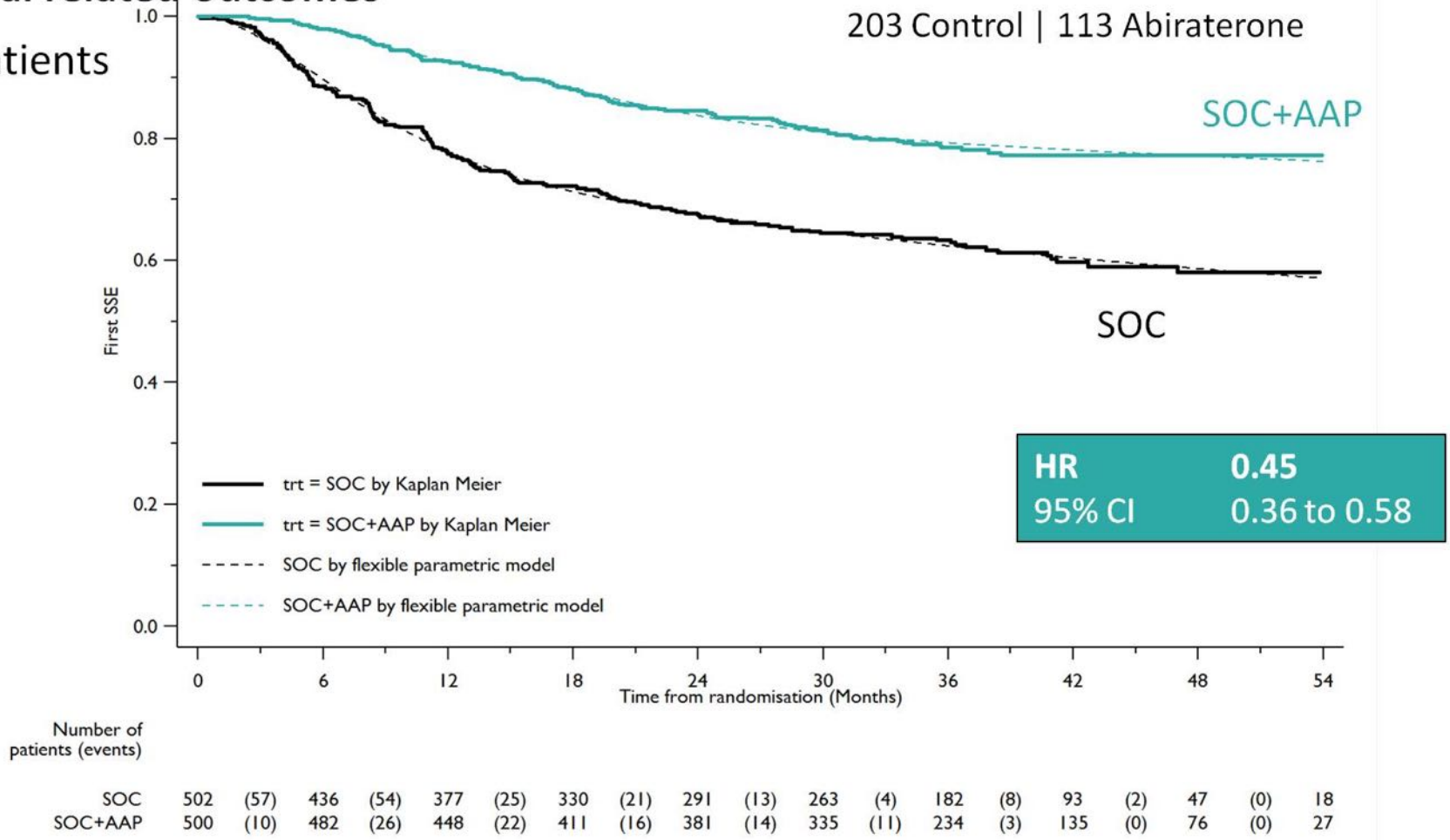

Presented By Nicholas James at 2017 ASCO Annual Meeting

# FFS – STAMPEDE "abiraterone comparison"



## Skeletal related outcomes

M1 patients




Presented By Nicholas James at 2017 ASCO Annual Meeting

| Qualità dell'evidenza SIGN | Raccomandazione | Forza della raccomandazione clinica |
|---|---|---|
| **Alta** | Nei pazienti metastatici alla diagnosi, con malattia ad alto rischio, può essere presa in considerazione la possibilità di associare alla terapia androgenosoppressiva upfront, un trattamento con Abiraterone acetato e prednisone o prednisolone [135, 136].<br>N.B. Secondo le vigenti disposizioni, in questa fase di malattia, abiraterone è prescrivibile al momento solo in regime di "off-label". | **Positiva debole** |

*La qualità viene definita alta in quanto l'evidenza è ottenuta da due studi prospettici e randomizzati che non presentano bias significativi.*

Business Wire
A Berkshire Hathaway Company



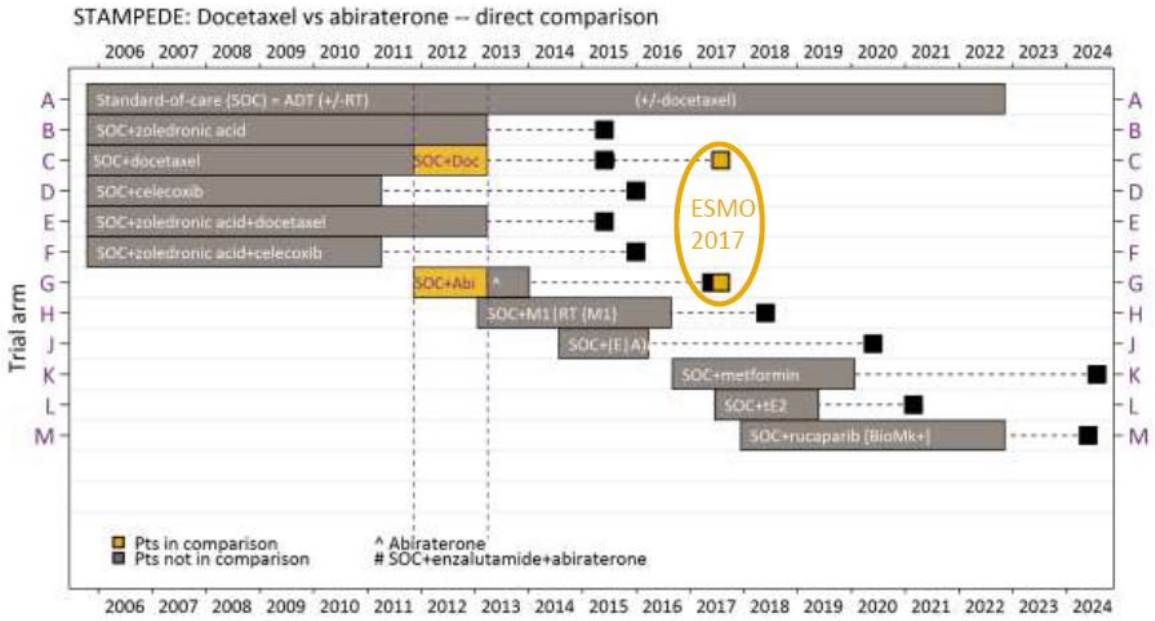
# European Commission Extends License for Janssen's ZYTIGA® Plus Prednisone / Prednisolone to Include Earlier Stage Prostate Cancer Patients

***Oral, Once-Daily Medication ZYTIGA® (abiraterone acetate) ® Plus Prednisone / Prednisolone Now Approved in Newly Diagnosed High-Risk Metastatic Hormone-Sensitive Prostate Cancer (mHSPC)***

November 20, 2017 08:30 AM Eastern Standard Time

# What is better for hormone naïve patients starting ADT? Doc or Abi???

# STAMPEDE: SOC+AAP vs SOC+DocP




**Recruitment:** Nov-2011 to Mar-2013

**Reported:** ESMO 2017

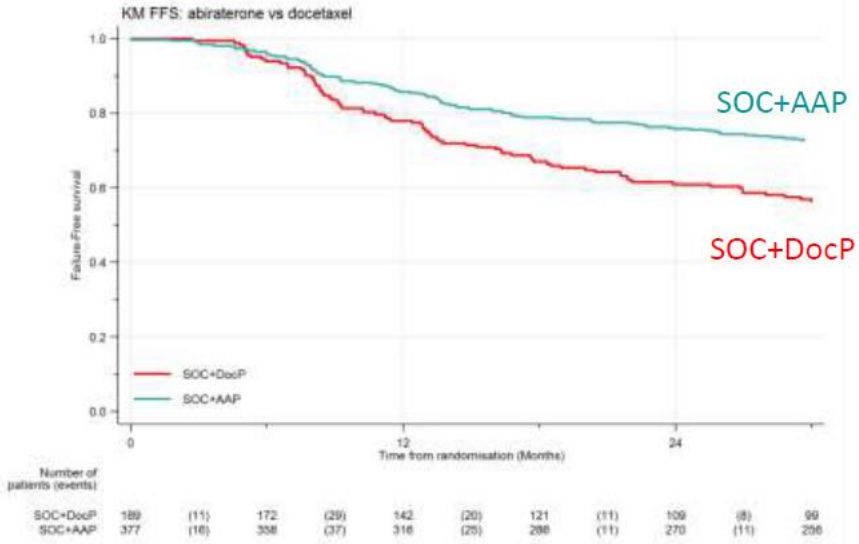
**Published:** (paper in development)

**Patients:** 189 SOC+DocP
377 SOC+AAP

566 patients randomised contemporaneously to either research arm

**Sydes M et al, ESMO 2017, abstract LBA31_PR**

# Failure-free survival [driven by PSA failure]




| | HR (95%CI) | P-val | *Interact$^n$ test* |
|---|---|---|---|
| All | **0.51** (0.39 to 0.67) | <0.001 | |
| M0 | **0.34** (0.16 to 0.69) | 0.003 | *0.17* |
| M1 | **0.56** (0.42 to 0.75) | <0.001 | |

| | SOC+DocP | | SOC+AAP | |
|---|---|---|---|---|
| | Events | Pts | Events | Pts |
| All | **97** | 189 | **122** | 377 |
| M0 | **18** | 74 | **13** | 150 |
| M1 | **79** | 115 | **109** | 227 |

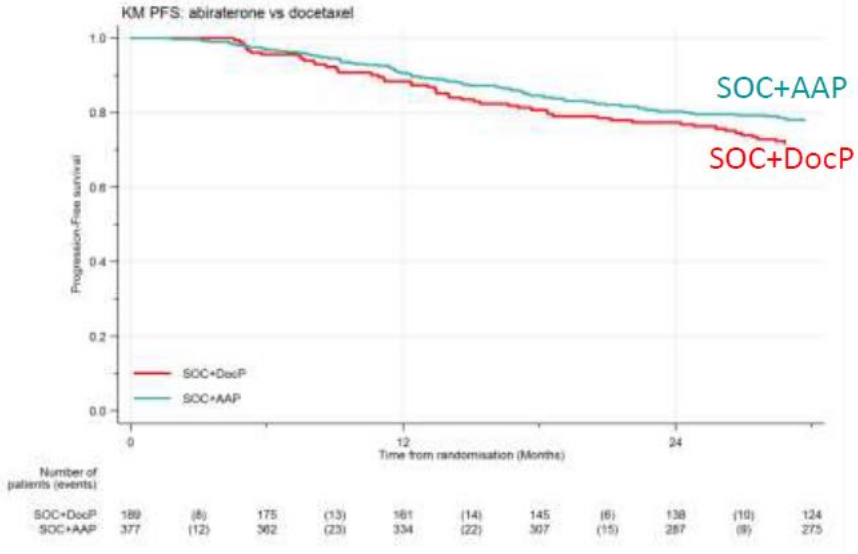
**Key:**
HR<1 favours SOC+AAP
HR>1 favours SOC+DocP

Interact$^n$ = test for interaction (heterogeneity of treatment effect)

**Sydes M et al, ESMO 2017, abstract LBA31_PR**

# Progression-free survival

PFS = FFS ignoring PSA failure




| | HR (95%CI) | P-val | *Interact$^n$ test* |
|---|---|---|---|
| All | **0.65** (0.48 to 0.88) | 0.005 | |
| M0 | **0.42** (0.17 to 1.05) | 0.06 | *0.32* |
| M1 | **0.69** (0.50 to 0.95) | 0.02 | |

| | SOC+DocP | | SOC+AAP | |
|---|---|---|---|---|
| | Events | Pts | Events | Pts |
| All | **72** | 189 | **103** | 377 |
| M0 | **10** | 74 | **9** | 150 |
| M1 | **62** | 115 | **94** | 227 |

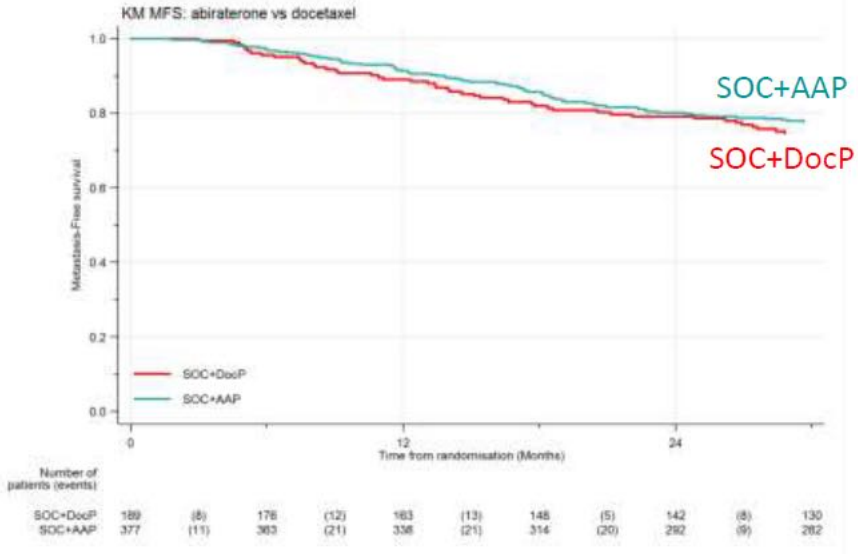
**Key:**
HR<1 favours SOC+AAP
HR>1 favours SOC+DocP

Interact$^n$ = test for interaction (heterogeneity of treatment effect)

**Sydes M et al, ESMO 2017, abstract LBA31_PR**

# Metastatic progression-free survival

MPFS = new or progression of metastases or death from any cause




| | HR (95%CI) | P-val | *Interact$^n$ test* |
|---|---|---|---|
| All | **0.77** (0.57 to 1.03) | 0.08 | |
| M0 | **0.91** (0.42 to 2.01) | 0.82 | *0.74* |
| M1 | **0.76** (0.55 to 1.04) | 0.09 | |

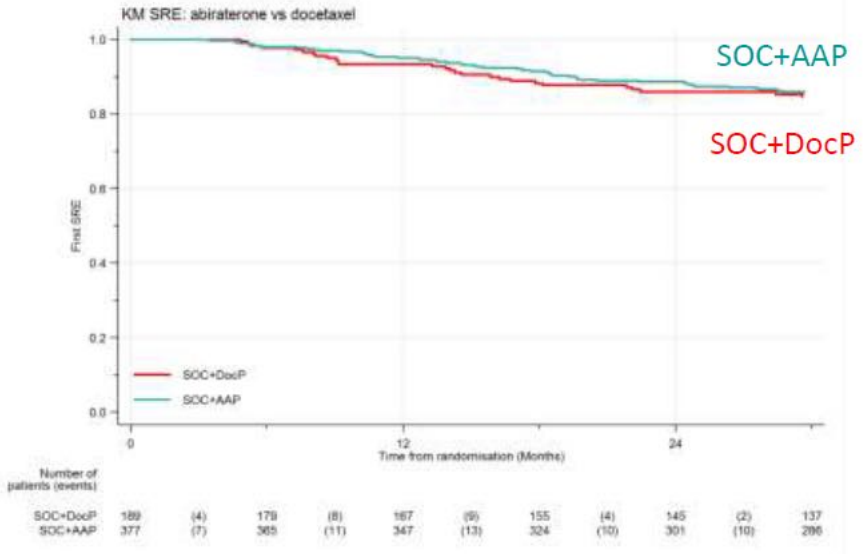
| | SOC+DocP | | SOC+AAP | |
|---|---|---|---|---|
| | Events | Pts | Events | Pts |
| All | **71** | 189 | **118** | 377 |
| M0 | **10** | 74 | **18** | 150 |
| M1 | **61** | 115 | **100** | 227 |

**Key:**
HR<1 favours SOC+AAP
HR>1 favours SOC+DocP

Interact$^n$ = test for interaction (heterogeneity of treatment effect)

**Sydes M et al, ESMO 2017, abstract LBA31_PR**

# Symptomatic skeletal events




| | HR (95%CI) | P-val | *Interact$^n$ test* |
|---|---|---|---|
| All | **0.83** (0.55 to 1.25) | 0.38 | |
| M0 | **1.28** (0.24 to 6.67) | 0.77 | *0.65* |
| M1 | **0.82** (0.53 to 1.25) | 0.35 | |

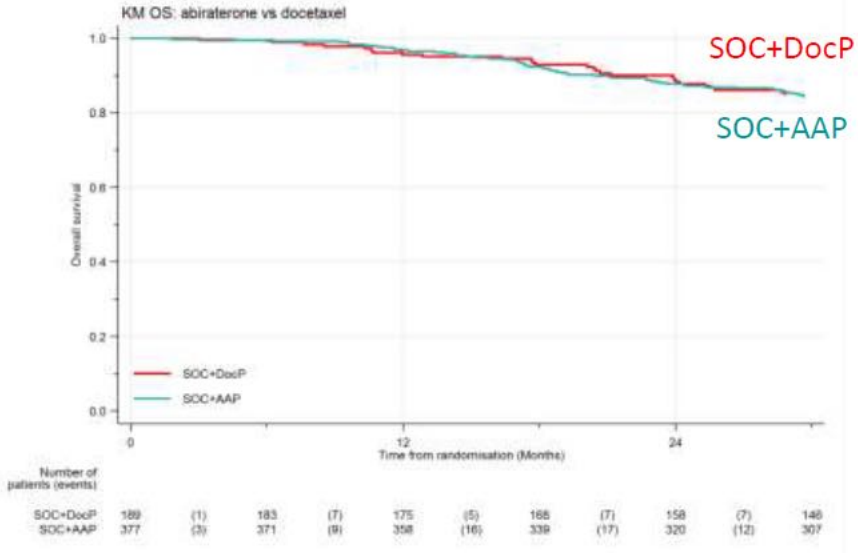
| | SOC+DocP | | SOC+AAP | |
|---|---|---|---|---|
| | Events | Pts | Events | Pts |
| All | **36** | 189 | **63** | 377 |
| M0 | **2** | 74 | **5** | 150 |
| M1 | **34** | 115 | **58** | 227 |

**Key:**
HR<1 favours SOC+AAP
HR>1 favours SOC+DocP

Interact$^n$ = test for interaction (heterogeneity of treatment effect)

**Sydes M et al, ESMO 2017, abstract LBA31_PR**

# Overall survival [primary outcome measure]




| | HR (95%CI) | P-val | Interact$^{n}$ test |
|---|---|---|---|
| All | **1.16** (0.82 to 1.65) | 0.40 | |
| M0 | 1.51 (0.58 to 3.93) | 0.40 | *0.69* |
| M1 | 1.13 (0.77 to 1.66) | 0.53 | |

| | SOC+DocP | | SOC+AAP | |
|---|---|---|---|---|
| | Events | Pts | Events | Pts |
| All | **44** | 189 | **105** | 377 |
| M0 | 6 | 74 | 16 | 150 |
| M1 | 38 | 115 | 89 | 227 |

**Key:**
HR<1 favours SOC+AAP
HR>1 favours SOC+DocP

Interact$^{n}$ = test for interaction (heterogeneity of treatment effect)

**Sydes M et al, ESMO 2017, abstract LBA31_PR**

# Adverse events – worst toxicity ever

| **Safety population** | **SOC+DocP** | **SOC+AAP** |
|---|---|---|
| Patients included in adverse event analysis | 172 (91%) | 373 (>99%) |
| Grade 1+ AE | 172 (100%) | 370 (99%) |
| Grade 3+ AE | 86 (50%) | 180 (48%) |
| **Grade 3+ AEs by category (*incl. expected AEs*)** | | |
| Endocrine disorder (*incl. hot flashes, impotence*) | 15 (9%) | 49 (13%) |
| Febrile neutropenia | 29 (**17**%) | 3 (**1**%) |
| Neutropenia | 22 (**13**%) | 4 (**1**%) |
| Musculoskeletal disorder: | 9 (5%) | 33 (9%) |
| Cardiovascular disorder (*incl. hypertension, MI, cardiac dysrhythmia*): | 6 (3%) | 32 (9%) |
| Gastrointestinal disorder: | 9 (5%) | 28 (8%) |
| Hepatic disorder (*incl. increased AST, increased ALT*): | 1 (1%) | 32 (9%) |
| General disorder (*incl. fatigue, oedema*): | 18 (10%) | 21 (6%) |
| Respiratory disorder (*incl. breathlessness*): | 12 (7%) | 11 (3%) |
| Renal disorder | 5 (3%) | 20 (5%) |
| Lab abnormalities (*incl. hypokalaemia*): | 9 (5%) | 11 (3%) |

**Sydes M et al, ESMO 2017, abstract LBA31_PR**

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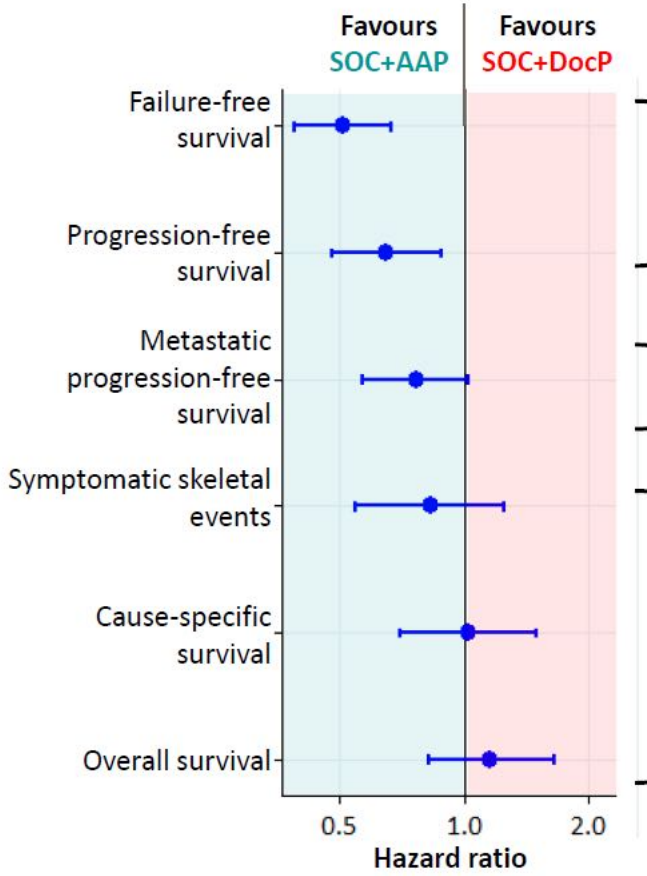
**Sydes M et al, ESMO 2017, abstract LBA31_PR**




# Summary

Head-to-head data in 566 pts (Nov-2011 to Mar-2013)

Strong evidence favouring AAP

Weak evidence favouring AAP

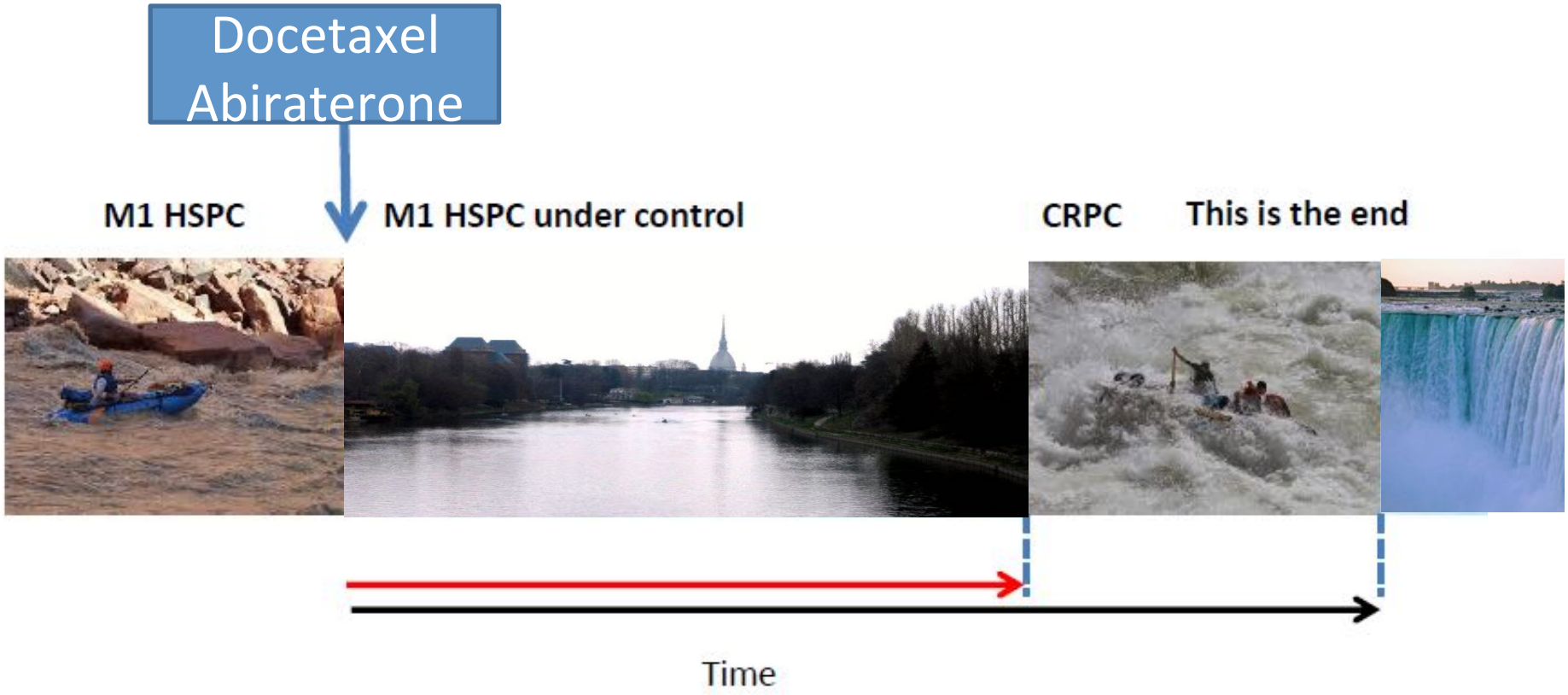
No good evidence of a difference

→ Proportionately different time spent in each disease state

Toxicity profiles quite different and well known

**Sydes M et al, ESMO 2017, abstract LBA31_PR**

# M1 HSPC: the good «window» to use docetaxel or abiraterone



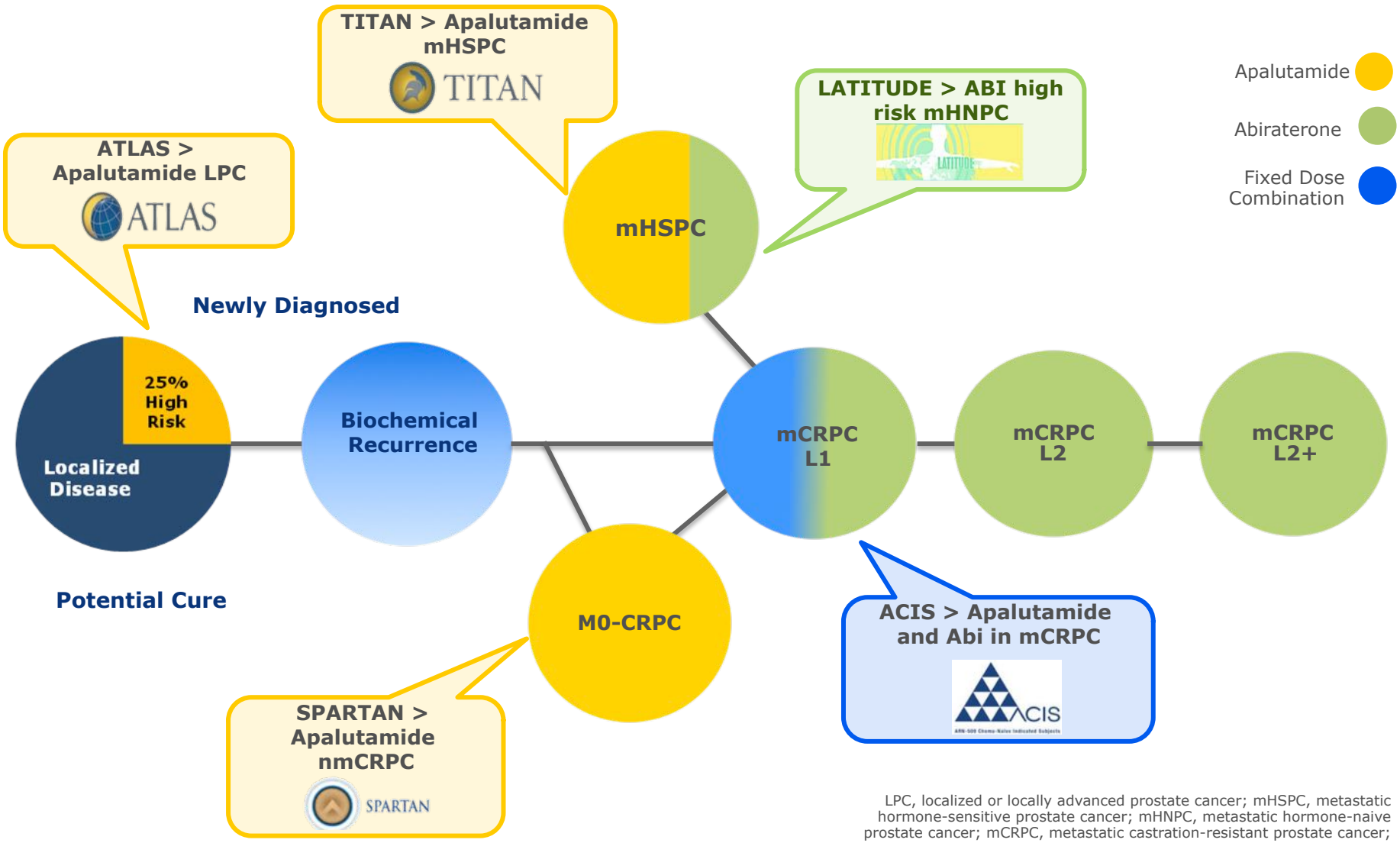
# Phase 3 Ongoing Combination Therapy Trials in HSPC

| Study | Identifier | Study Drugs | Pts (N) | Primary End Point | Status/Read Out |
|---|---|---|---|---|---|
| **LATITUDE** | NCT01715285 | ADT ± **AA** | 1209 | rPFS, OS | ASCO 2017 |
| **STAMPEDE (Arm G)** | NCT00268476 | ADT ± **AA** | 1800 | OS | LBA ASCO 2017 |
| **PEACE-1** | NCT01957436 | ADT ± DOC vs ADT + **AA** ± DOC (± local RT) | 916 | PFS, OS | Recruiting/2020 |
| **STAMPEDE (Arm J)** | NCT00268476 | ADT ± **AA + ENZ*** | 1800 | OS | Closed-will report in 2-3 yrs |
| **SWOG-1216** | NCT01809691 | ADT + **TAK-700** vs ADT + BIC | 1304 | OS | Recruiting/2027 |
| **ENZAMET** | NCT02446405 | ADT + **ENZ** vs ADT + antiandrogen | 1100 | OS | Recruiting/2020 |
| **TITAN** | NCT02489318 | ADT ± **APA (ARN 509)** | 1000 | rPFS, OS | Recruiting/ 2021 |
| **ARCHES** | NCT02677896 | ADT ± **ENZ** | 1100 | rPFS | Recruiting/ 2023 |
| **ARASENS** | NCT02799602 | ADT + DOC ± **ODM-201** | 1300 | OS | Recruiting/2022 |

*Includes upfront Doc

*Modified from and courtesy of K. Fizazi*

# Phase 3 Studies with ARTA




LPC, localized or locally advanced prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; mHNPC, metastatic hormone-naive prostate cancer; mCRPC, metastatic castration-resistant prostate cancer; M0-CRPC, non-metastatic CRPC