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10th edition
GLOBAL CONGRESS ON PROSTATE CANCER
JUBILEE EDITION

# Systemic treatment in high-risk localized prostate cancer

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# Disclosures

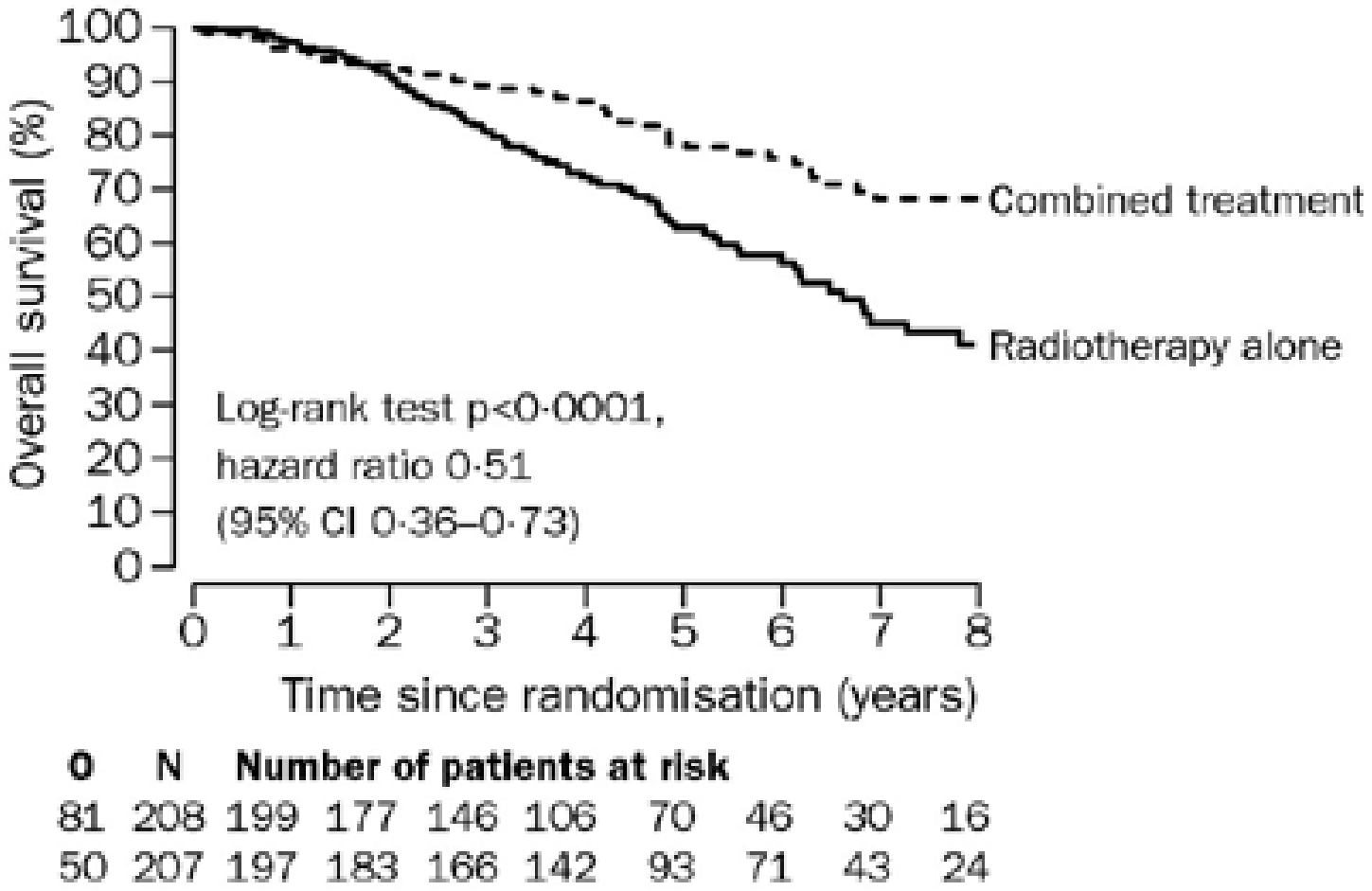
Participation to advisory boards and talks for:

Amgen, Astellas, Astrazeneca, Bayer, Clovis, Janssen, MSD, Novartis/AAA, Sanofi

Honoraria go to Gustave Roussy, my institution.

Participation to advisory boards with personal honorarium for CureVac and Orion.

# High-risk localized Prostate Cancer: Systemic ADT you shall give with RXT

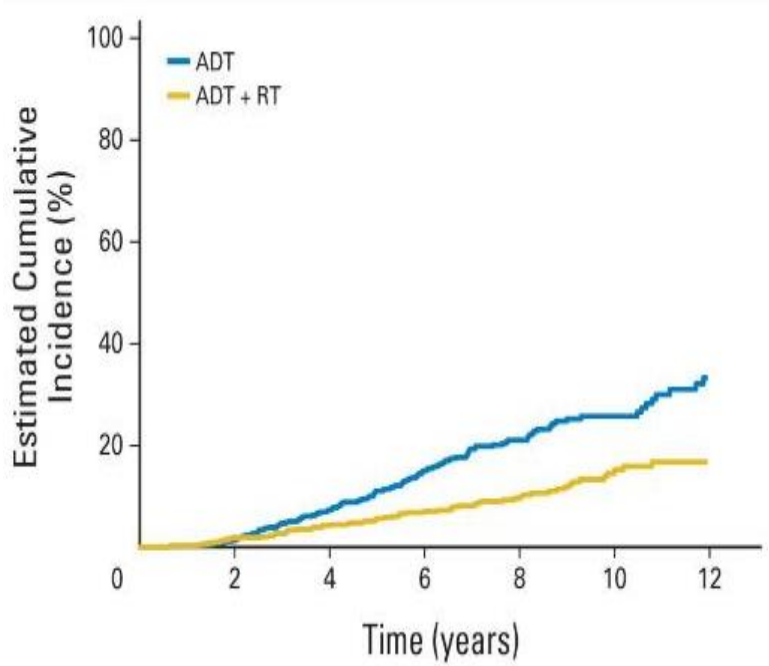



Bolla M et al. *Lancet*. 2002;360:103-108.

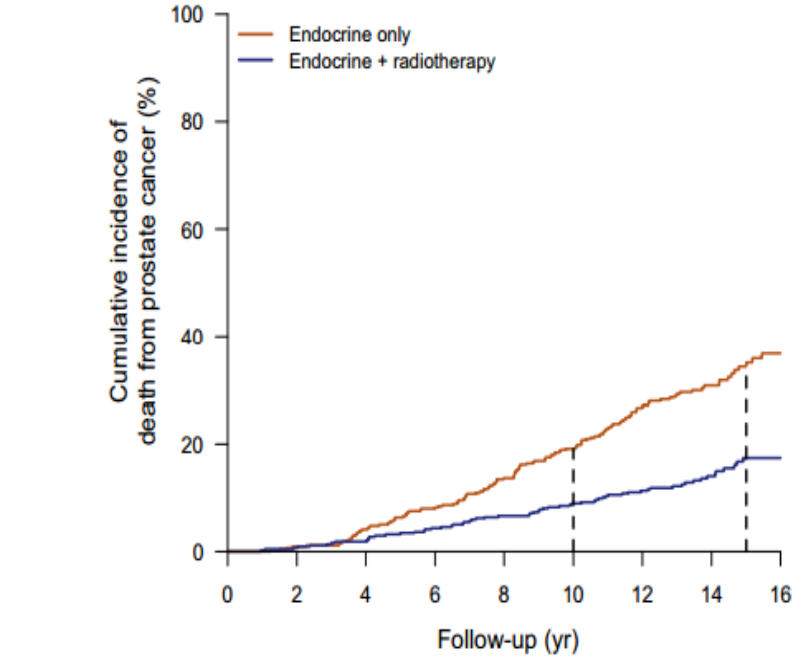
# High-Risk Localized Prostate Cancer: A Local Treatment to Give With ADT

## Deaths from Prostate Cancer

### NCIC CTG PR.3/MRC PR07/Int T94-0110



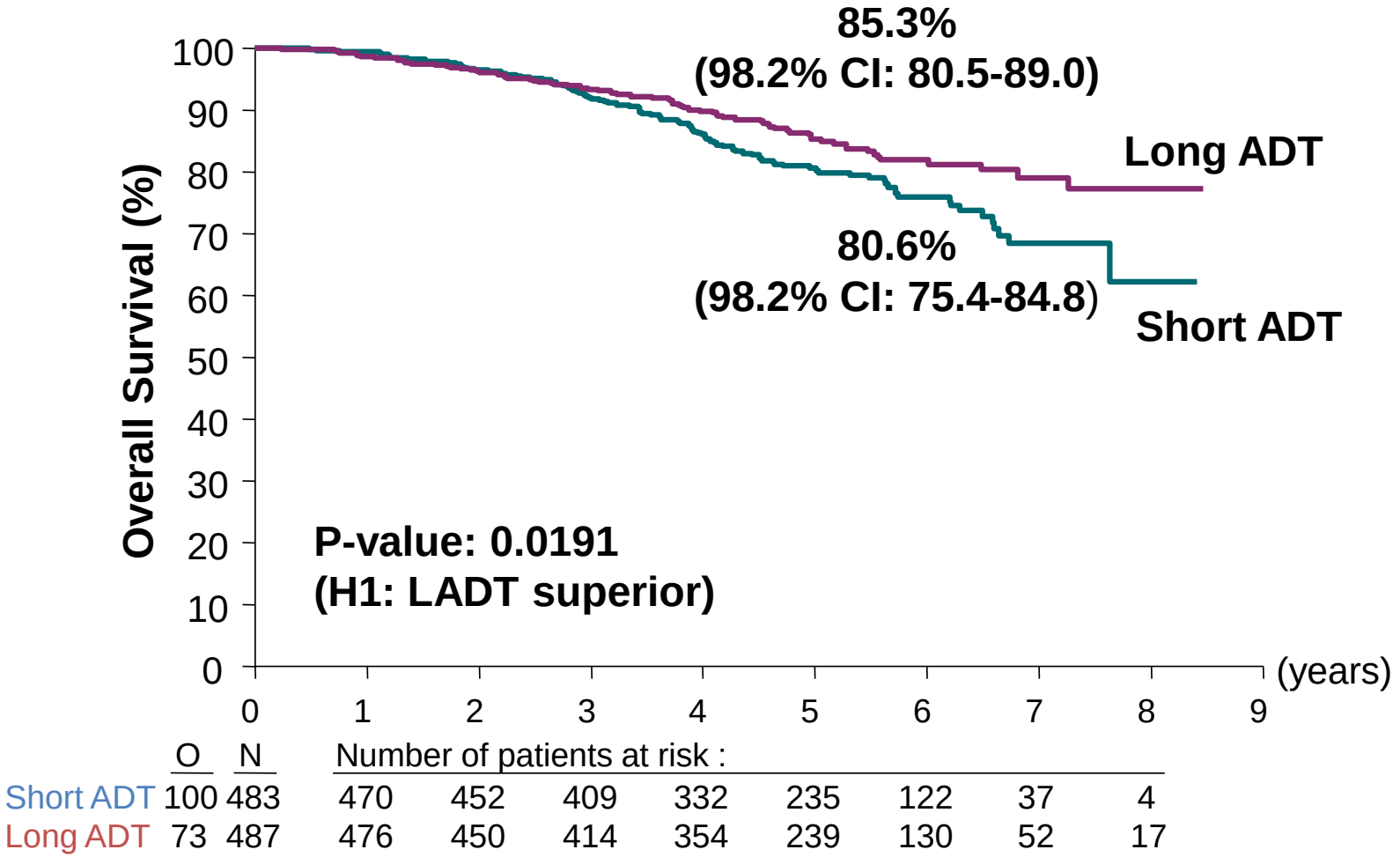

### SPCG-7





Mason et al. *J Clin Oncol*. 2015;33:2143-50.
Fossa et al. *Eur Urol*. 2016;70:684-91.

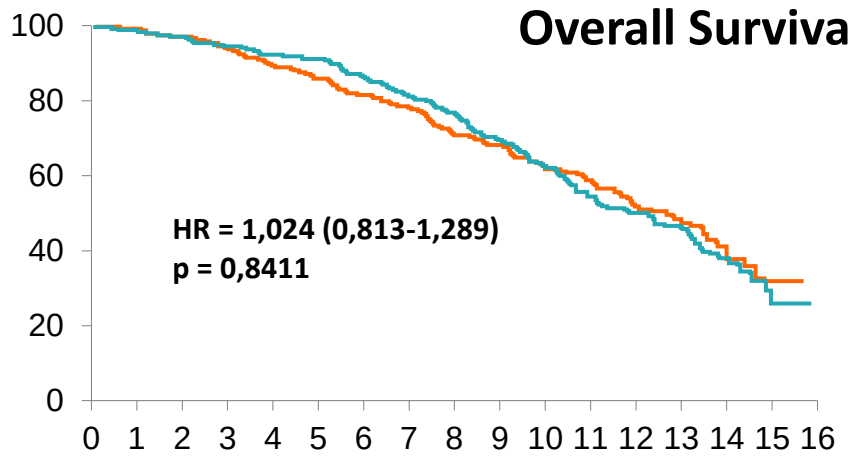
# ADT + RXT: 3 Years > 6 Months (OS)

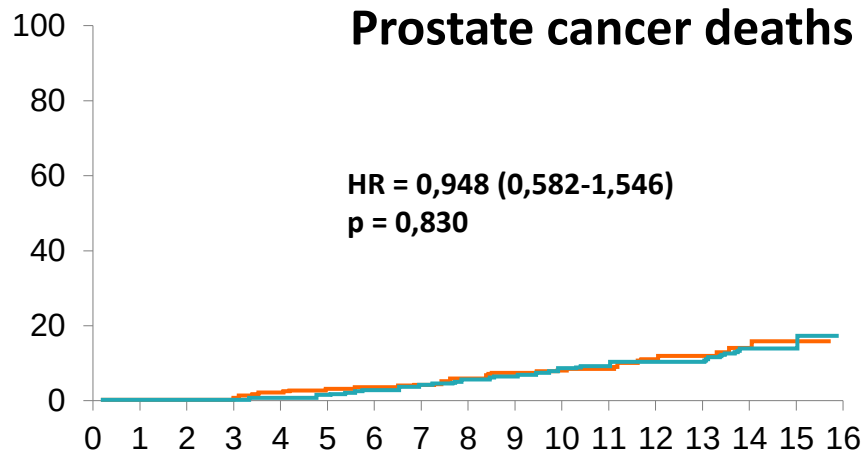



Bolla, *NEJM*. 2009;360:2516-27.

# Duration of ADT with RXT: 18 months or 36 months?

n=630 pts, N0M0, age ≤ 80 y
T3-T4, PSA > 20 ng/ml, Gleason ≥8

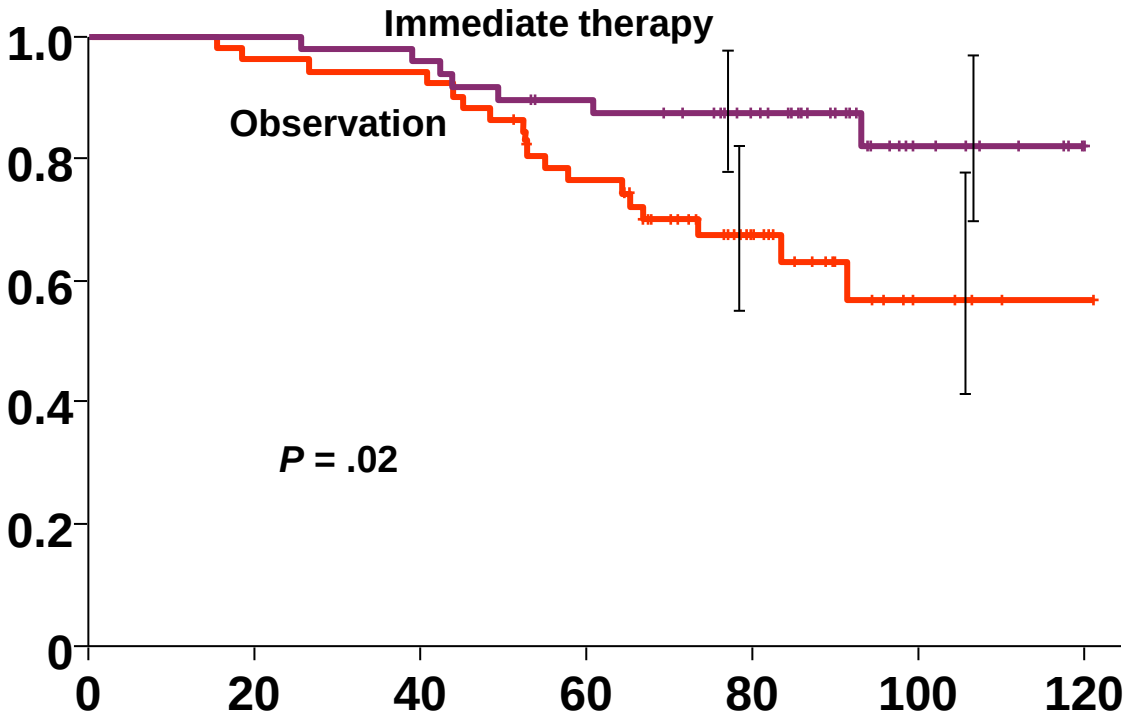



- Relapse-free survival better with 36 months (HR 0,714, IC95% 0,532-0,952, p=0,024)
- No benefit in MFS, OS or specific survival
- QOL better with 18 months

Nabid A et al., ASCO 2017, Abstr. 5008

# Immediate ADT improves OS in pN+ patients post RP




| Patients (n) | | | | |
|---|---|---|---|---|
| Immediate therapy | 47 | 47 | 40 | 8 |
| Observation | 51 | 49 | 37 | 5 |

Messing EM, et al. *New Engl J Med*. 1999;341(24):1781-1788.

# Should adjuvant ADT be used after prostatectomy for high-risk patients?

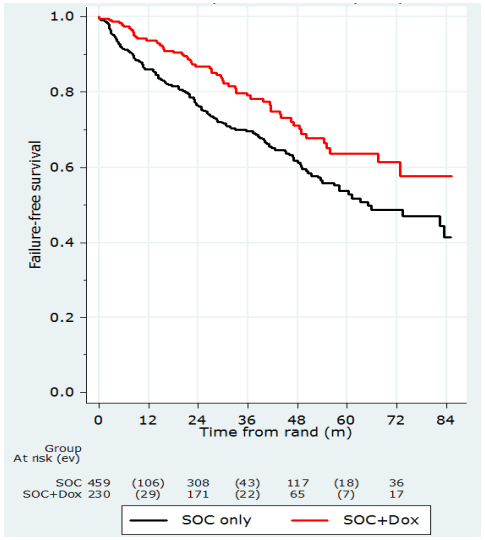
**Ongoing GETUG 20 trial:**

pT3b or Gleason 8
pN0 or pNx, PSA undetectable

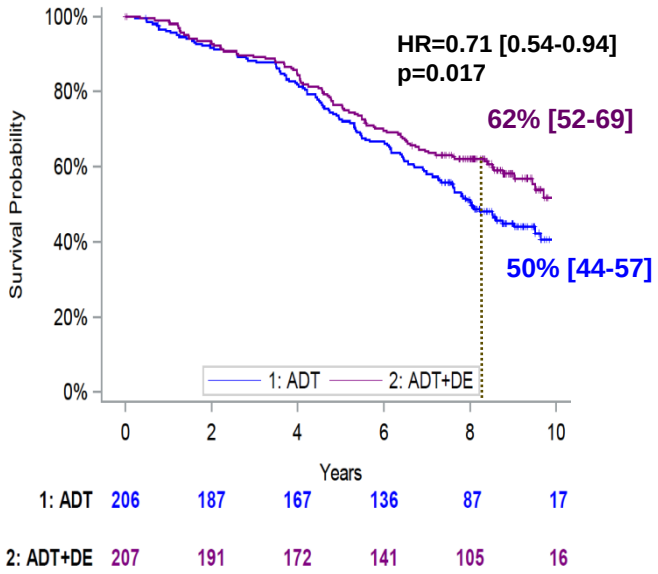
n=700 planned pts

# Docetaxel trials (with ADT) in high-risk localized prostate cancer: RFS

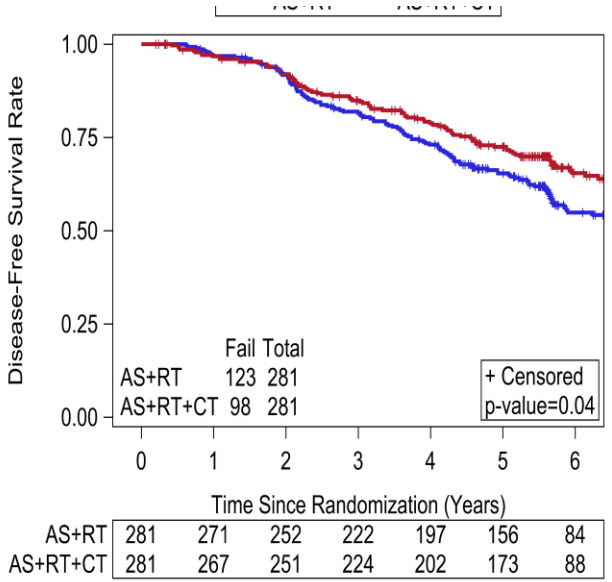
**STAMPEDE**




**GETUG 12**




**RTOG 0521**

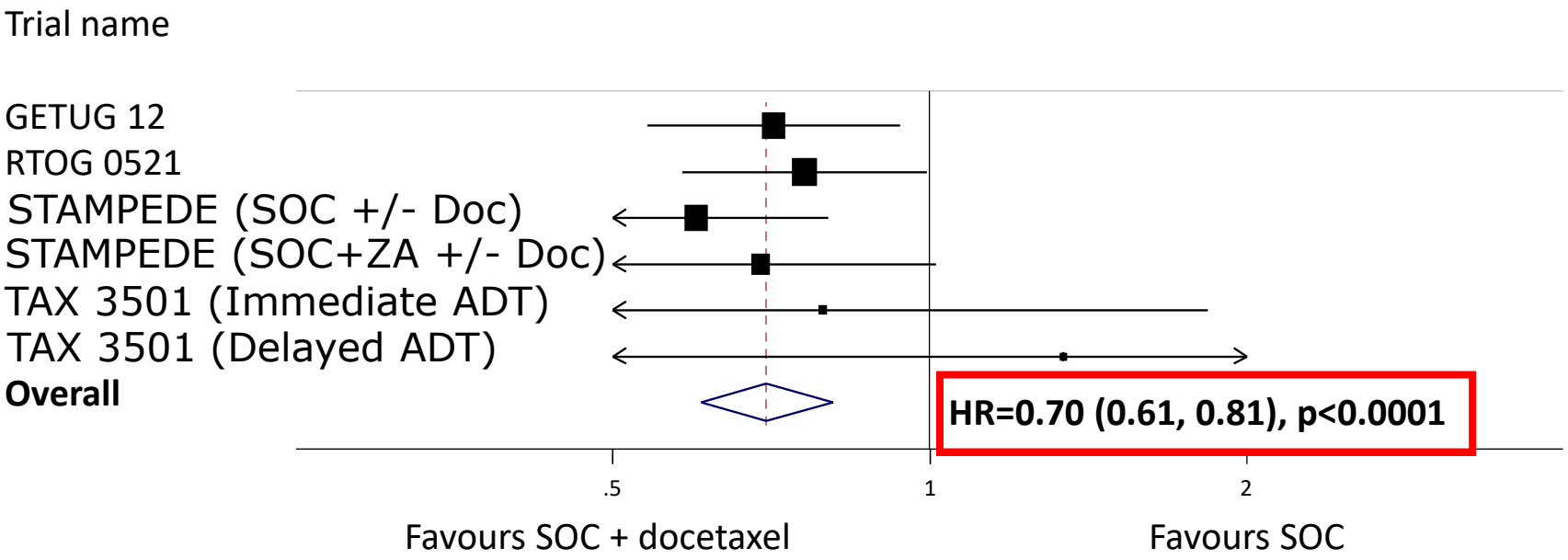



**2016 Meta-analysis: HR=0.70 (0.61, 0.81) for RFS, p<0.0001**

Fizazi K, Lancet Oncol 2015
James N, Lancet 2016 (Figure courtesy of Nick James)
Sandler H, ASCO 2015
Vale C, Lancet Oncol 2016

# Docetaxel in localized prostate cancer: “Failure-free survival”

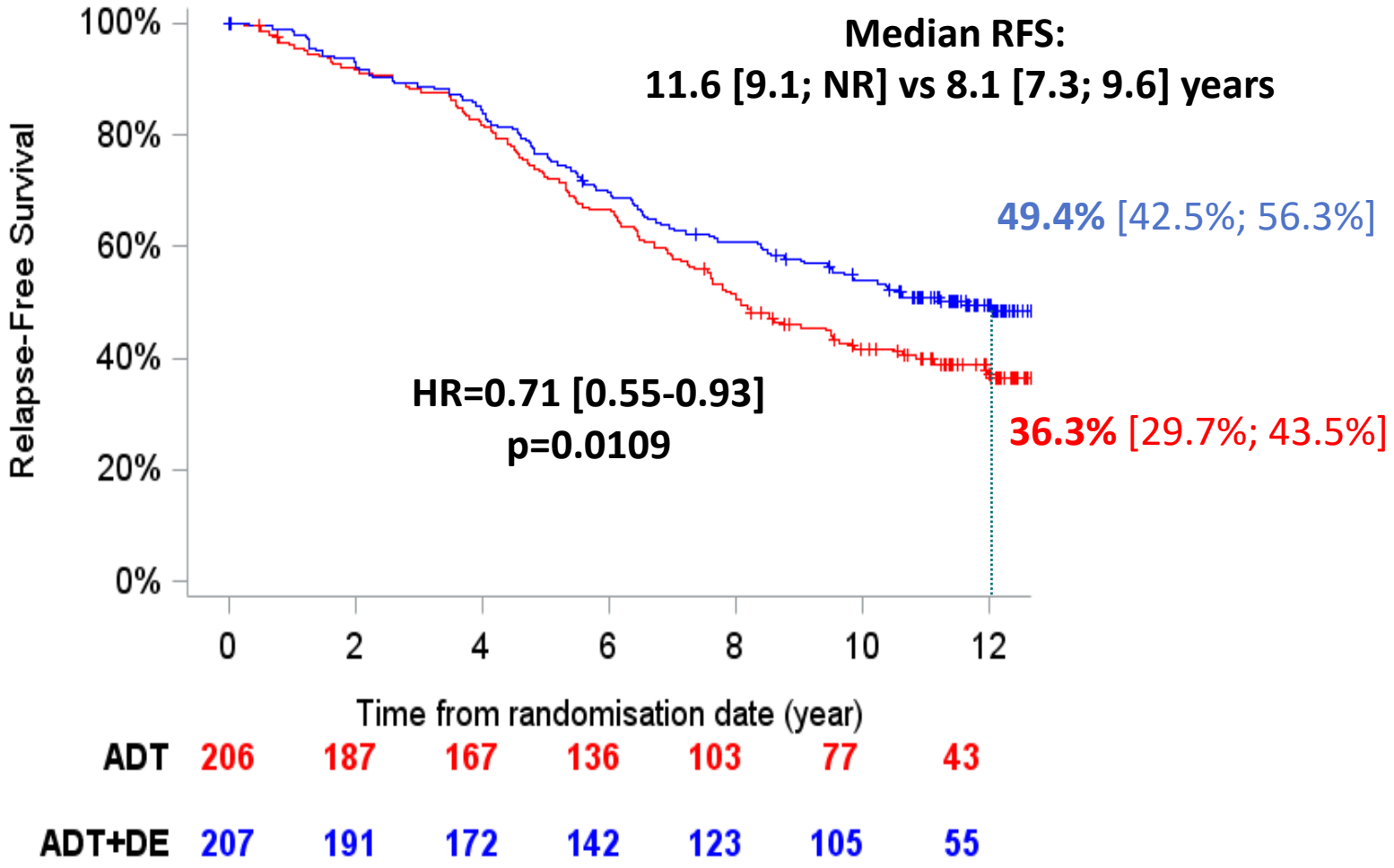
## Results based on 2348 men / 842 events




**8% absolute reduction in failure (from 70% to 62%) at 4 years**

Vale C, Lancet Oncol 2016; 17: 243-56

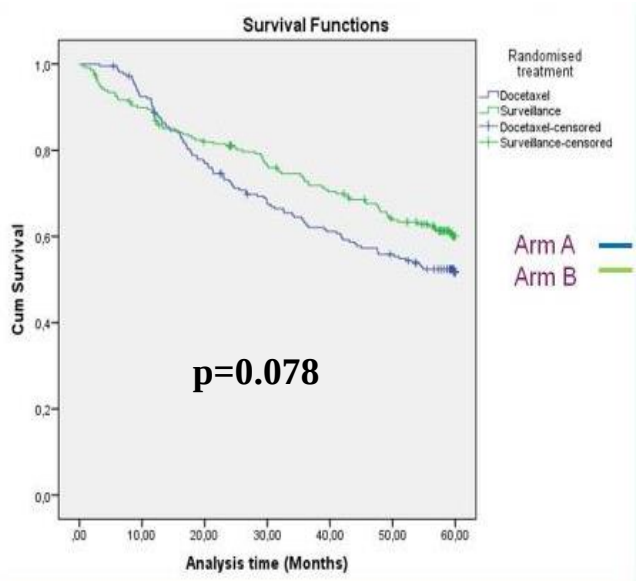
# UPDATED ANALYSIS OF GETUG-12: RELAPSE-FREE SURVIVAL (RFS) (233 events)



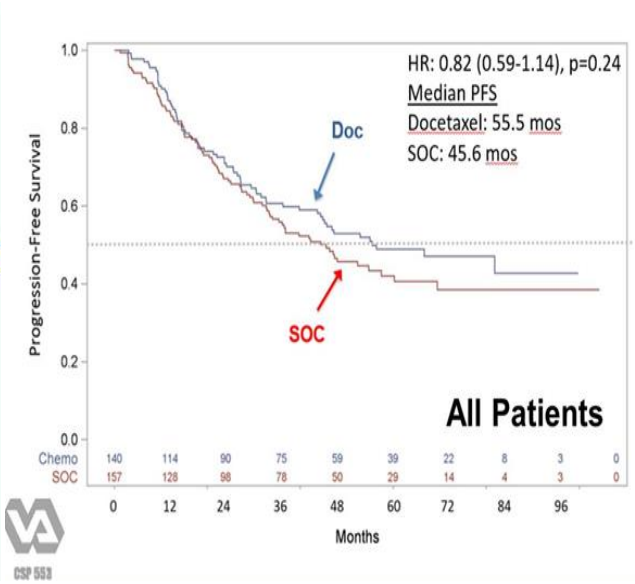

Fizazi K, ESMO 2018

# Other docetaxel trials in high-risk localized prostate cancer: RFS

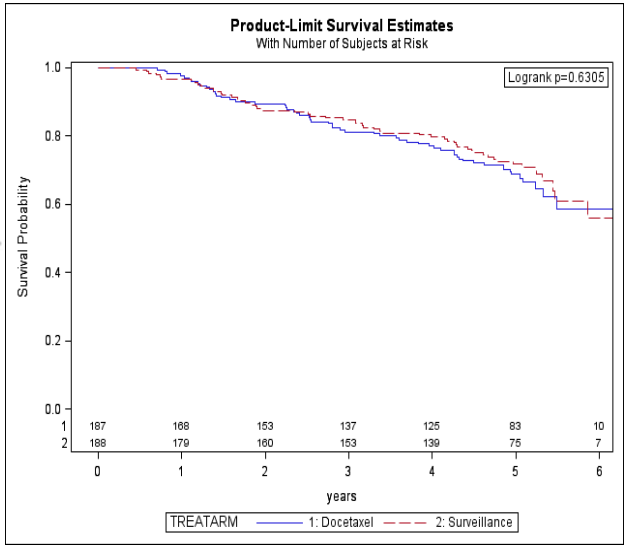
**SPCG12/Ad Pro (n=459)**




**VA CSP #553 (n=297)**



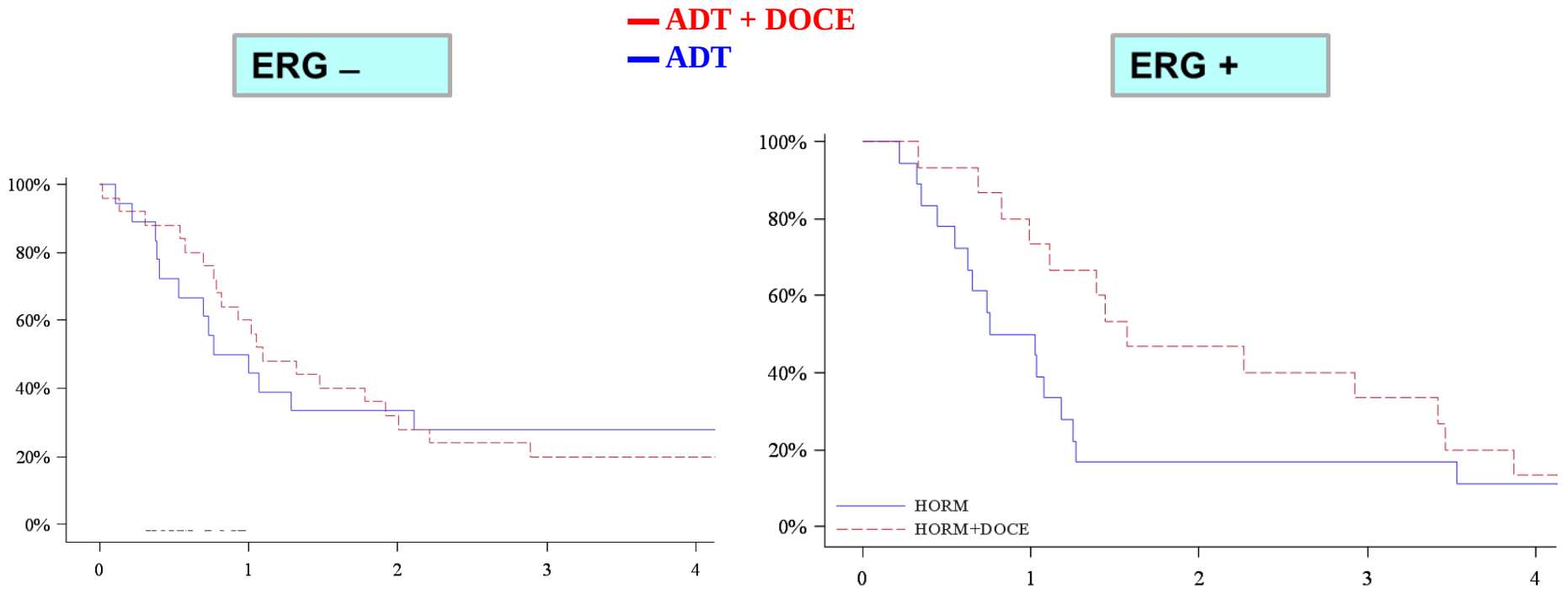

**SPCG13/Ad Rad (n=375)**




Ahlgren et al. ASCO 2016 (abstr 5001)
Lin et al. AUA 2016 (abstr 740)

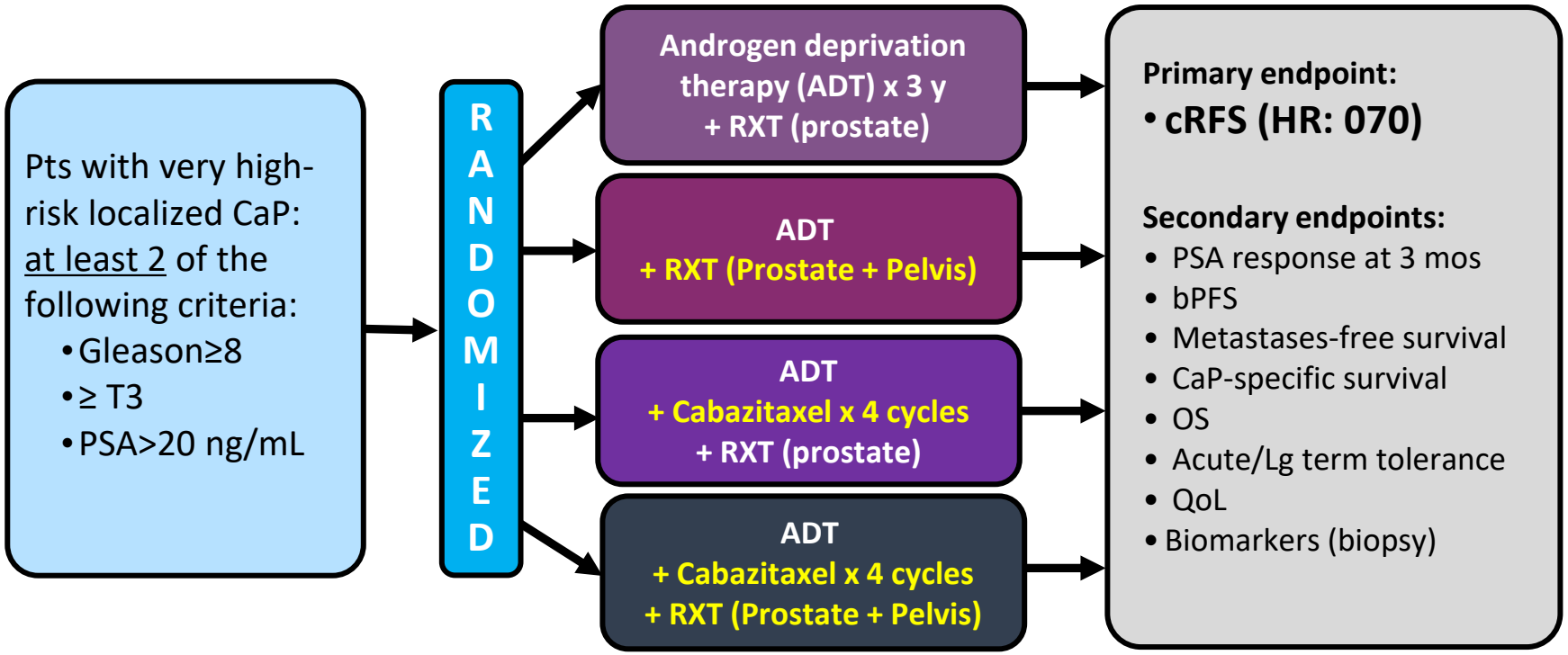
Kellokumpu-Lehtinen et al. ASCO 2018 (abstr 5000)

# Sensitivity to docetaxel predicted by ERG expression? (GETUG 15)




Rajpar S, ASCO 2017

# PEACE-2: European Phase III Trial of Cabazitaxel and Pelvic Irradiation in Patients With High-risk Localized Prostate Cancer

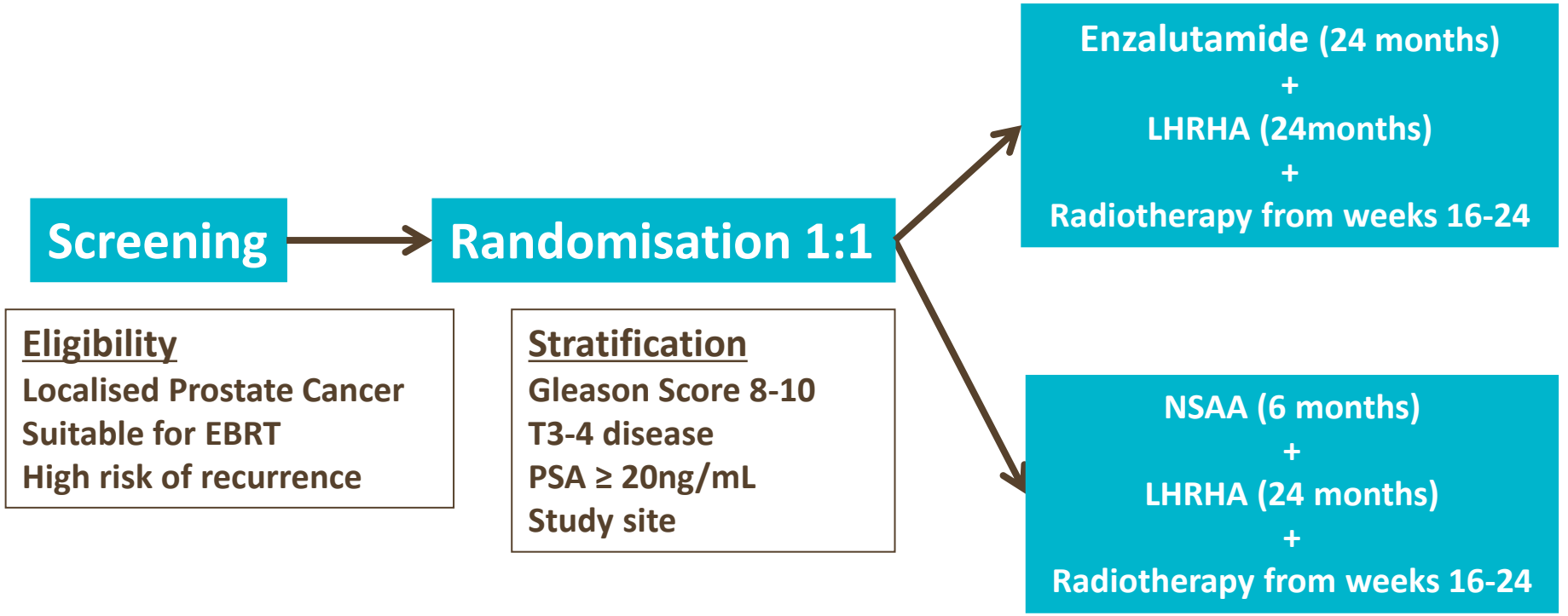



Study sponsor: Unicancer

**n= 750 pts recruited**

NCT01952223

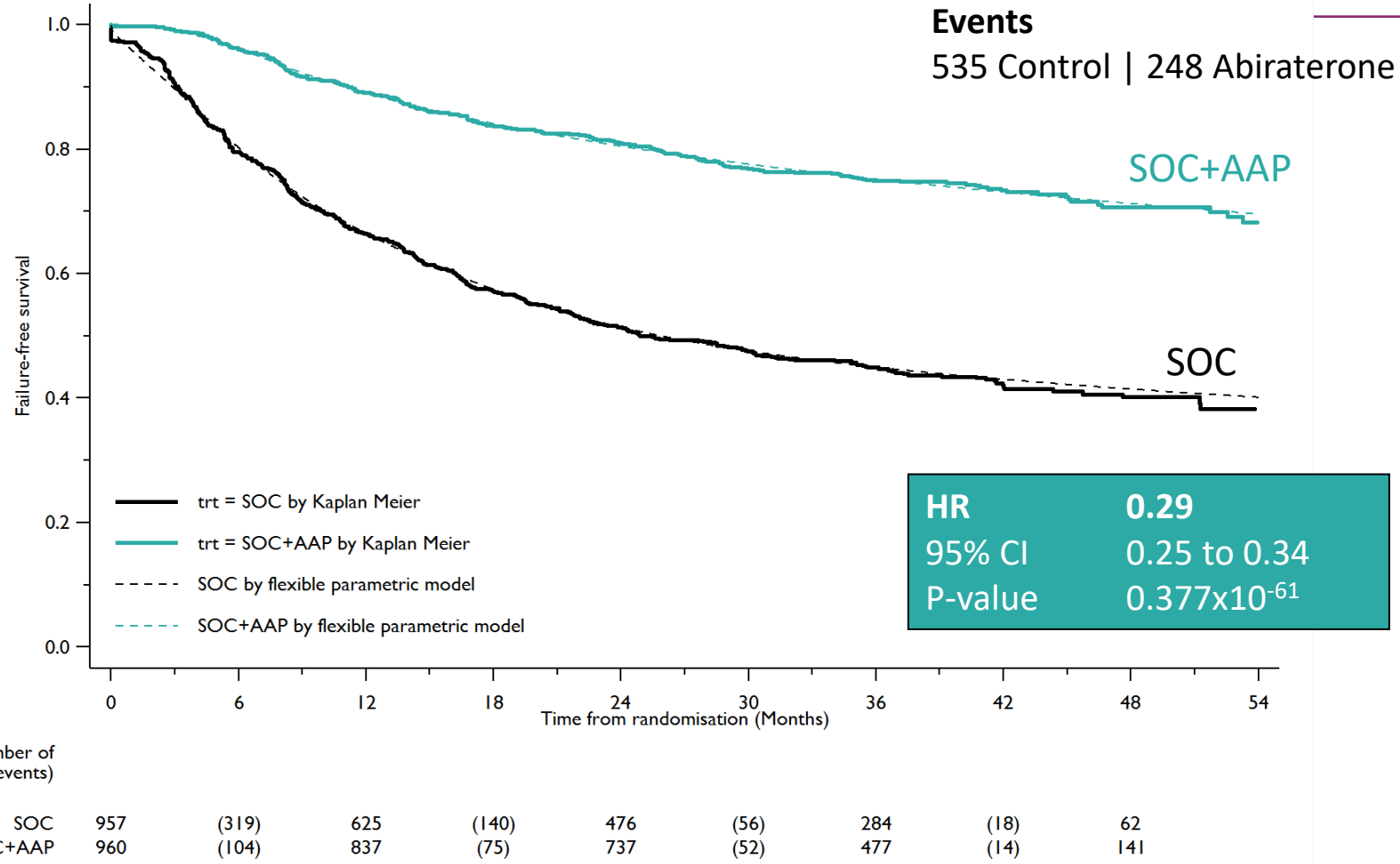
# ENZARAD




**n=800 planned pts**

# STAMPEDE Abiraterone: Localized (M0) CaP

**FFS**




| | |
|---|---|
| **HR** | **0.29** |
| 95% CI | 0.25 to 0.34 |
| P-value | $0.377 \times 10^{-61}$ |

**This represents a 71% improvement in time to failure**

James N, ESMO 2017

# Abiraterone acetate plus prednisolone with or without enzalutamide added to androgen deprivation therapy compared to ADT alone for men with high-risk nonmetastatic prostate cancer: primary combined analysis from two comparisons in the STAMPEDE platform protocol

Gerhardt Attard, Louise Brown, Noel Clarke, Laura Murphy, William Cross, Rob Jones, Silke Gillessen, J.Martin Russell, Adrian Cook, Jo Bowen, Anna Lydon, Ian Pedley, Omi Parikh, Simon Chowdhury, Zafar Malik, David Matheson, Chris Parker, Matthew Sydes, Mahesh Parmar, Nicholas James **on behalf of the STAMPEDE investigators***

Conducted by Medical Research Council Trials Unit at University College London, U.K.

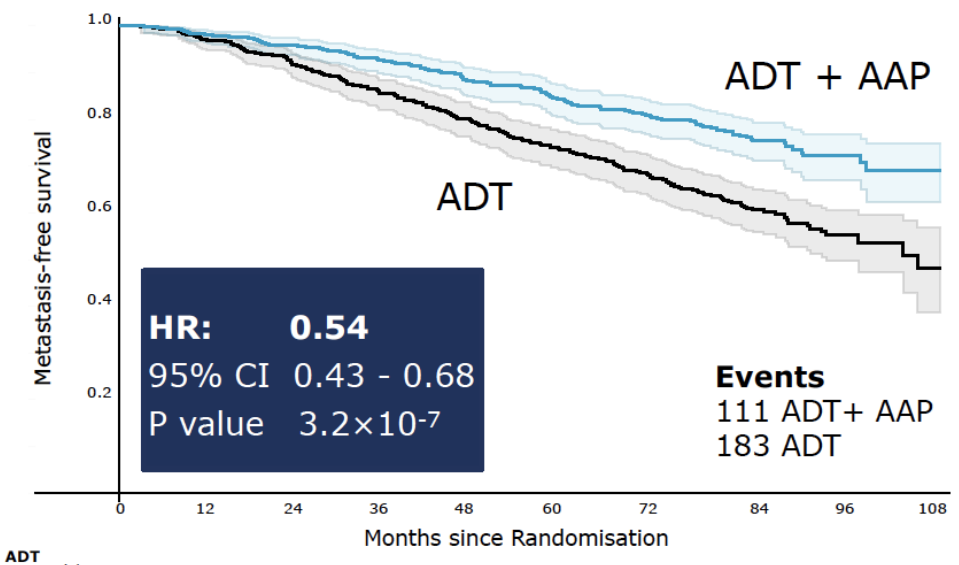
ClinicalTrials.gov number, NCT00268476 & Current Controlled Trials number, ISRCTN78818544

*113 U.K. and Swiss sites: list of investigators and collaborators at www.stampedetrial.org

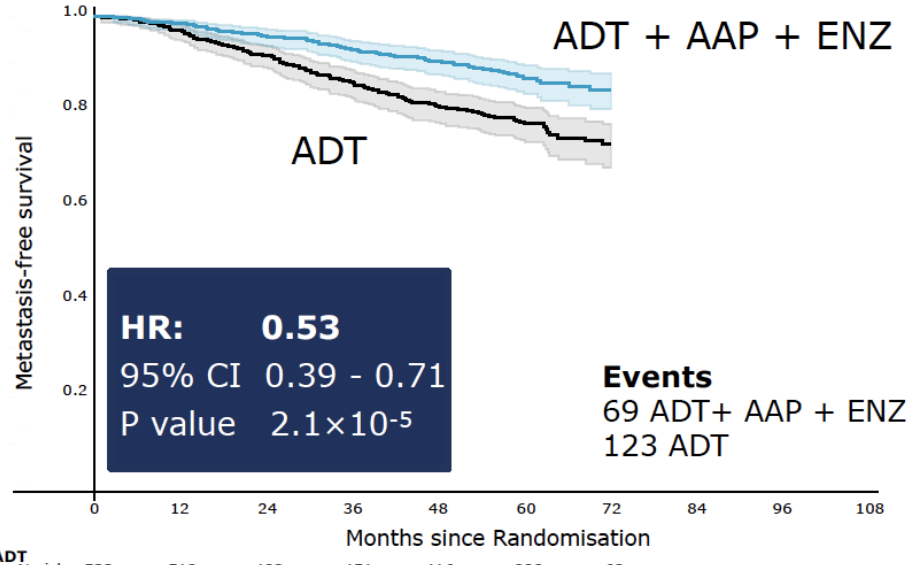
www.stampedetrial.org

2021 ESMO congress

# Metastasis-free survival by randomisation period




| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **ADT** | | | | | | | | | | |
| At-risk | 455 | 438 | 411 | 385 | 351 | 318 | 266 | 172 | 53 | 9 |
| Censored | 0 | 3 | 4 | 5 | 8 | 15 | 40 | 112 | 222 | 263 |
| Event | 0 | 14 | 40 | 65 | 96 | 122 | 149 | 171 | 180 | 183 |
| **ADT+AAP** | | | | | | | | | | |
| At-risk | 459 | 441 | 426 | 411 | 391 | 362 | 312 | 198 | 71 | 14 |
| Censored | 0 | 9 | 13 | 13 | 14 | 22 | 58 | 157 | 279 | 334 |
| Event | 0 | 9 | 20 | 35 | 54 | 75 | 89 | 104 | 109 | 111 |

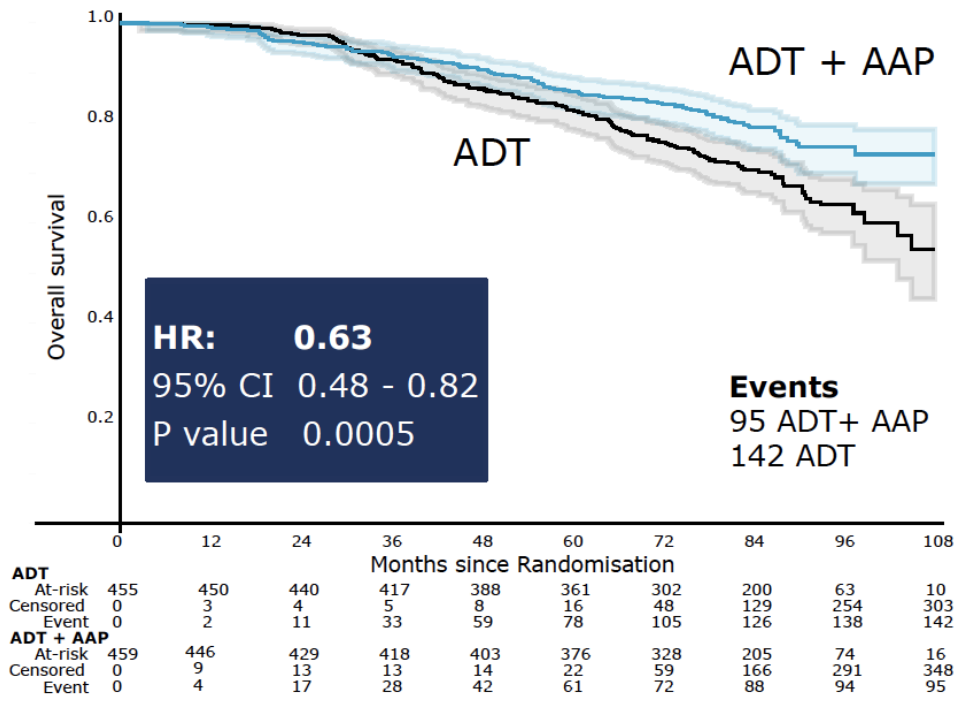


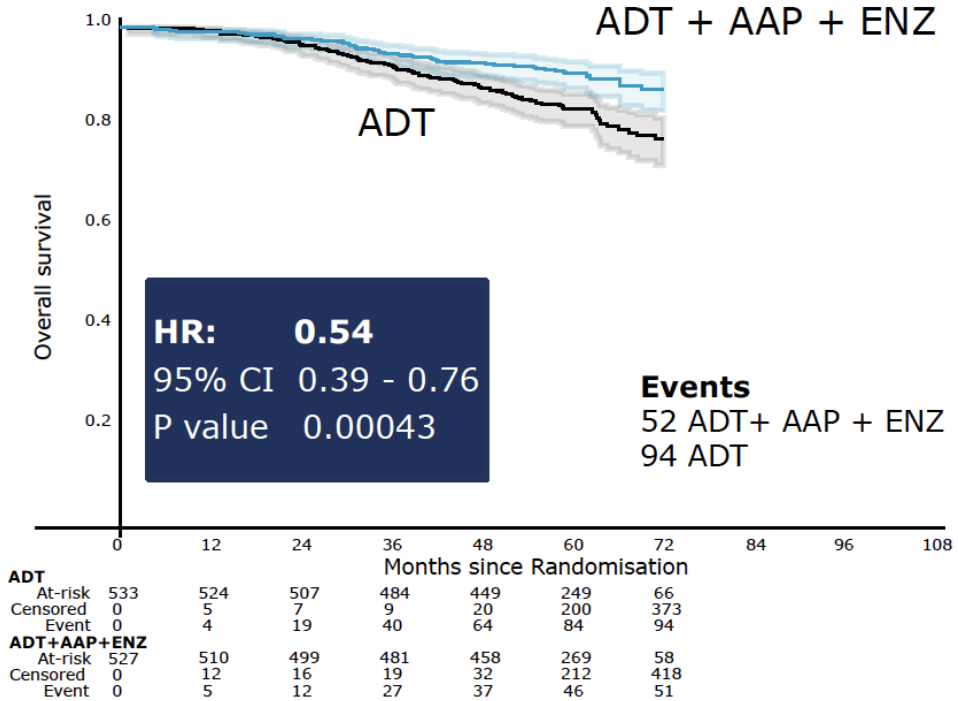

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **ADT** | | | | | | | |
| At-risk | 533 | 512 | 483 | 451 | 416 | 232 | 63 |
| Censored | 0 | 5 | 7 | 9 | 18 | 186 | 347 |
| Event | 0 | 16 | 43 | 73 | 99 | 115 | 123 |
| **ADT+AAP+ENZ** | | | | | | | |
| At-risk | 527 | 507 | 491 | 473 | 448 | 260 | 57 |
| Censored | 0 | 12 | 15 | 18 | 31 | 203 | 402 |
| Event | 0 | 8 | 21 | 36 | 48 | 64 | 68 |

Kaplan-Meier estimates with 95% CI in lighter shade

**Interaction HR: 1.02, 95% CI: 0.70 – 1.50, P=0.908**

# Overall survival by randomisation period




Kaplan-Meier estimates with 95% CI in lighter shade

Interaction between comparisons, P=0.5

# Adverse events

| Worst toxicity grade in 1st 2 years | ADT only (AAP comparison) | | ADT only (AAP + ENZ comparison) | | AAP | | AAP + ENZ | |
|---|---|---|---|---|---|---|---|---|
| | N (454) | % | N (530) | % | N (456) | % | N (522) | % |
| 3 | 118 | 26 | 160 | 30 | 151 | 33 | **277** | **53** |
| 4 | 12 | 3 | 12 | 2 | 17 | 4 | **23**[¶] | **4** |
| 5 | 0 | 0 | 0 | 0 | **3*** | **1** | **4^** | **1** |

[¶]Toxicities with the largest difference between AAP vs AAP+ENZ = (Gr 3) erectile dysfunction, hypertension, fatigue, (Gr 3/4) transaminitis

*1 event each of rectal adenocarcinoma, pulmonary haemorrhage and a respiratory disorder

^2 events each of septic shock and sudden death

# Conclusion: Systemic treatment in high-risk localized prostate cancer

- ADT+RXT to be privileged if life expectancy >5-10 years
- Duration of ADT: 18-36 months, likely to be adjusted based on comorbidities and individual risk
- Docetaxel improves RFS, but MFS/OS unclear
- Abiraterone added to ADT+ RXT improves dramatically both MFS and OS: new standard of care (in my opinion)