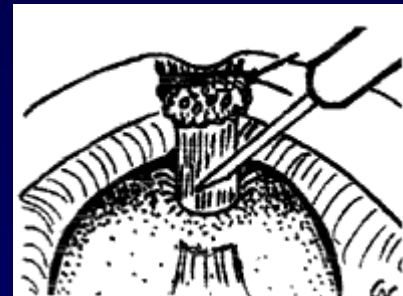


# Important Ongoing Clinical Trials in High Risk Localized Prostate Cancer

**Karim Fizazi, MD, PhD**  
**Institut Gustave Roussy**  
**Villejuif, France**

# High Risk Localized CaP



**Docetaxel after prostatectomy**

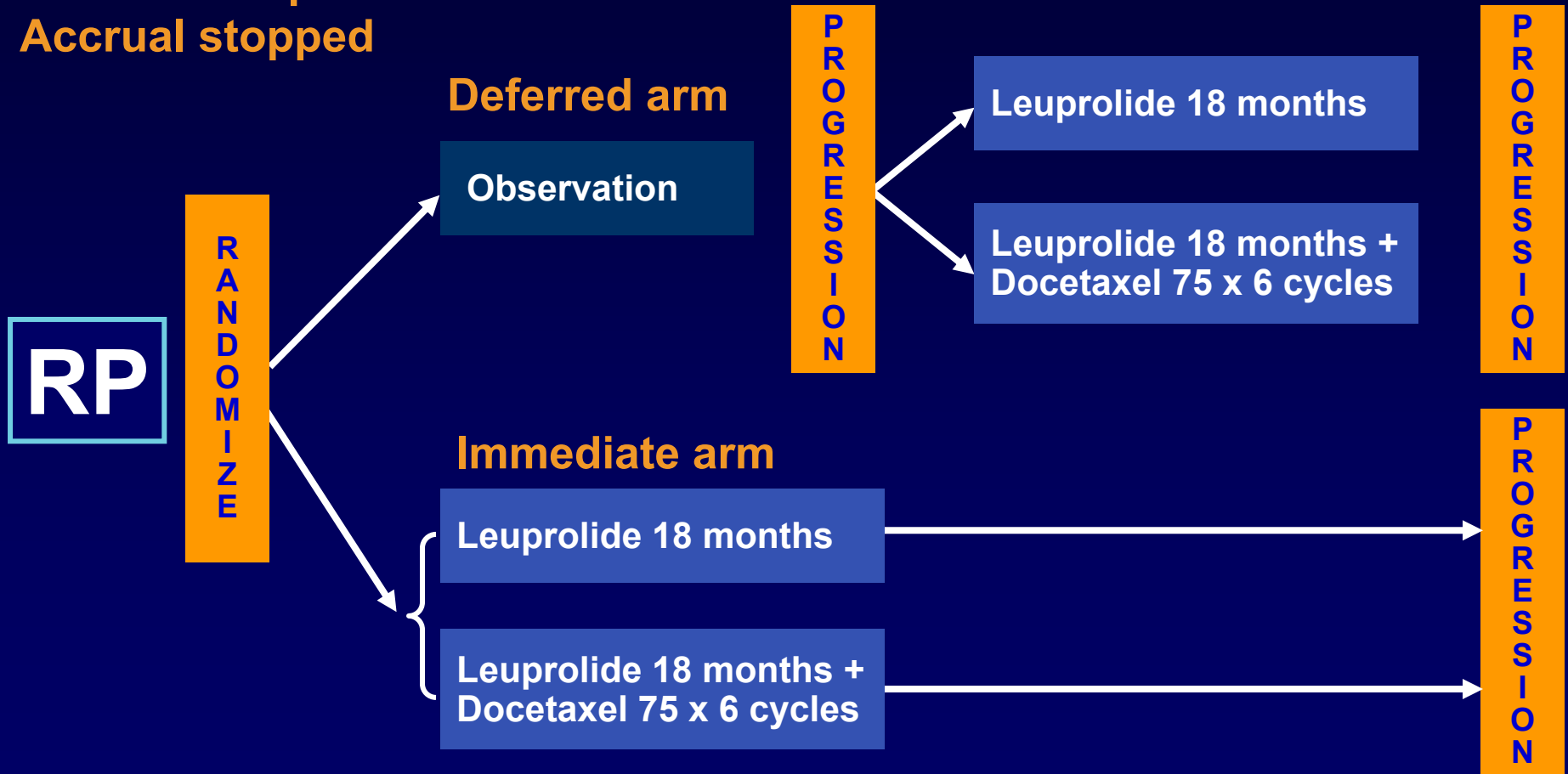
# TAX 3501

PI: M. Eisenberger (USA)

Primary Endpoint: PFS

n=228 /1696 pts

Accrual stopped



# AdPro

PI: Drs Ahlgren and Westman (Sweden)

Primary Endpoint: TTF

n=154/396

Started 10/05

Prostatectomy and  
post-op PSA<0.5

High risk:

- pT2 GS 4+3
- G 8-10 & SM +
- pT3 and GS  $\geq 7$
  
- if pre op PSA  $\geq 10$ ,  
LN Dissection

R  
A  
N  
D  
O  
M  
I  
Z  
E

```
graph LR; A[Prostatectomy and post-op PSA<0.5  
High risk:  
- pT2 GS 4+3  
- G 8-10 & SM +  
- pT3 and GS ≥ 7  
- if pre op PSA ≥ 10,  
LN Dissection] --> B[R  
A  
N  
D  
O  
M  
I  
Z  
E]; B --> C[Docetaxel 75 / 3 w  
x 6 cycles]; B --> D[Surveillance];
```

Docetaxel 75 / 3 w  
x 6 cycles

Surveillance

# VA # 553 CAP Montgomery (USA)

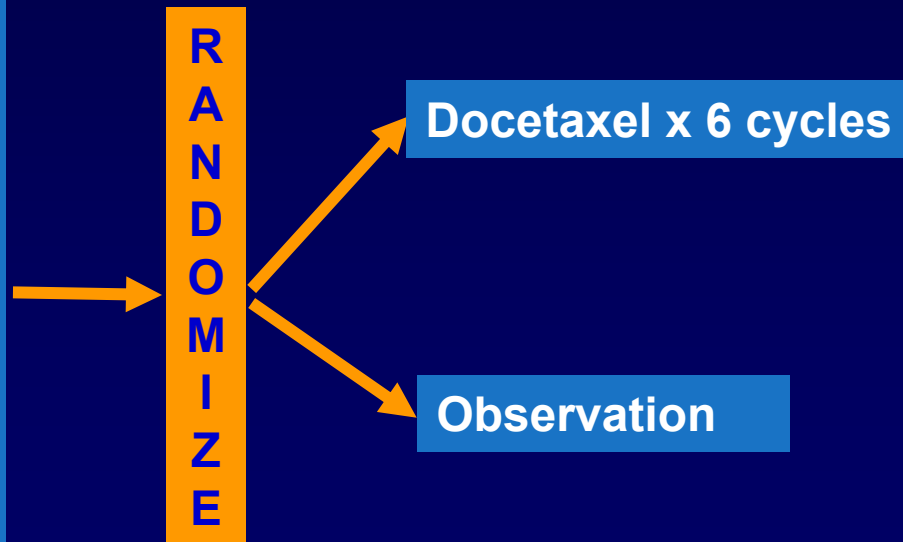
Primary endpoint: PFS (45% to 60%)

n=65/636

Prostatectomy and  
post-op PSA<0.1

High risk: any of:

- pT3b or pT4
- pT3a and GS  $\geq$  7
- Pre-op PSA>20
- Risk of relapse>50%  
(Kattan nomogram)



# High Risk Localized CaP



**Docetaxel after Radiotherapy**

# RTOG 0521

## PI: H Sandler (USA)

**Primary Endpoint: 4 year OS**

**n=260/600**

Neo-adj ADT 2 months + RT

Any of:

- GS 9-10 & PSA <100
- GS 8, PSA<20, T2-T3
- GS 8, PSA>20
- GS 7, PSA>20

PSA<150 and N-

R  
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Docetaxel 75 mg/3 w x 6 cycles  
+ ADT (2 years)

ADT (2 years)

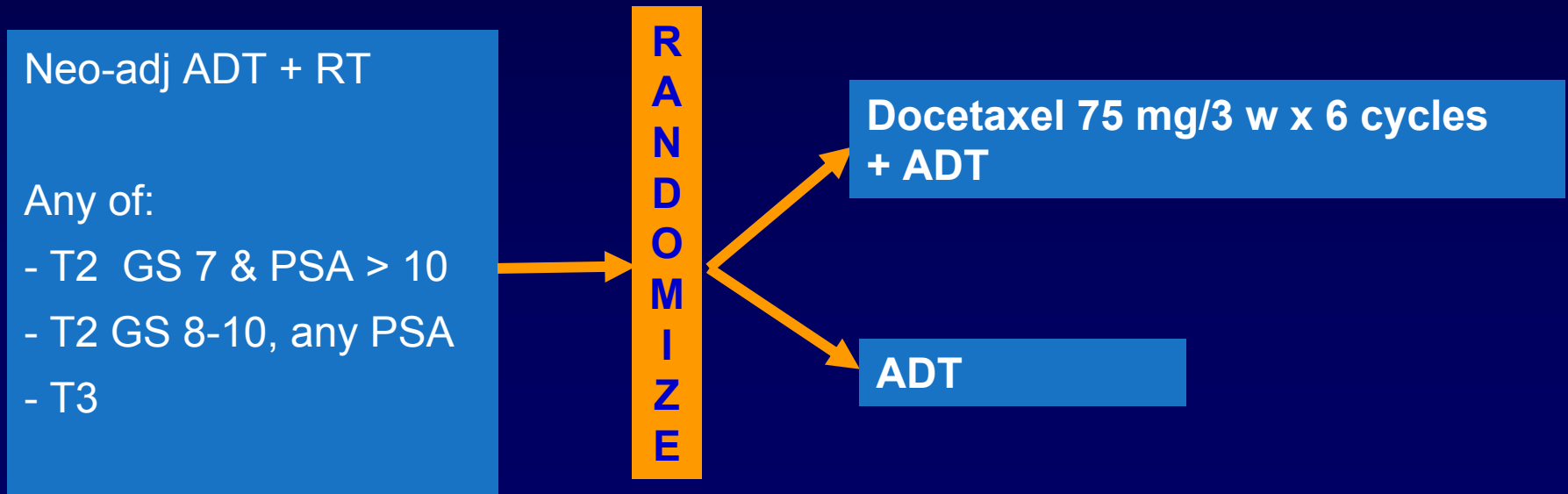
# AdRad

PI: PL Kellokumpu-Lehtinen (Finland)

n=9/924

Started late 2007

Intermediate/High risk



# High Risk Localized CaP



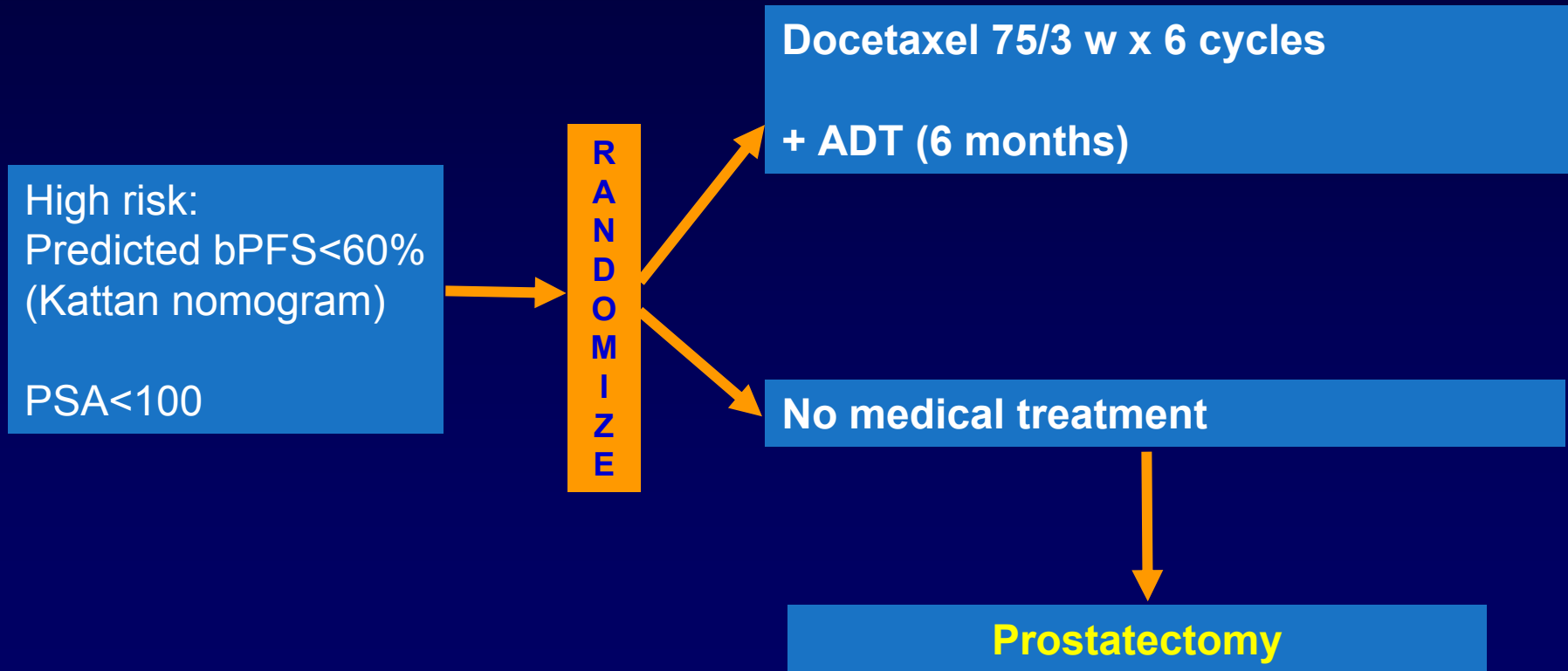
**Docetaxel before Prostatectomy**

# CALGB 90203

PI: J Eastham (USA)

Primary Endpoint: 3 year bPFS

n=14/750



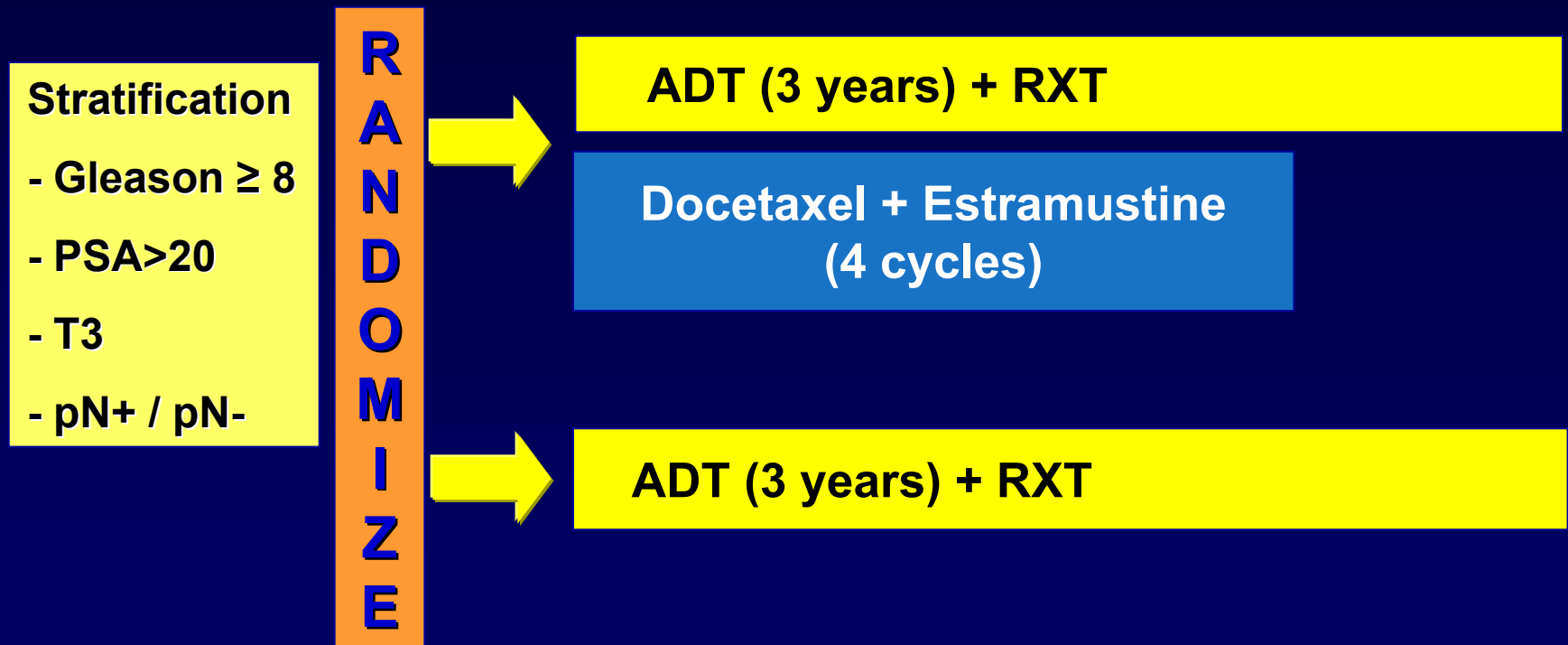
# High Risk Localized CaP



**Docetaxel before Radiotherapy**

# High Risk Localized Prostate Cancer GETUG 12 Trial

Primary endpoint: PFS  
n=413/400 pts

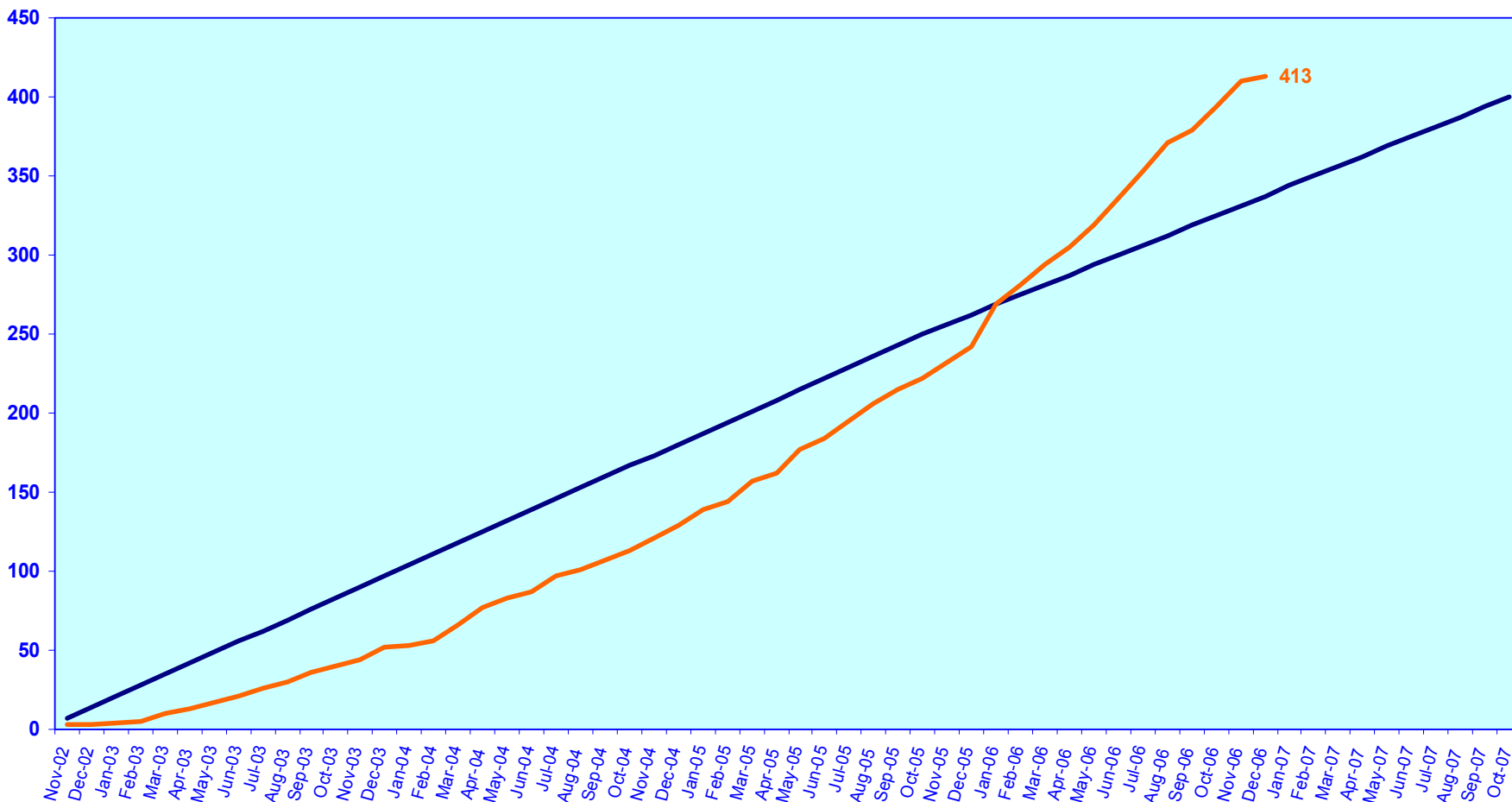


PI: K. Fizazi

# GETUG 12 Trial

Accrual completed in 11/2006

GETUG 12/0203 - Courbe des inclusions



# GETUG 12 Trial: Population

- T3 67%
- PSA > 20 59%
- Gleason  $\geq$  8 42%
- pN+ 28%

## # Adverse Factors

1	36%
2	39%
3	18%
4	6%

# 05-043 Dana-Farber

PI: A D'Amico (USA)

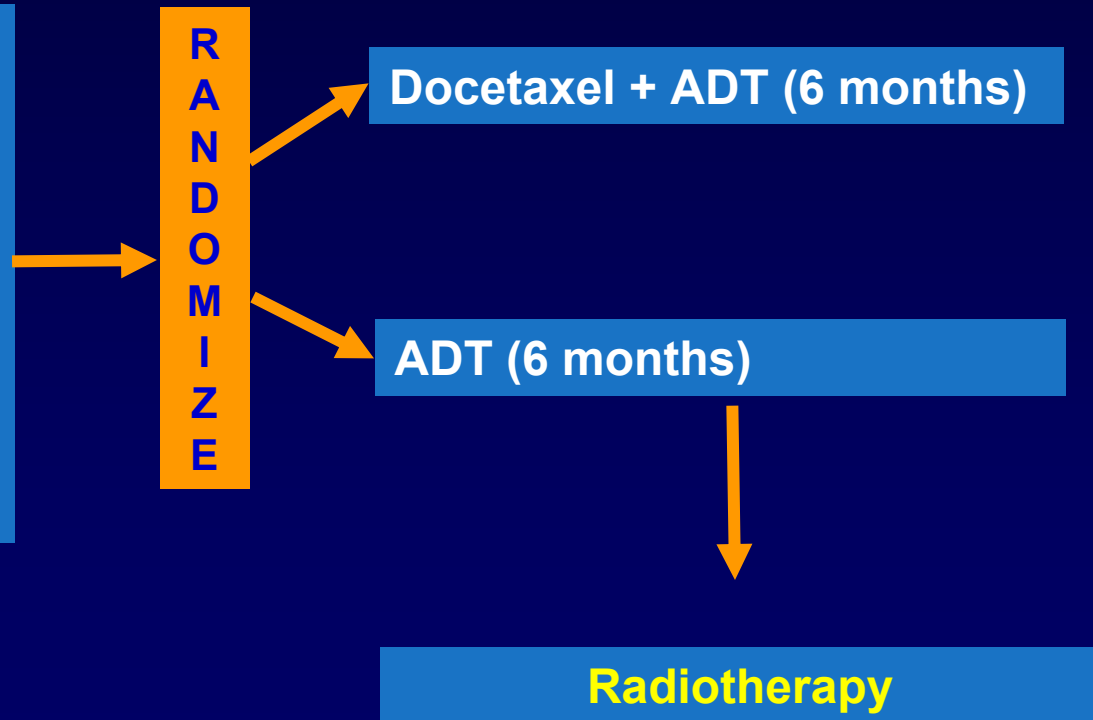
n=100 /350

Endpoint: OS

Inclusion criteria:

Intermediate-high risks:

- Gleason  $\geq 7$
- T3-T4
- PSA > 10
- PSA velocity > 2 ng/mL/year



# Phase III Trials of Docetaxel in Localized Prostate Cancer

Study name	PI	Local treatment	# Patients (enrolled/planned)	Status
GETUG 12	K. Fizazi (France)	XRT	413/400	Accrual completed
RTOG 0521	H. Sandler (USA)	XRT	260/600	Ongoing
TAX 3501	M. Eisenberger (USA)	RP	228/1700	Early enrolment termination
AdPro	Ahlgren (Sweden)	RP	154/396	Ongoing
DOCET-L-02357	A. D'Amico (USA)	XRT	100/350	Ongoing
VA # 553 CAP	Montgomery (USA)	RP	65/636	Ongoing
CALGB 90203	Eastham (USA)	RP	14/750	Ongoing
AdRad	Kellokumpu-Lehtinen (Fin)	XRT	9/924	Ongoing

# Zoledronic Acid-Preventing Bone Metastasis in the Adjuvant Setting

# Prostate Cancer: *ZEUS*

## Key endpoints

Primary: Time to bone metastases (4 year)

Others: Overall survival, PSA doubling time, substudies on bone markers

**1,433** patients

Prostate cancer, M0

+/- previous local curative treatment, +/- ADT

High risk PCa with at least one of the following criteria:

- Gleason Score 8-10
- pN+
- PSA  $\geq$  20 at diagnosis

R

Zoledronic acid 4 mg q 3 months

No Zoledronic acid\*

Treatment duration 4 years

# Prostate Cancer: *RADAR*

## Key endpoints:

Primary: **PSA Relapse free survival (5 year)**

Secondary: Overall survival QOL, bone metastases free survival, BMD

**1,000 patients**

**Prostate Cancer**

T2a (Gleason score  $\geq 7$  and PSA  $\geq 10$ ), T2b-4, N0, M0

Stratification:

- T2a/T2b/T3,4
- <60 y/60-70 y/>70 y
- Gleason primary pattern 1-3/4,5
- PSA <10/10-20/>20
- Treatment center

R

Short term AD (STAD) – LHRH analogue for 5 mo prior to and during first mo of radiation treatment (total 6 mo)

Short term AD (STAD) – LHRH analogue for 5 mo prior to and during first mo of radiation treatment (total 6 mo)

+ **Zoledronic Acid 4 mg q 3 mo / 18 mo**

Intermediate term AD – LHRH analogue as for STAD arm, but continued for further 12 mo (total 18 mo)

Intermediate term AD – LHRH analogue as for STAD arm, but continued for 12 mo (total 18 mo)

+ **Zoledronic Acid 4 mg q 3 mo / 18 mo**

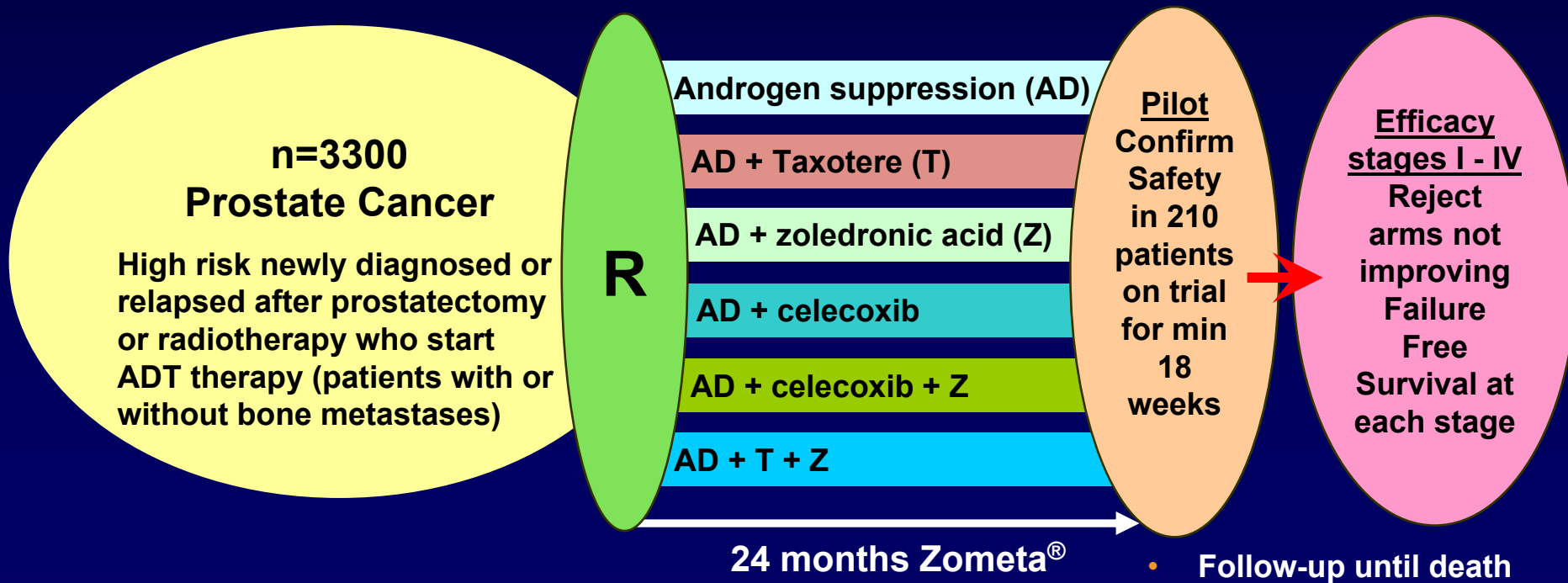
Treatment 18 mo/follow-up > 5 years

# Prostate Cancer: *STAMPEDE*

## Key endpoints:

Primary: Failure free survival

Secondary: QOL, cost effectiveness, toxicity, SREs, overall survival



# Conclusions

- **Docetaxel-based chemotherapy and zoledronic acid have demonstrated efficacy and are registered in castration-resistant prostate cancer.**
- **A series of large ongoing phase III trials are testing their potential impact in high risk localized prostate cancer.**
- **First results are awaited around 2010.**