

# Prostatacancer

*Patientens vej gennem sygdommen set fra onkologens vinkel*

Per Kongsted, overlæge, PhD

Afdeling for kræftbehandling, Klinik 4, Herlev og Gentofte Hospital

Oktober 2025

# Nøgletal

Incidens (2023): **4.404 / år**

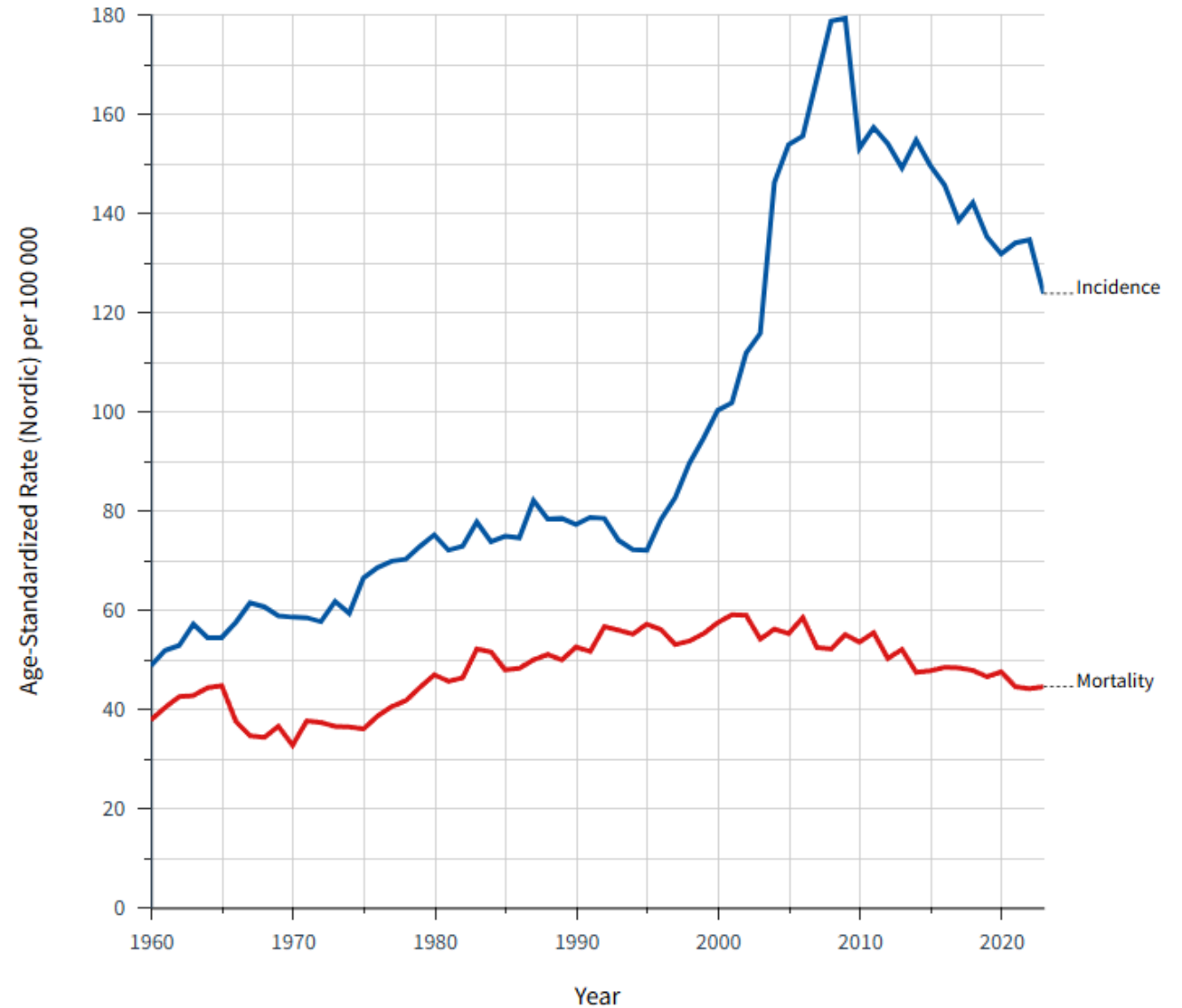
Prævalens (2023): **49.917**

Andel af alle mandlige kræfttilfælde: **~20%**

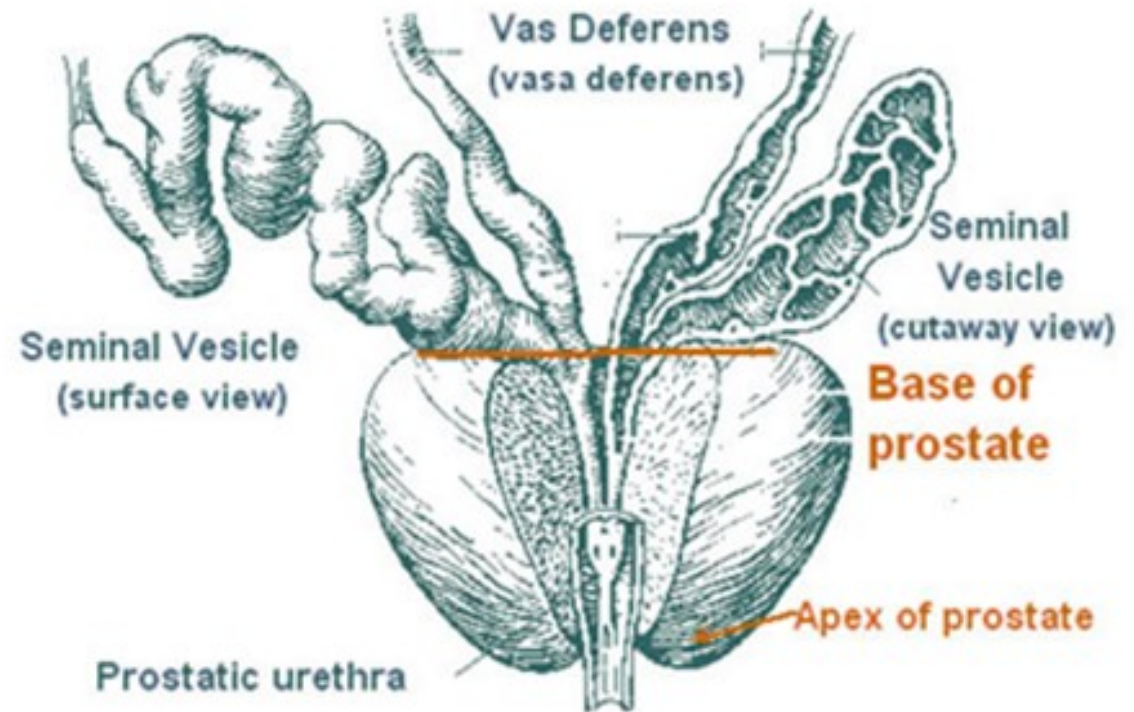
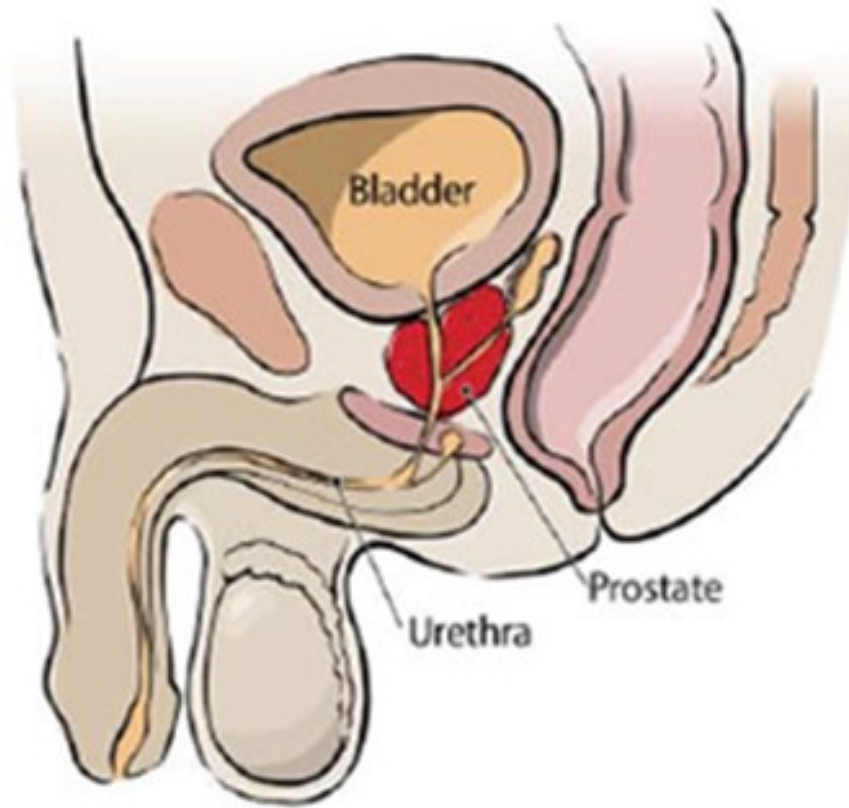
Relativ overlevelse (2019-2023)

1 år **98,7%**

5 år **90,7%**



# Anatomi



# Udredning

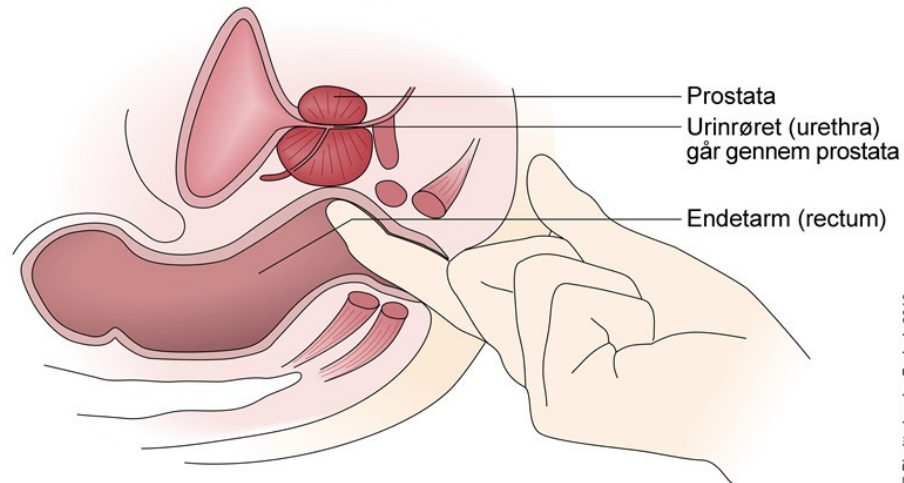


PSA forhøjet og/eller symptomer

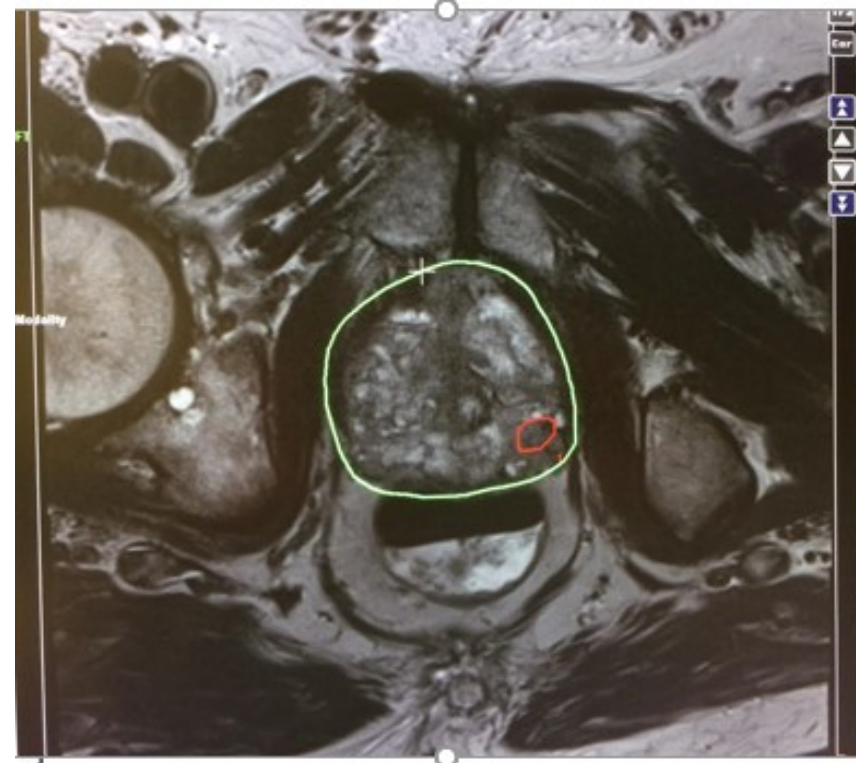
→ Rektal eksploration

→ MR-scanning af prostata

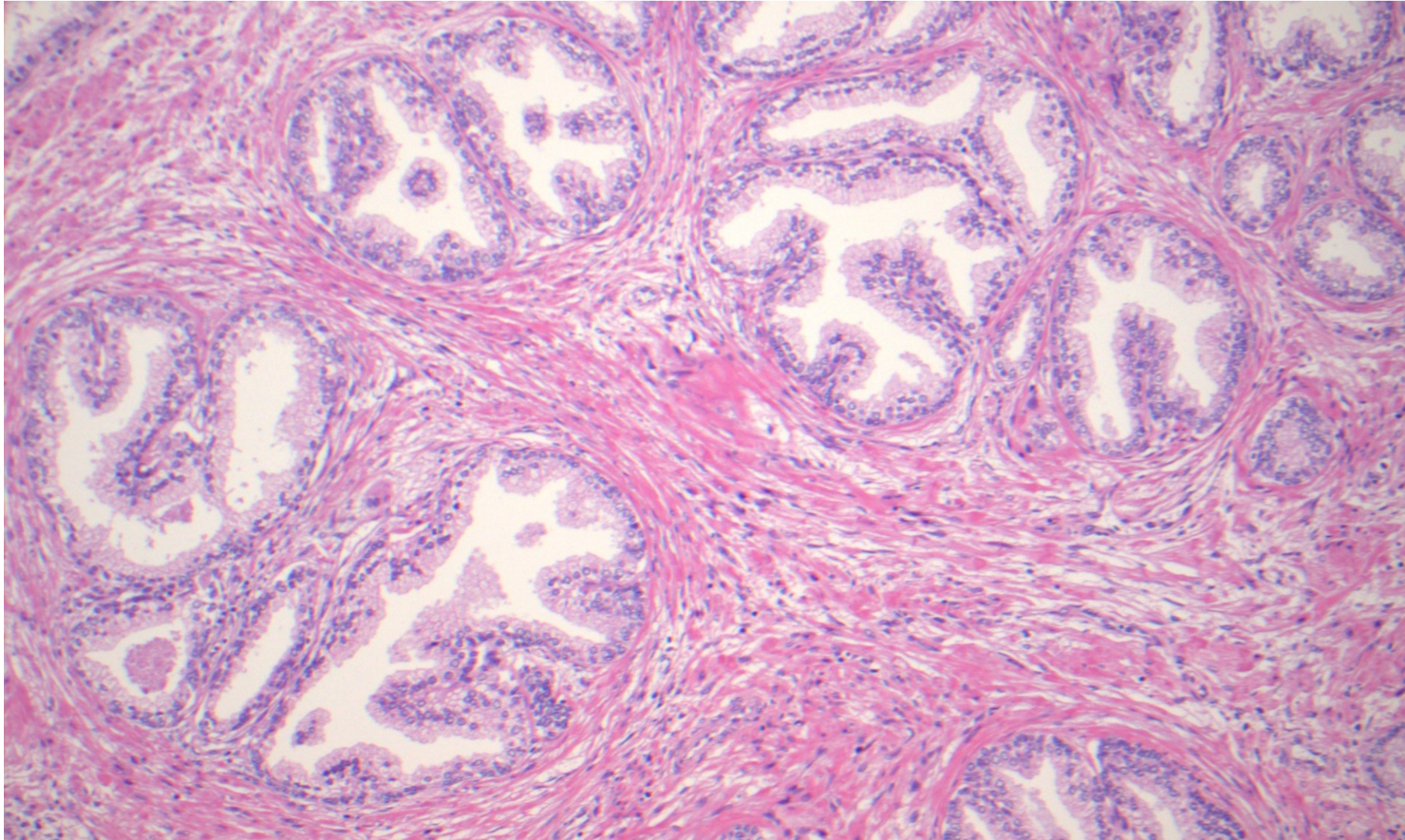
→ Transrektal ultralyds undersøgelse (TRUS) med biopsier (MR-guidede) via perineum



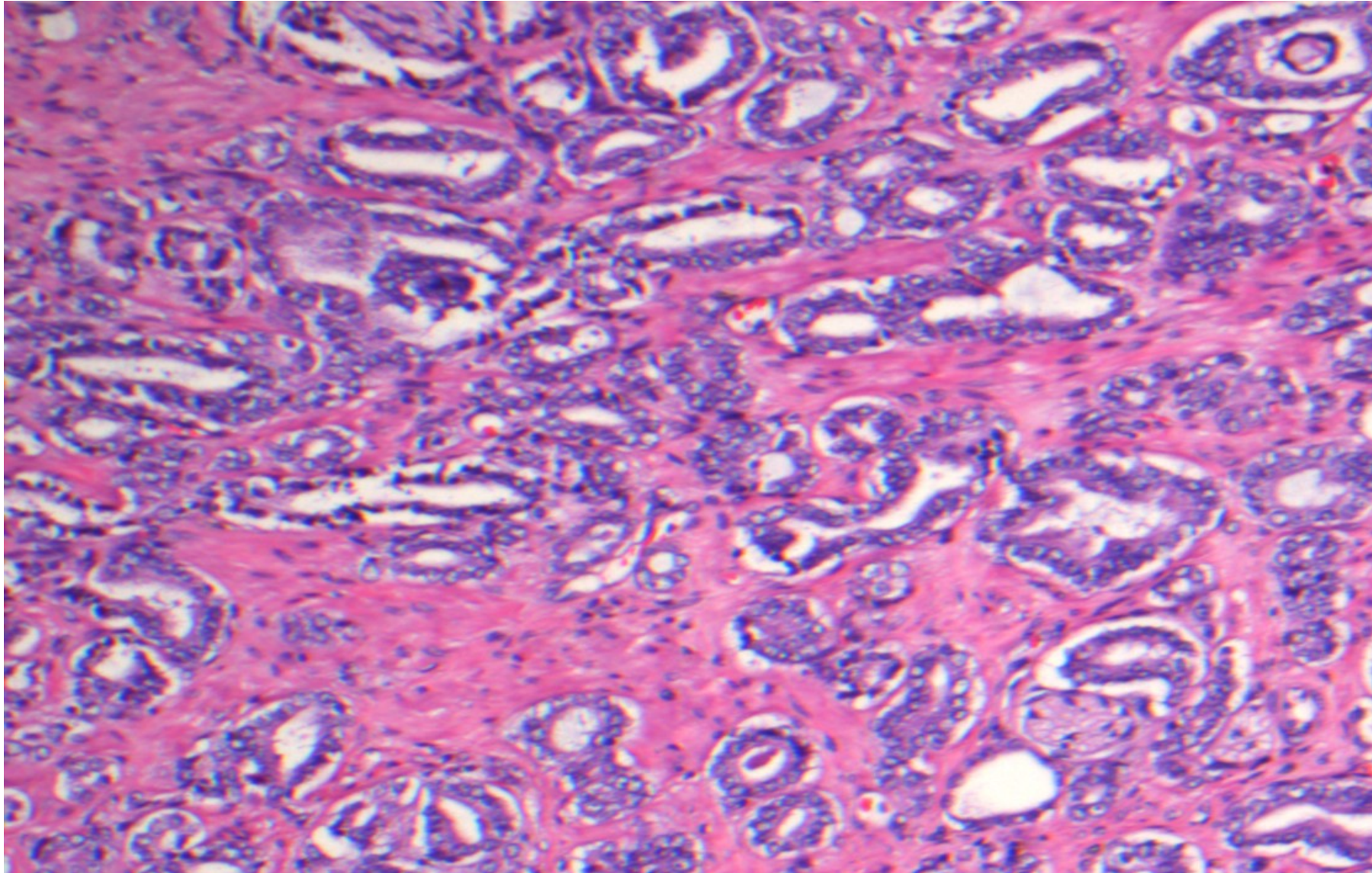
© Birgitte Lerche-Barlach 2010  
© Danske Regioner



# Normalt prostatavæv



# Adenocarcinoma prostatae, Gleason grading 1-5



# Kurativ behandling



PSA forhøjet eller symptomer  
→TRUS og biopsier:

klinisk T-stadie  
adenocarcinom (Gleason Score)

Klinisk lokaliseret sygdom?



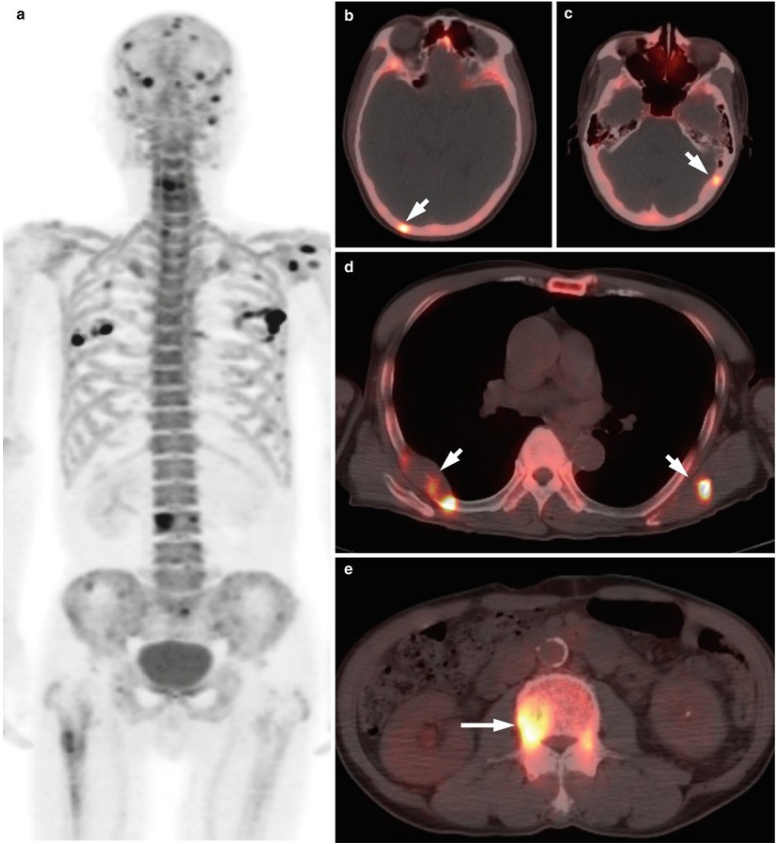
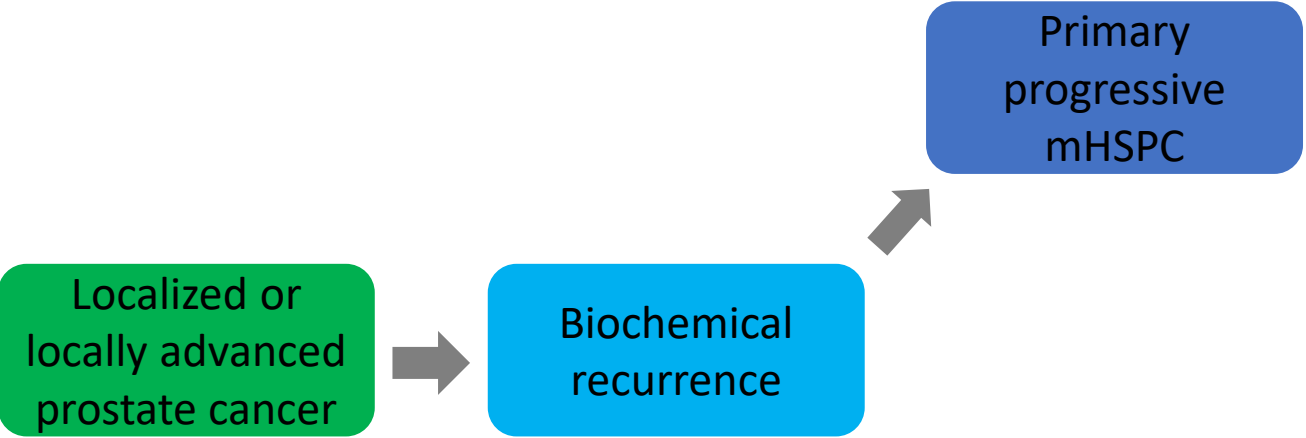
NaF-PET-CT-scanning



E b **KURATIV BEHANDLING** i

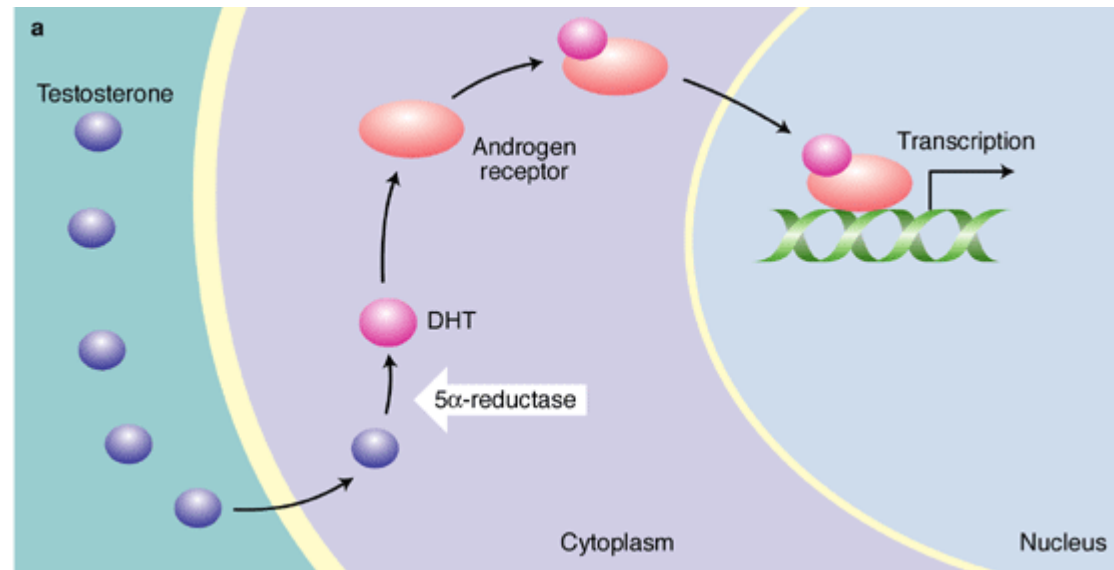


# The course of prostate cancer



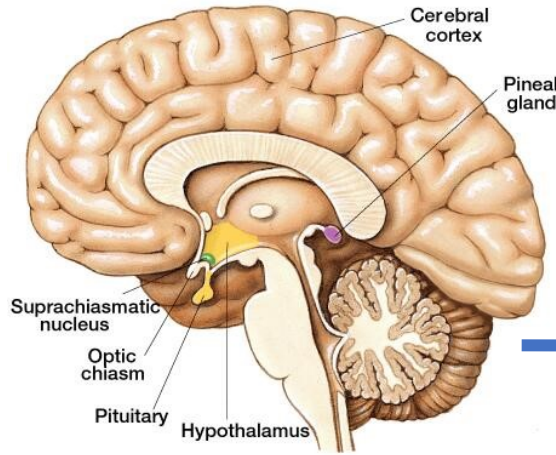
# Prostata

- en hormonafhængig kirtel

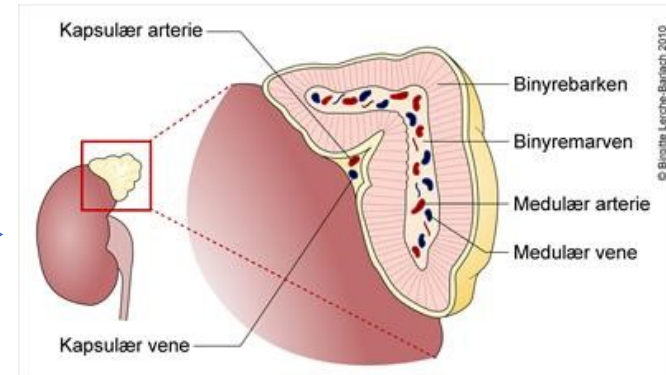


Androgenreceptorer i cytoplasmaet  
i kirtel og støttevæv

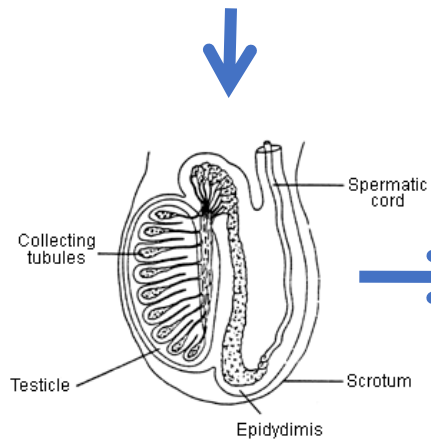
# Hypothalamus-hypofyse akserne



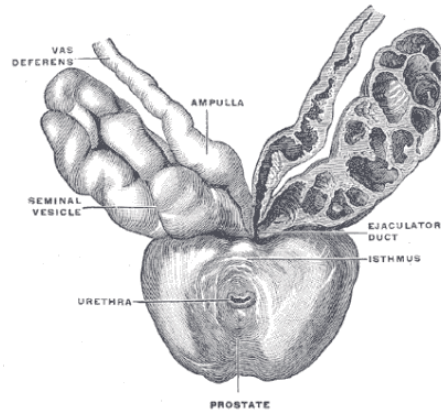
Adrenocortikotrop  
Hormon



Follikel Stimulerende Hormon  
Luteiniserende Hormon

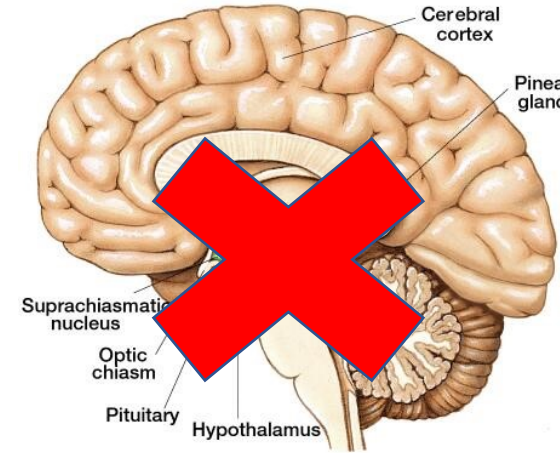
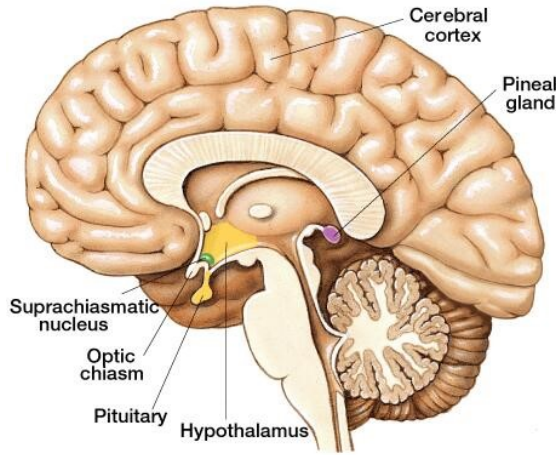


Testosteron

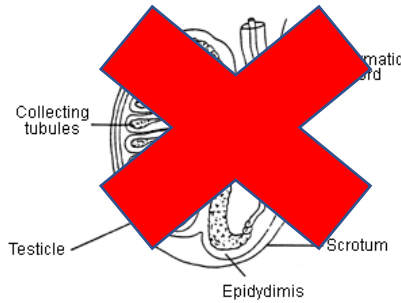


Androstenedion  
Dehydroepiandrosteron

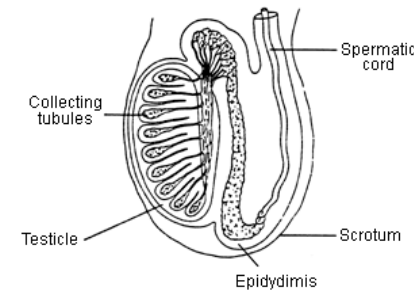
# Endokrin behandling (kastration)



Depot LHRH  
injektionsbehandling  
(medicinsk kastration)



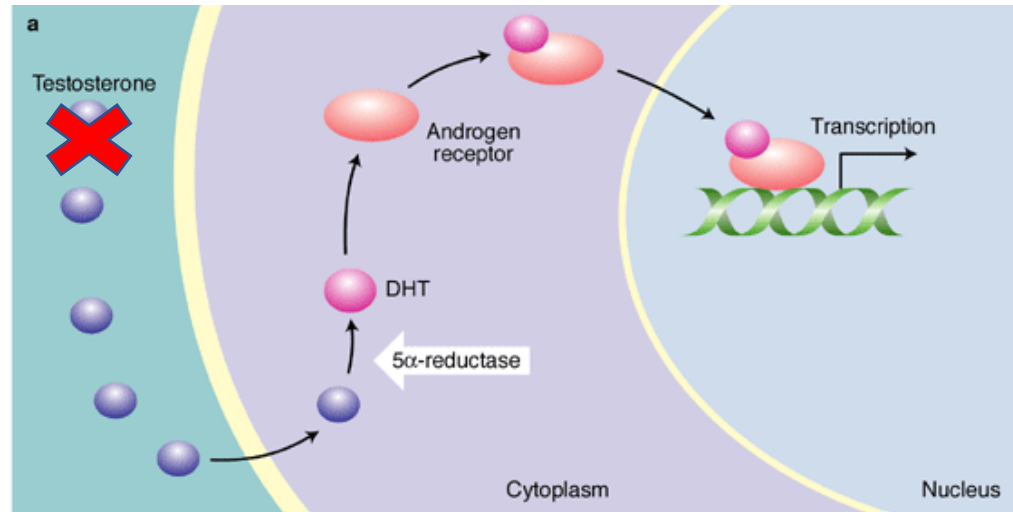
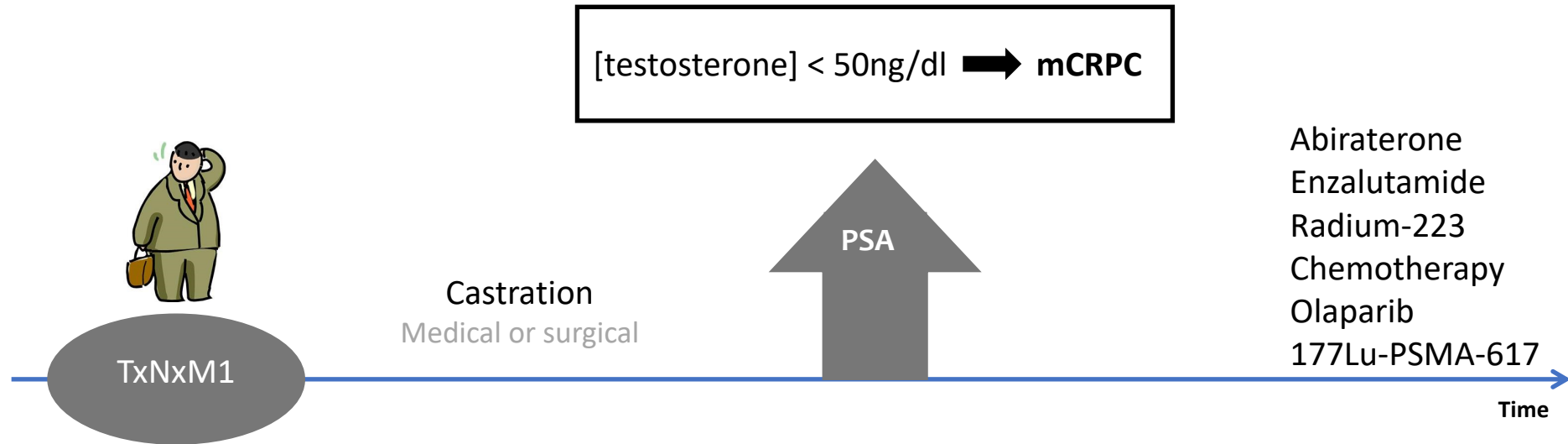
Orkiektomi  
(kirurgisk kastration)



# Bivirkninger til kastrationsbehandling

- Nedsat libido og impotens, hede/svedeture, brystømhed, vægtøgning med mindsket muskelmasse, anæmi, humørsvingninger, depression, knogleskørhed
- Øget risiko for metabolisk syndrom (forhøjet BS, hyperkolæsterolæmi og hypertension) samt AMI

# metastatic Castration-Resistant Prostate Cancer



Median overall survival<sup>1</sup>:

**~ 30 months**

<sup>1</sup>James et 2015, *Eur Urol*

# Case 1

- 79-årig mand, c. prostatae siden 2011, adenocarc., cT3aN0M0, Gleason Score 7 (3+4), PSA 18.
- Primært beh. med EBRT + ADT
- PSA recidiv i 2015. Påbegynder bicalutamid.
- PSA gradvis stigende til 60 i 2017. 18F-NaF PET-CT med 2 knoglemets. (vertebrae), ingen lymfeknudemets. eller viscerale mets.
- Behandles med medicinsk kastration, PSA nadir 5.
- Nu PSA stigning (17) efter 15 mdr. samt tiltagende knoglemets. på NaF-PET-CT scanning.
- God AT, PS 0. Tager paracetamol for smerter.
- Ingen ko-morb. fraset hypertension.



No new lesion on bonescan

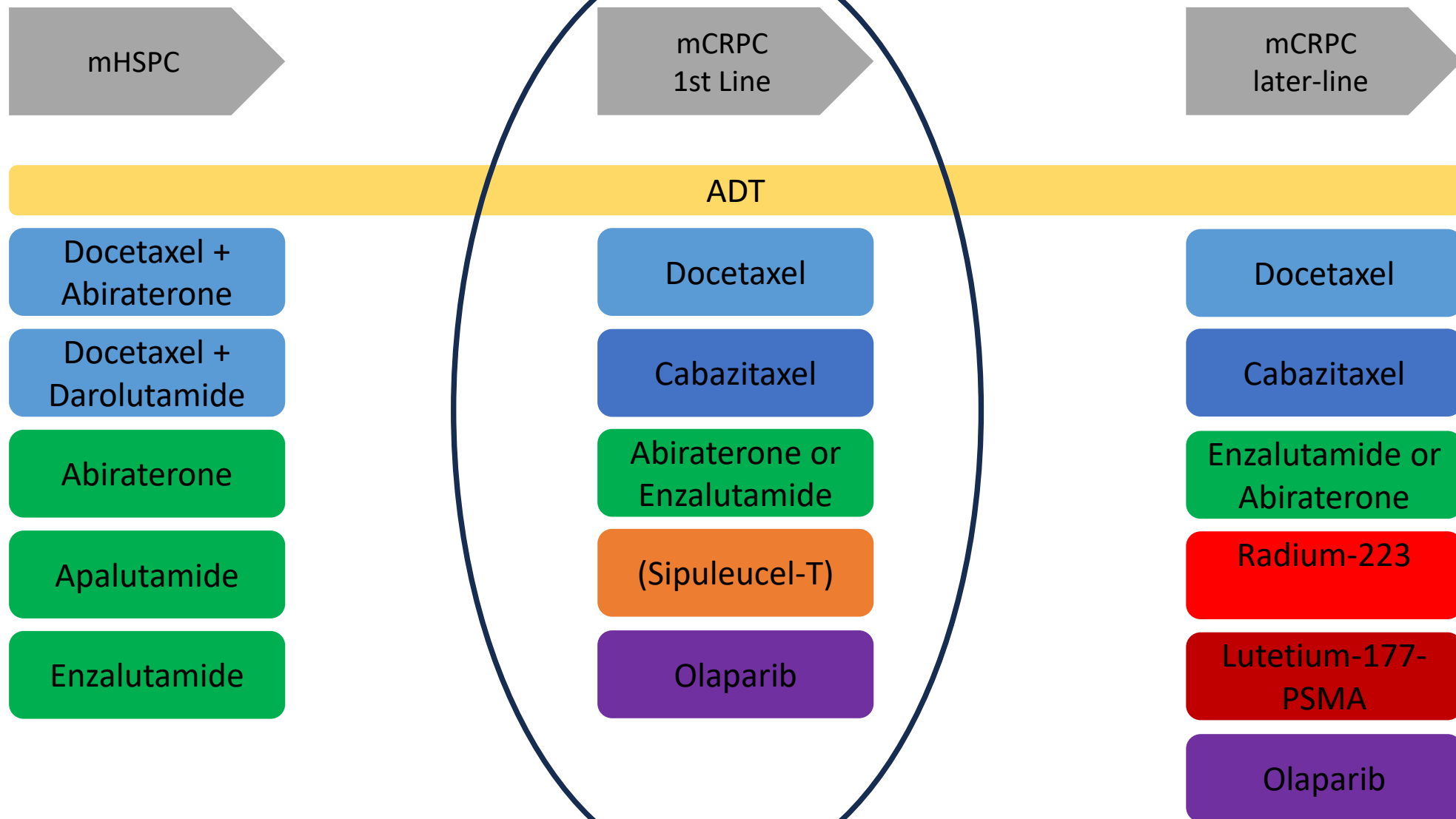


No lesions on CT-TA



New lesions on bonescan

[testosterone]  $\leq 1.7$  nmol per liter



AR-targeting therapy



Chemotherapy



Cellular therapy



Radioisotope



Targeted Therapy

# Phase III trials with a survival advantage in mCRPC

Trial	Disease state	Trial design	HR	Median survival, mo
TAX 327 <sup>1</sup> (n=1006)	mCRPC with or without symptoms	docetaxel/prednisone vs mitoxantrone/prednisone	0.76	18.9 vs 16.5 Δ 2.4
IMPACT <sup>2</sup> (n=512)	Few symptoms mCRPC	sipuleucel-T vs control	0.78	25.8 vs 21.7 Δ 4.1
TROPIC <sup>3</sup> (n=755)	Post-docetaxel	cabazitaxel/prednisolone vs mitoxantrone/prednisone	0.70	15.1 vs 12.7 Δ 2.4
COU-AA-301 <sup>4</sup> (n=1195)	Post-docetaxel	abiraterone/low-dose prednisolone vs placebo/low-dose prednisolone	0.74	15.8 vs 11.2 Δ 4.6
AFFIRM <sup>5</sup> (n=1199)	Post-docetaxel	enzalutamide vs placebo	0.63	18.4 vs 13.6 Δ 4.8
ALSYMPCA <sup>6</sup> (n=921)	Post-docetaxel (or docetaxel-unsuitable)	radium 223/BSC* vs placebo/BSC	0.70	14.9 vs 11.3 Δ 3.6
PREVAIL <sup>7</sup> (n=1717)	Post-ADT in asymptomatic or mildly symptomatic (mCRPC)	enzalutamide vs placebo	0.71	32.4 vs 30.2 Δ 2.2
COU-AA-302 <sup>8</sup> (n=1088)	Post-ADT in asymptomatic or mildly symptomatic (mCRPC)	abiraterone/low-dose prednisolone vs placebo/low-dose prednisolone	0.81	34.7 vs 30.3 Δ 4.4

\*BSC: best supportive care; HR: hazard ratio; mCRPC: metastatic CRPC

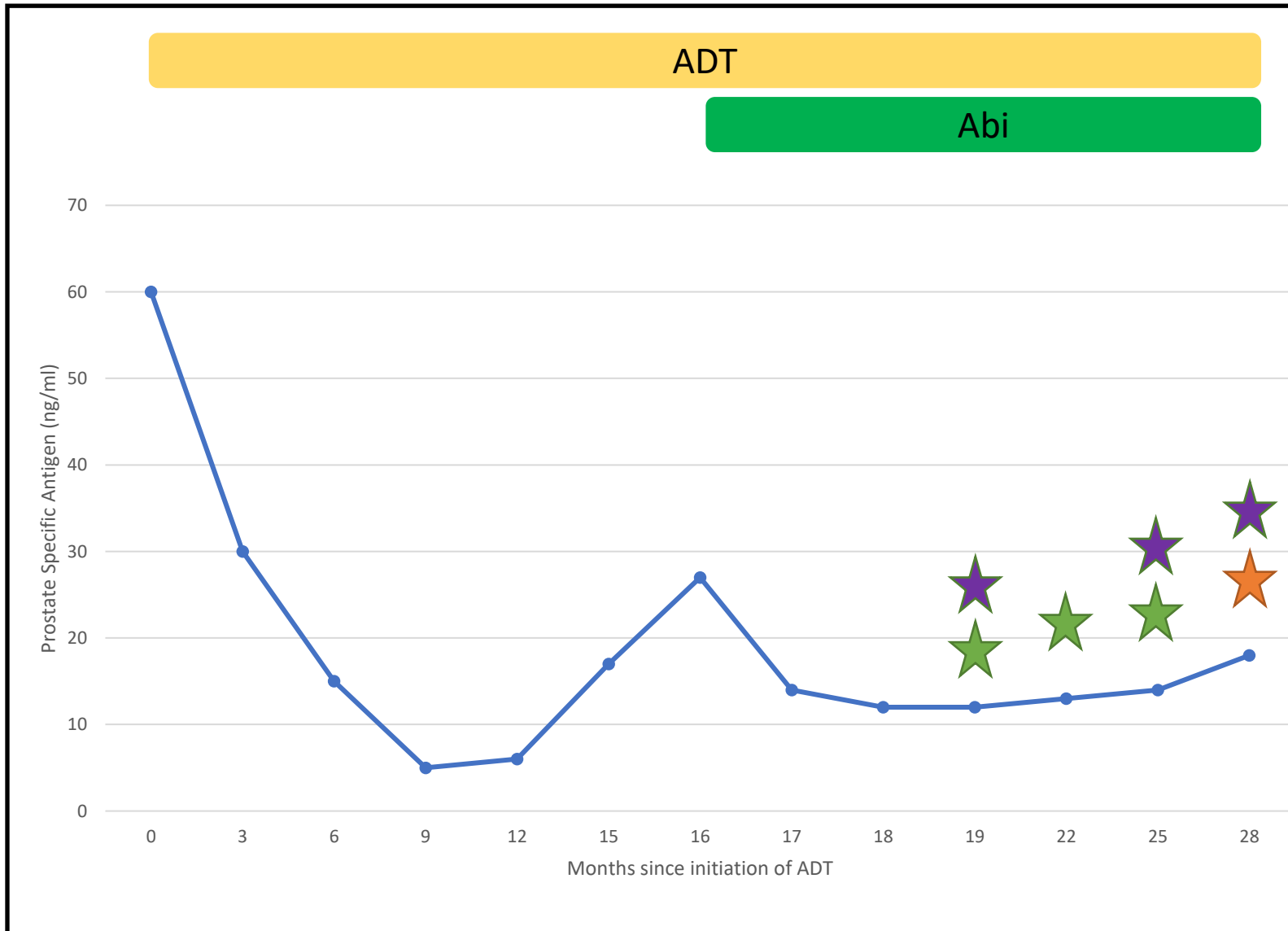
Table adapted from N James, ESMO 2018

<sup>1</sup>Tannock IF et al. N Engl J Med 2004;351:1502-12; <sup>2</sup>Kantoff PW et al. N Engl J Med 2010;363:411-22; <sup>3</sup>de Bono JS et al. Lancet 2010;376:1147-54;

<sup>4</sup>Fizazi K et al. Lancet Oncol 2012;13:983-92; <sup>5</sup>Scher HI et al. N Engl J Med 2012;367:1187-97; <sup>6</sup>Parker C et al. Engl J Med 2013;369:213-23

# Behandling med Abirateron (CYP17A1 inhibitor)

- Tabletbehandling, 1000 mg x 1 dagligt + 10 mg prednisolone (kontinuerligt)
- En behandlingsserie varer 28 dage / 4 uger
- Medicinen udleveres af læge forudgået af klinisk kontrol, blodprøver og evt. NaF-PET-CT-scanning
- Bivirkninger:
  - Hypertension, ødemer, hypokaliæmi, forhøjede transaminaser, hyperglykæmi



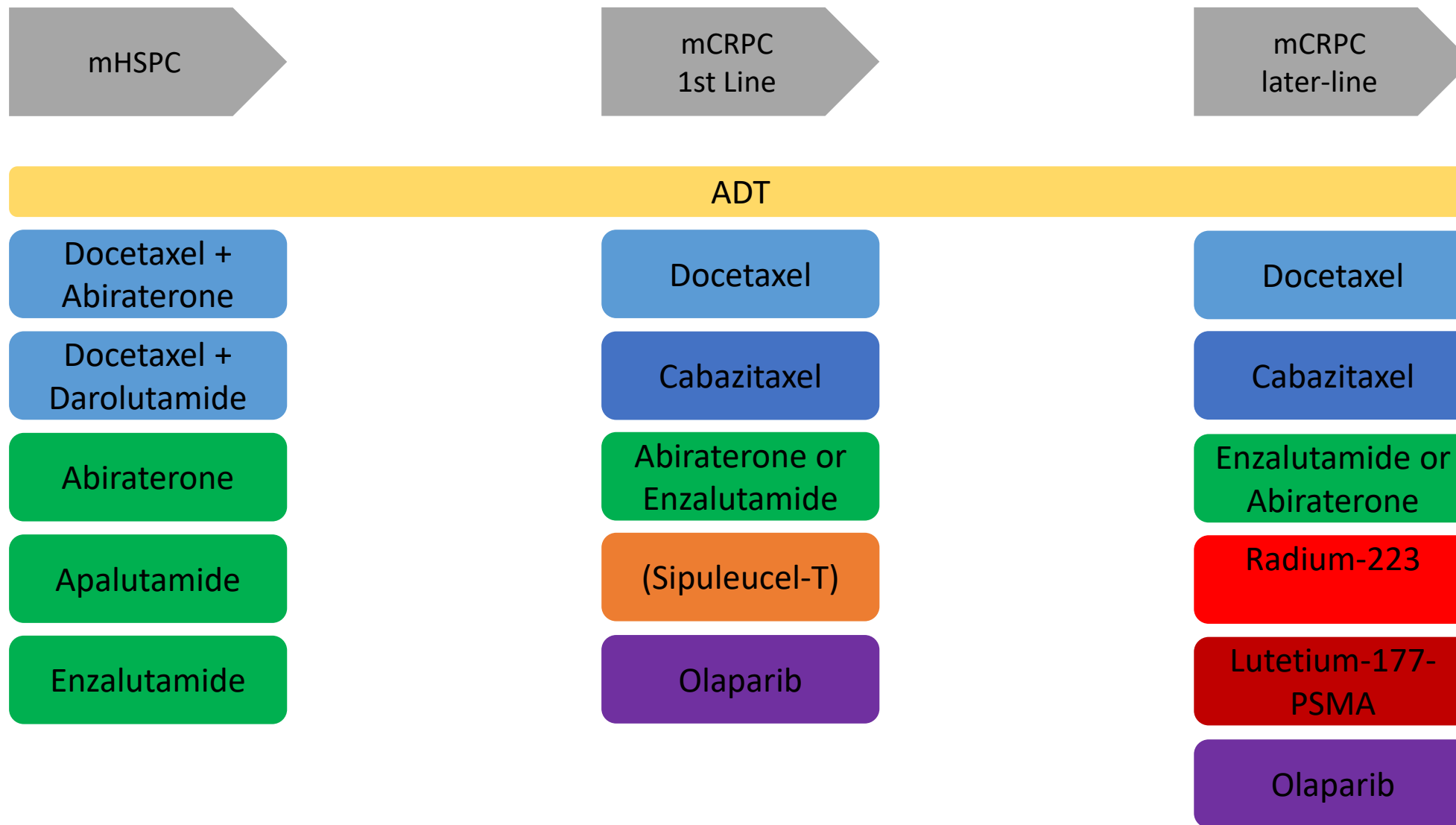
No new lesion on bonescan



New lesions on bonescan



No lesions on CT-TA



AR-targeting therapy



Chemotherapy



Cellular therapy



Radioisotope

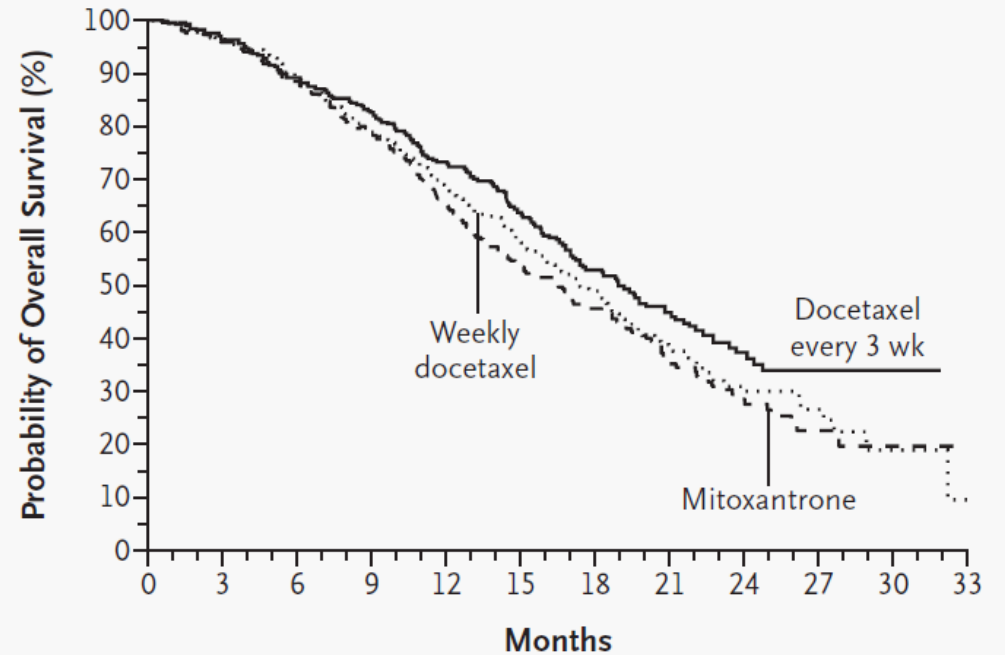


Targeted Therapy

ORIGINAL ARTICLE

# Docetaxel plus Prednisone or Mitoxantrone plus Prednisone for Advanced Prostate Cancer

Ian F. Tannock, M.D., Ph.D., Ronald de Wit, M.D., William R. Berry, M.D., Jozsef Horti, M.D., Anna Pluzanska, M.D., Kim N. Chi, M.D., Stephane Oudard, M.D., Christine Théodore, M.D., Nicholas D. James, M.D., Ph.D., Ingela Turesson, M.D., Ph.D., Mark A. Rosenthal, M.D., Ph.D., and Mario A. Eisenberger, M.D., for the TAX 327 Investigators



**No. at Risk**

	0	3	6	9	12	15	18	21	24	27	30	33
Docetaxel every 3 wk	335	296	217	104	37	5						
Weekly docetaxel	334	297	200	105	29	4						
Mitoxantrone	337	297	192	95	29	3						

# Docetaxel

Semisyntetisk cytostatikum, der påvirker mitosen og cellulære funktioner i interfase ved at

- fremme polymerisering af tubulinproteiner til stabile mikrotubuli
- hæmme depolymeriseringen af mikrotubuli

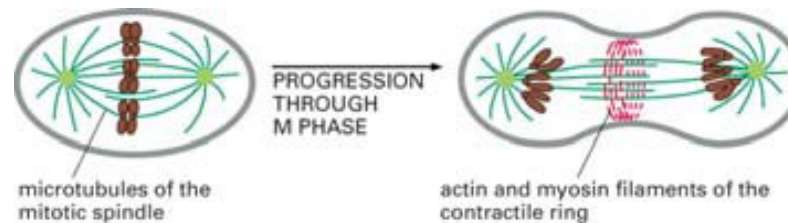
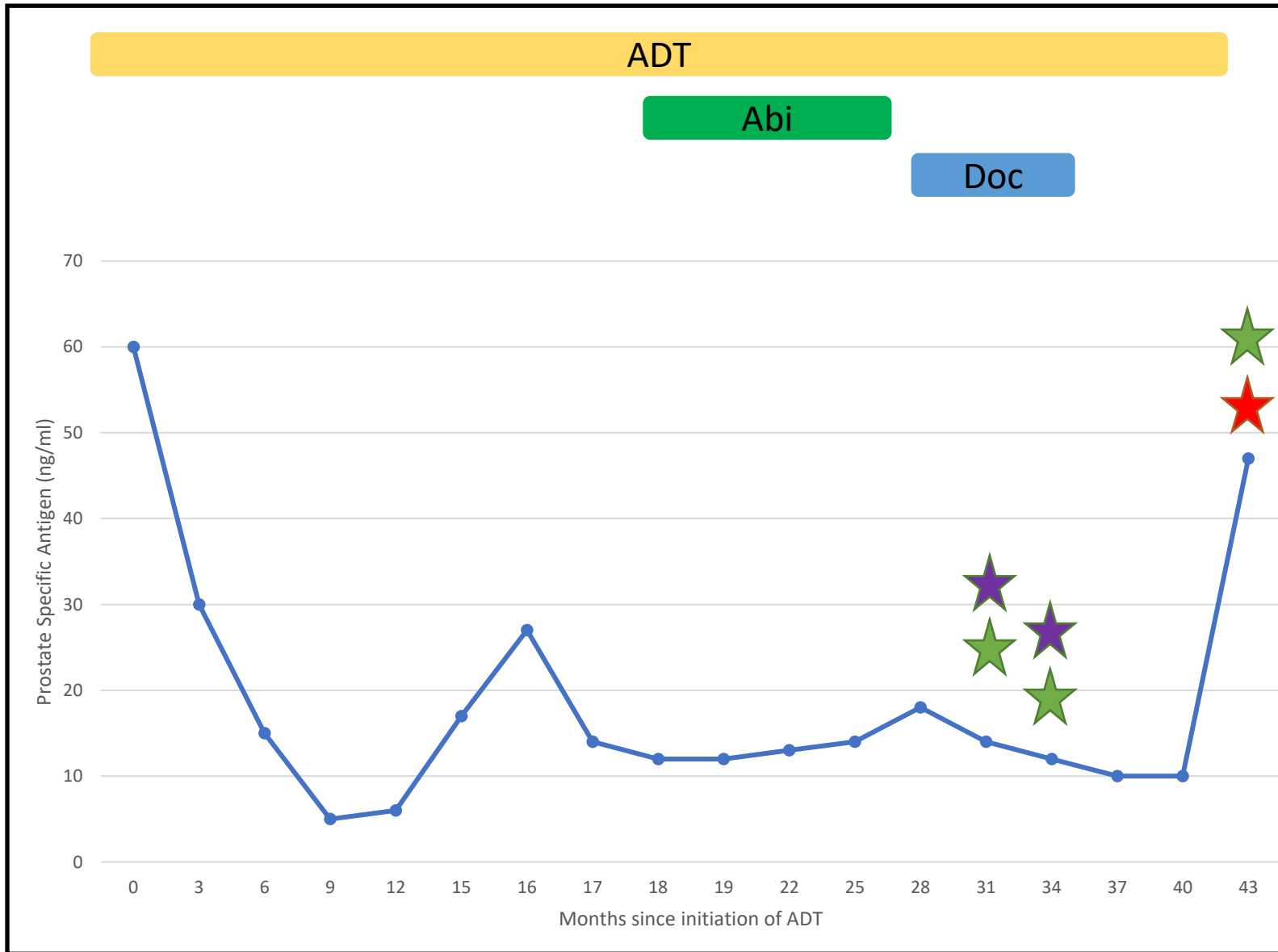


Figure 18-4. Molecular Biology of the Cell, 4th Edition.

# Administration og bivirkninger til kemoterapi

- Gives intravenøst hver 3. uge (maksimalt 10 behandlinger) forudgået af klinisk kontrol, blodprøver og evt. NaF-PET-CT-scanning
- Behandlingen suppleres med tbl. prednisolon 10 mg x 1 dagligt
- Forud for hver behandling tages moderate doser steroid for at forebygge en evt. allergisk reaktion
  
- Bivirkninger
  - Hårudtynding, træthed, smagsændringer, kvalme, diare, negleforandringer og neuropati
  - Knoglemarvssuppression (risiko for infektion / blødning)



No new lesion on bonescan



No lesions on CT-TA



New lesions on bonescan



Clinical progression and liver metastases

# Tværsnit / truende tværsnit

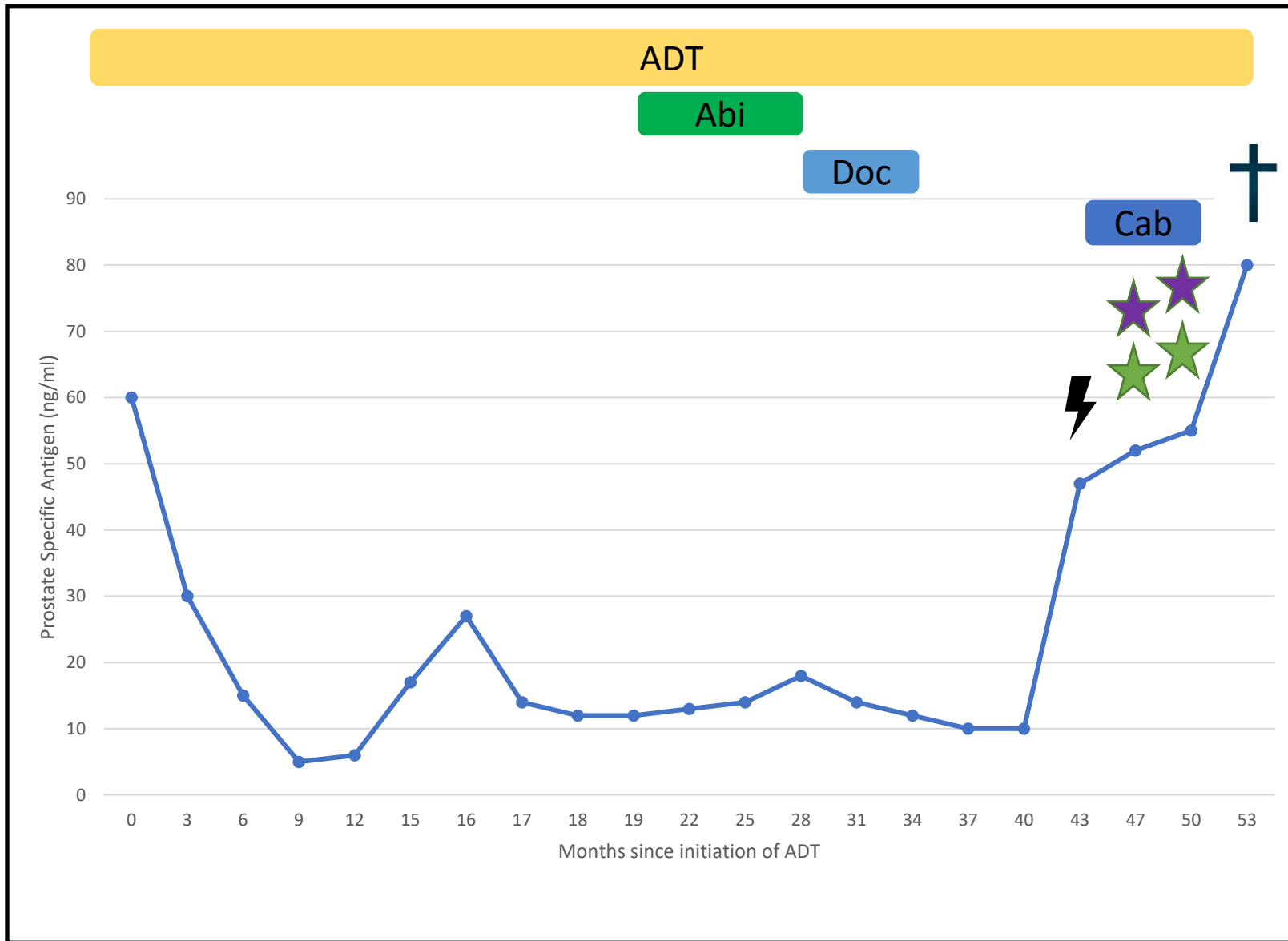
## Symptomer

Rygsmertter, føleforstyrrelser, nedsat styrke i arme / ben, inkontinens

## Behandling

Pallierende strålebehandling (typisk 3 Gy x 10) eller ryggkirurgi med efterfølgende supplerende strålebehandling





No new lesion on bonescan



New lesions on bonescan

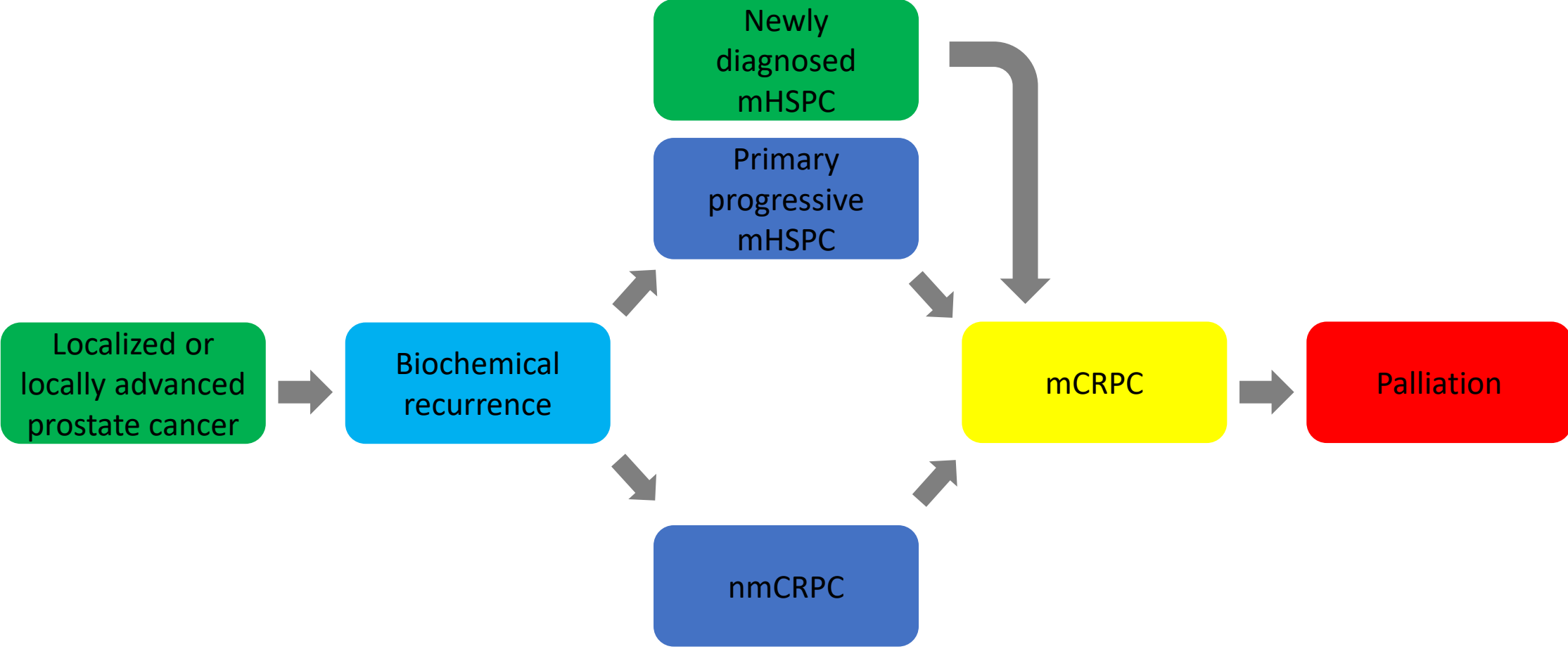


No lesions on CT-TA



Radiation therapy

# The course of prostate cancer

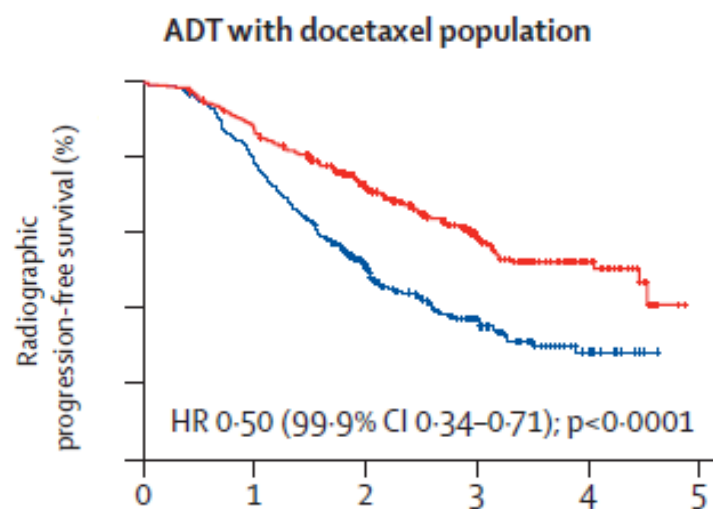


# Case 2

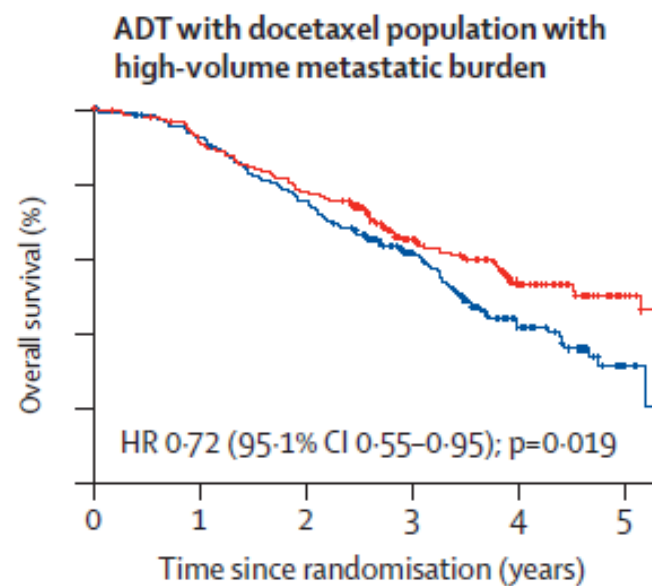
- 62-årig mand
- Nydiagnosticeret c. prostatae, adenocarcinom, Gleason Score 9 (5+4), PSA 750.
- 15 knoglemets. (rygsøjlen, ribben og lårbenet) på 18F-NaF PET-CT scanningen samt betydelig lymfeknudemetastaser i retroperitoneum (> 2 cm).
- Nogenlunde AT, PS 1. Startet tbl. morfin 10 mg for smerter.
- Komorbiditet omfatter hypertension og AF (NOAK).

# Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2 × 2 factorial design

Karim Fizazi, Stéphanie Foulon, Joan Carles, Guilhem Roubaud, Ray McDermott, Aude Fléchon, Bertrand Tombal, Stéphane Supiot, Dominik Berthold, Philippe Ronchin, Gabriel Kacso, Gwenaëlle Gravis, Fabio Calabro, Jean-François Berdah, Ali Hasbini, Marlon Silva, Antoine Thiery-Vuillemin, Igor Latorzeff, Loïc Mourey, Brigitte Laguerre, Sophie Abadie-Lacourtoisie, Etienne Martin, Claude El Kouri, Anne Escande, Alvar Rosello, Nicolas Magne, Friederike Schlurmann, Frank Priou, Marie-Eve Chand-Fouche, Salvador Villà Freixa, Muhammad Jamaluddin, Isabelle Rieger, Alberto Bossi, on behalf of the PEACE-1 investigators\*

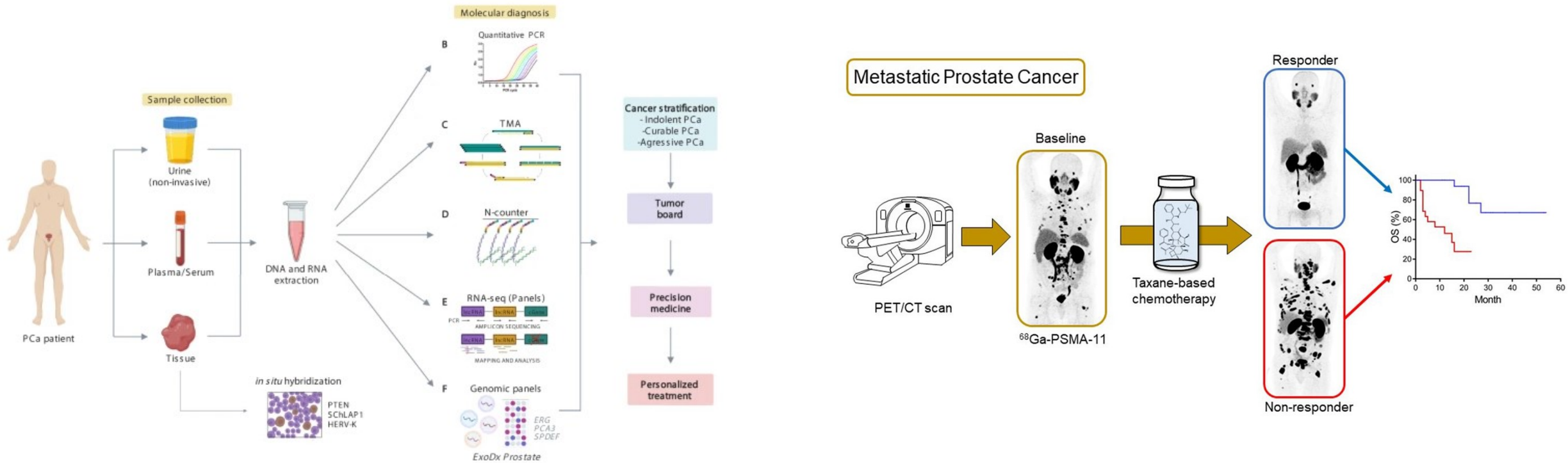


355	274	137	61	16	0
355	303	200	105	35	0



232	210	171	101	39	6
224	201	171	103	57	16

# Hvad med prædiktive biomarkører i klinisk praksis?



## 150 patients with mCRPC; pre and post treatment with abiraterone or enzalutamide

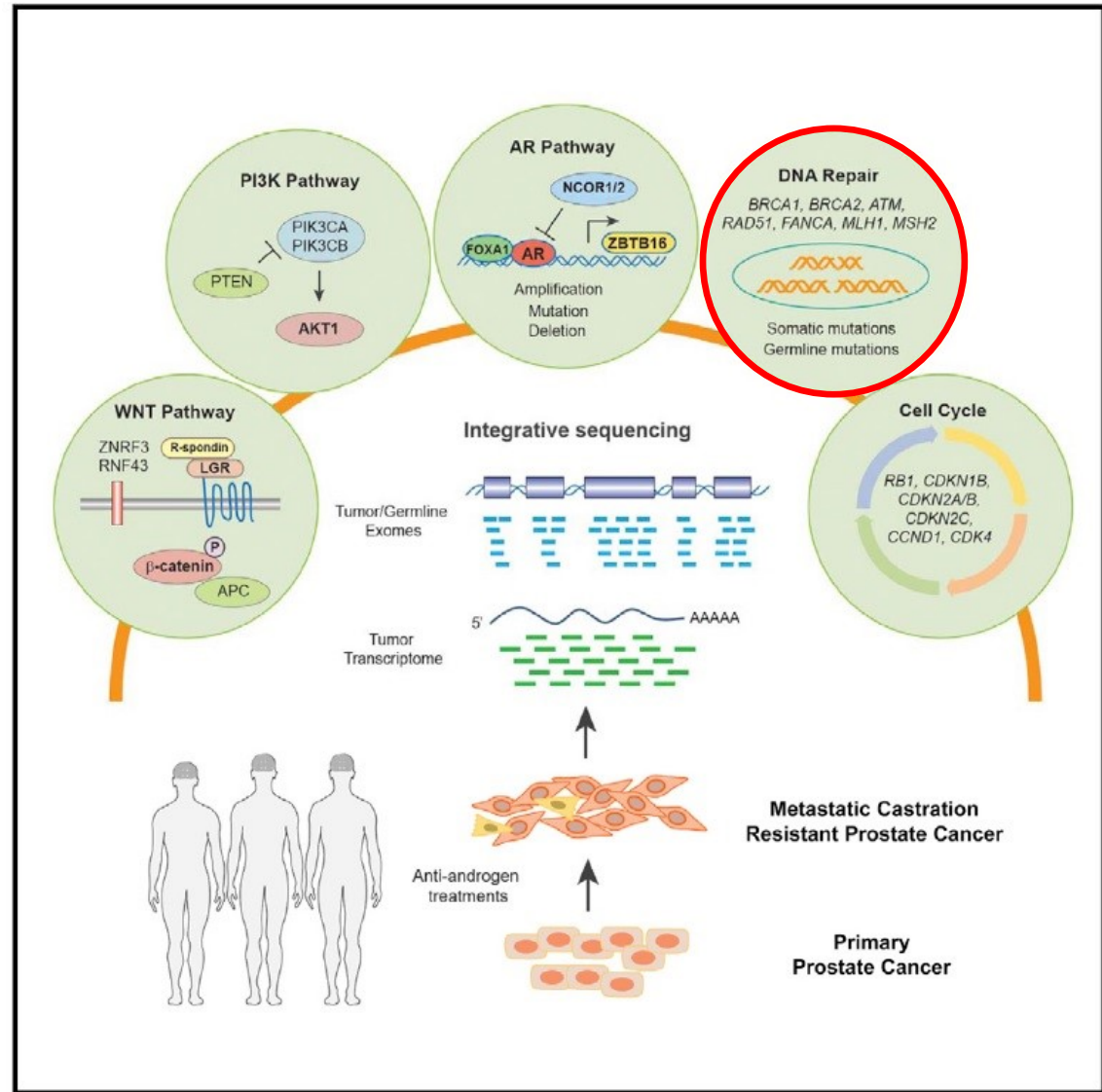
Biopsy samples obtained from bone- and soft tissue (mostly bone- and lymph node metastases)

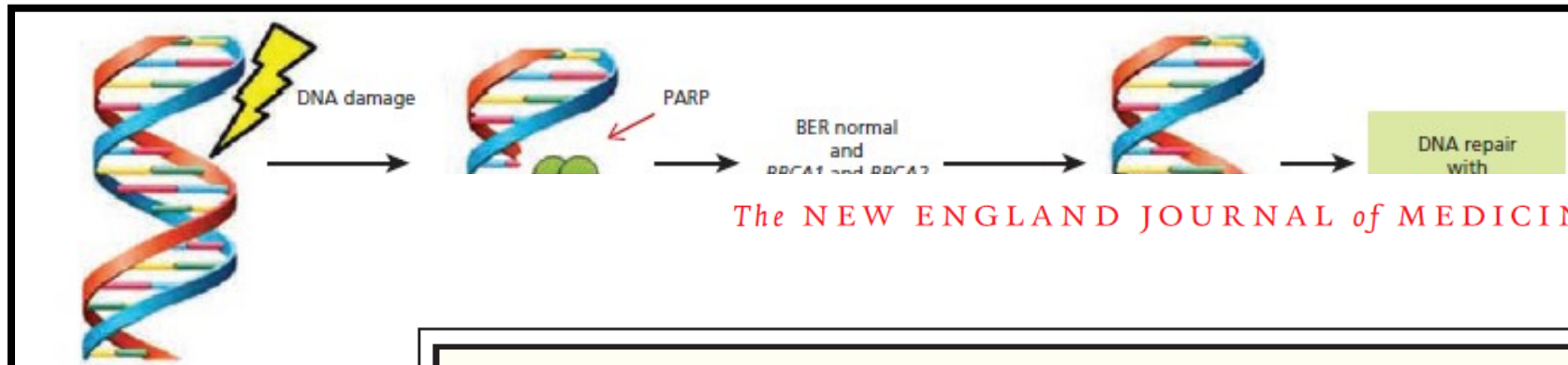
The most frequently aberrant genes included AR (63%), TP53 (53%) and PTEN (40.7%)

19% had aberrations in **BRCA2 (13%), BRCA1** and **ATM**

5% harbored pathogenic germline BRCA2 mutations with a subsequent somatic event that resulted in biallelic loss

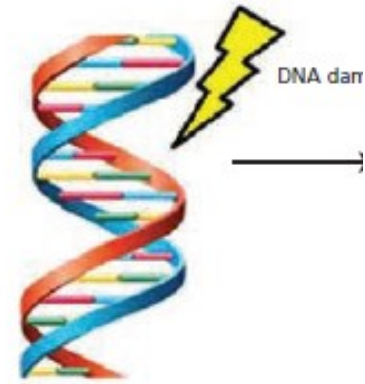
Almost 4% had small cell neuroendocrine carcinoma / adenocarcinoma with neuroendocrine differentiation (3%)





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE



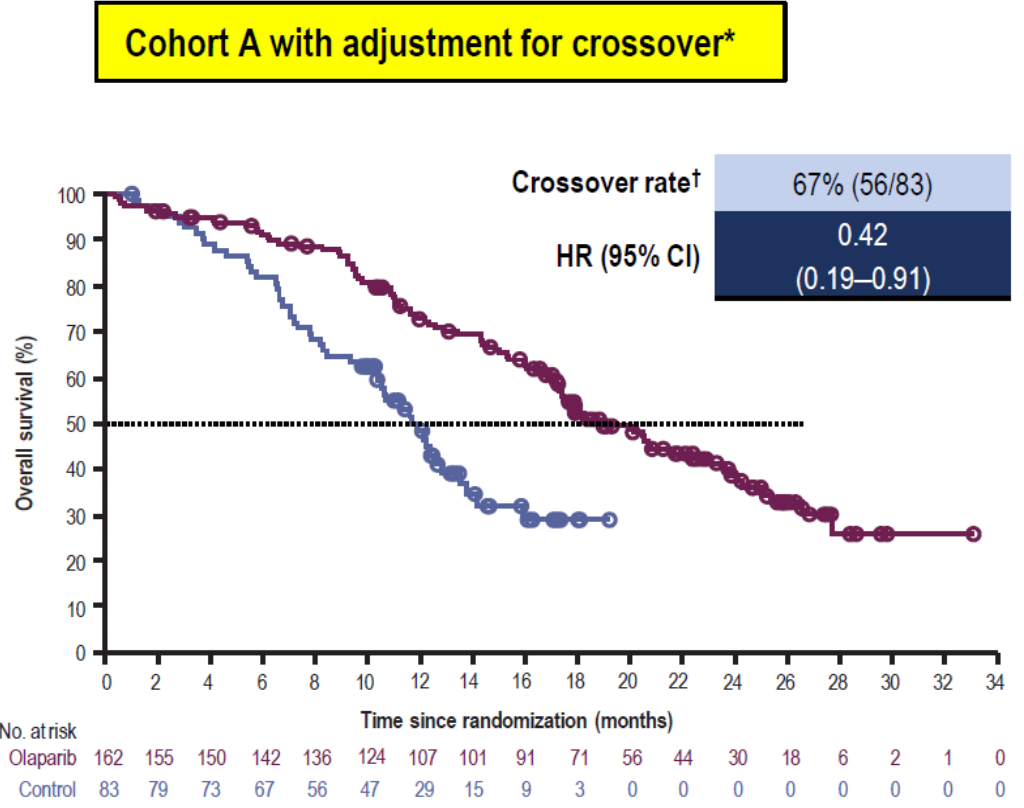
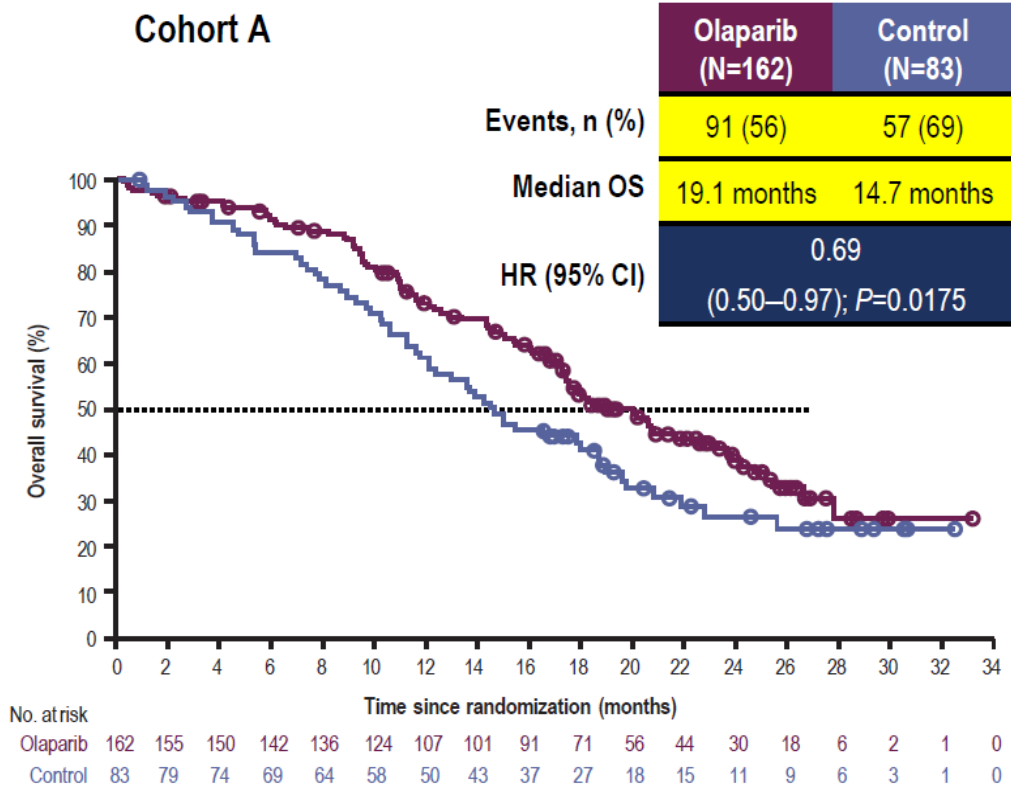
# Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

M. Hussain, J. Mateo, K. Fizazi, F. Saad, N. Shore, S. Sandhu, K.N. Chi, O. Sartor, N. Agarwal, D. Olmos, A. Thiery-Vuillemin, P. Twardowski, G. Roubaud, M. Özgüroğlu, J. Kang, J. Burgents, C. Gresty, C. Corcoran, C.A. Adelman, and J. de Bono, for the PROfound Trial Investigators\*

Figure 1. Mechanism of action of PARP  
Abbreviations: BER, base excision repair

# Olaparib improved OS in Cohort A (*BRCA1, BRCA2* or *ATM*)

Prespecified adjustment for crossover (final prespecified analysis)



Median follow-up duration for censored patients was 21.9 months for the olaparib arm and 21.0 months for the control arm.

\*Re-censored; conducted using RPSFTM to demonstrate the impact on OS of crossover of patients from the control arm to receive olaparib as a first subsequent anticancer therapy. <sup>†</sup>Patients receiving olaparib at any time.

# Nyere kombinationsbehandlinger

---



## Olaparib plus abiraterone versus placebo plus abiraterone in metastatic castration-resistant prostate cancer (PROpel): final prespecified overall survival results of a randomised, double-blind, phase 3 trial

*Fred Saad, Noel W Clarke, Mototsugu Oya, Neal Shore, Giuseppe Procopio, João Daniel Guedes, Cagatay Arslan, Niven Mehra, Francis Parnis, Emma Brown, Friederike Schlürmann, Jae Young Joung, Mikio Sugimoto, Oliver Sartor, Yu-Zhen Liu, Christian Poehlein, Laura Barker, Paula Michelle del Rosario, Andrew J Armstrong*



## First-line talazoparib plus enzalutamide versus placebo plus enzalutamide in men with metastatic castration-resistant prostate cancer and homologous recombination repair gene alterations: patient-reported outcomes from the randomised, double-blind, placebo-controlled, phase 3 TALAPRO-2 trial

*Andre P Fay\*, Karim Fizazi, Nobuaki Matsubara, Arun A Azad, Fred Saad, Ugo De Giorgi, Jae Young Joung, Peter C C Fong, Robert J Jones, Stefanie Zschäbitz, Jan Oldenburg, Neal D Shore, Curtis Dunshee, Joan Carles, Paul Cislo, Jane Chang, Cynthia G Healy, Alexander Niyazov, Neeraj Agarwal\**

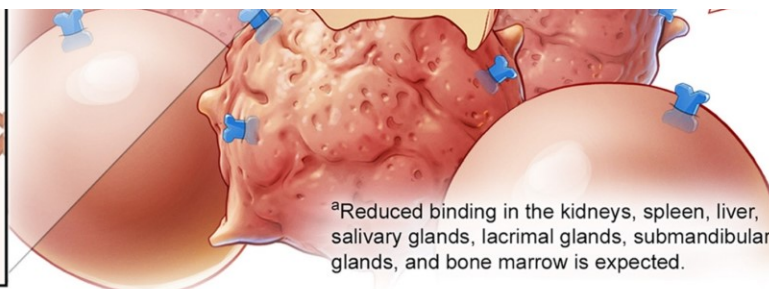
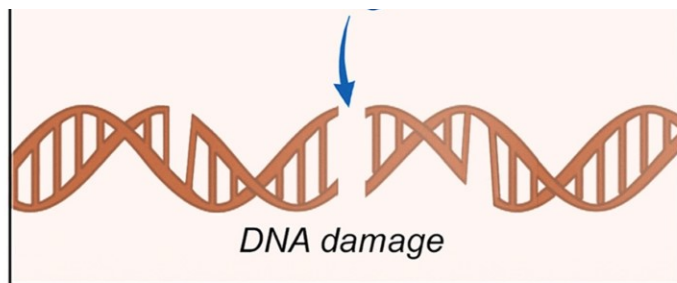
## Niraparib and Abiraterone Acetate for Metastatic Castration-Resistant Prostate Cancer

*Kim N. Chi, MD<sup>1</sup>; Dana Rathkopf, MD<sup>2</sup>; Matthew R. Smith, MD<sup>3</sup>; Eleni Efstathiou, MD<sup>4</sup>; Gerhardt Attard, MD<sup>5</sup>; David Olmos, MD<sup>6</sup>; Ji Youl Lee, MD<sup>7</sup>; Eric J. Small, MD<sup>8</sup>; Andrea J. Pereira de Santana Gomes, MD<sup>9</sup>; Guilhem Roubaud, MD<sup>10</sup>; Marniza Saad, MD<sup>11</sup>; Bogdan Zurawski, MD<sup>12</sup>; Valerii Sakalo, MD<sup>13</sup>; Gary E. Mason, MD<sup>14</sup>; Peter Francis, MD<sup>15</sup>; George Wang, MS, MAS<sup>14</sup>; Daphne Wu, PhD<sup>16</sup>; Brooke Diorio, PhD<sup>17</sup>; Angela Lopez-Gitlitz, MD<sup>18</sup>; and Shahneen Sandhu, MD<sup>18</sup>; on behalf of the MAGNITUDE Principal Investigators*

ORIGINAL ARTICLE

# Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer

O. Sartor, J. de Bono, K.N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S.T. Tagawa, L.T. Nordquist, N. Vaishampayan, G. El-Haddad, C.H. Park, T.M. Beer, A. Armour, W.J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R.A. Messmann, M.J. Morris, and B.J. Krause, for the VISION Investigators\*



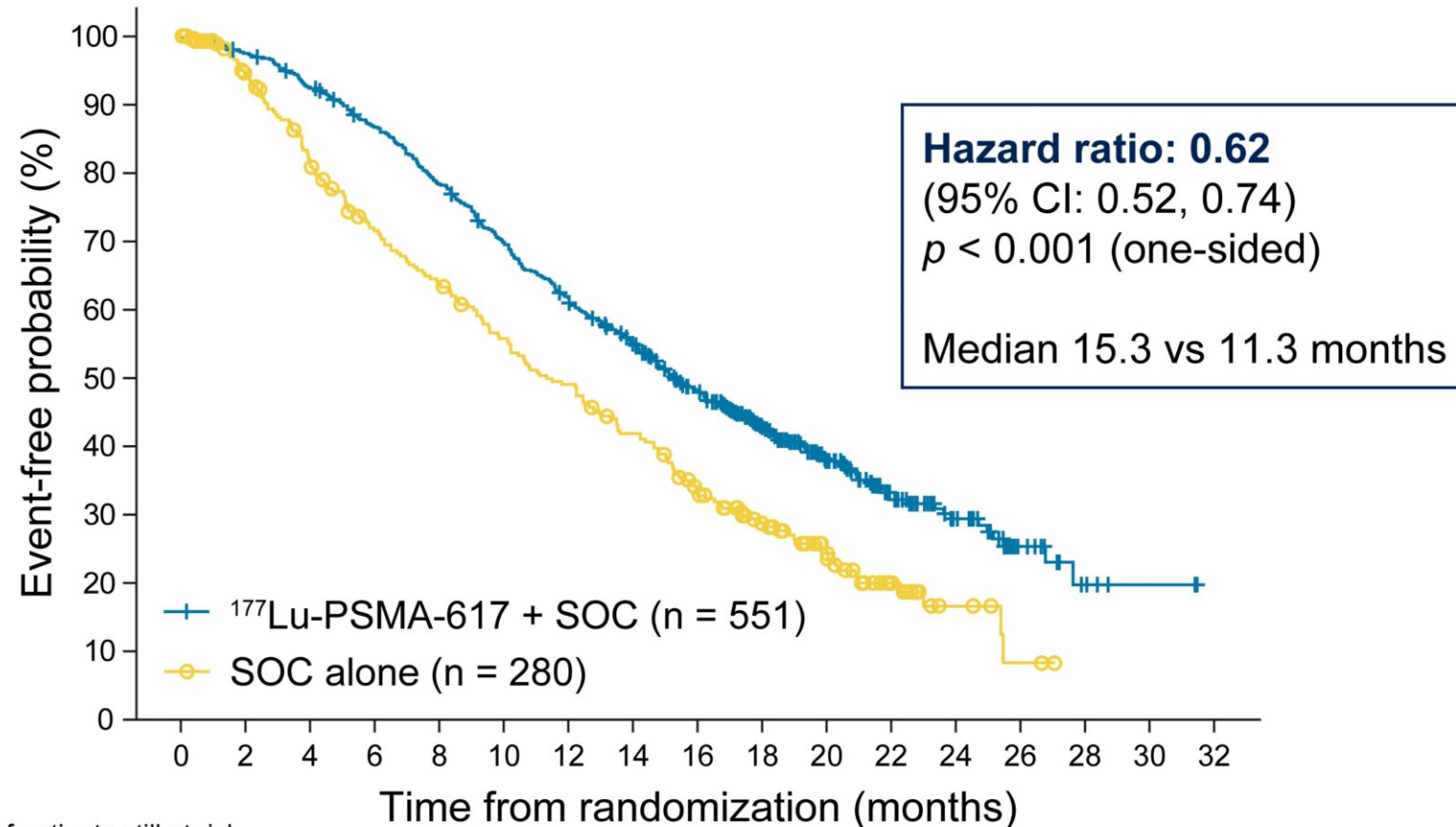
Prostate cancer cell and neighbouring cell death

\*Reduced binding in the kidneys, spleen, liver, salivary glands, lacrimal glands, submandibular glands, and bone marrow is expected.

# Primary endpoints: $^{177}\text{Lu}$ -PSMA-617 prolonged OS

## Primary analysis

All randomized patients  
(N = 831)



Number of patients still at risk

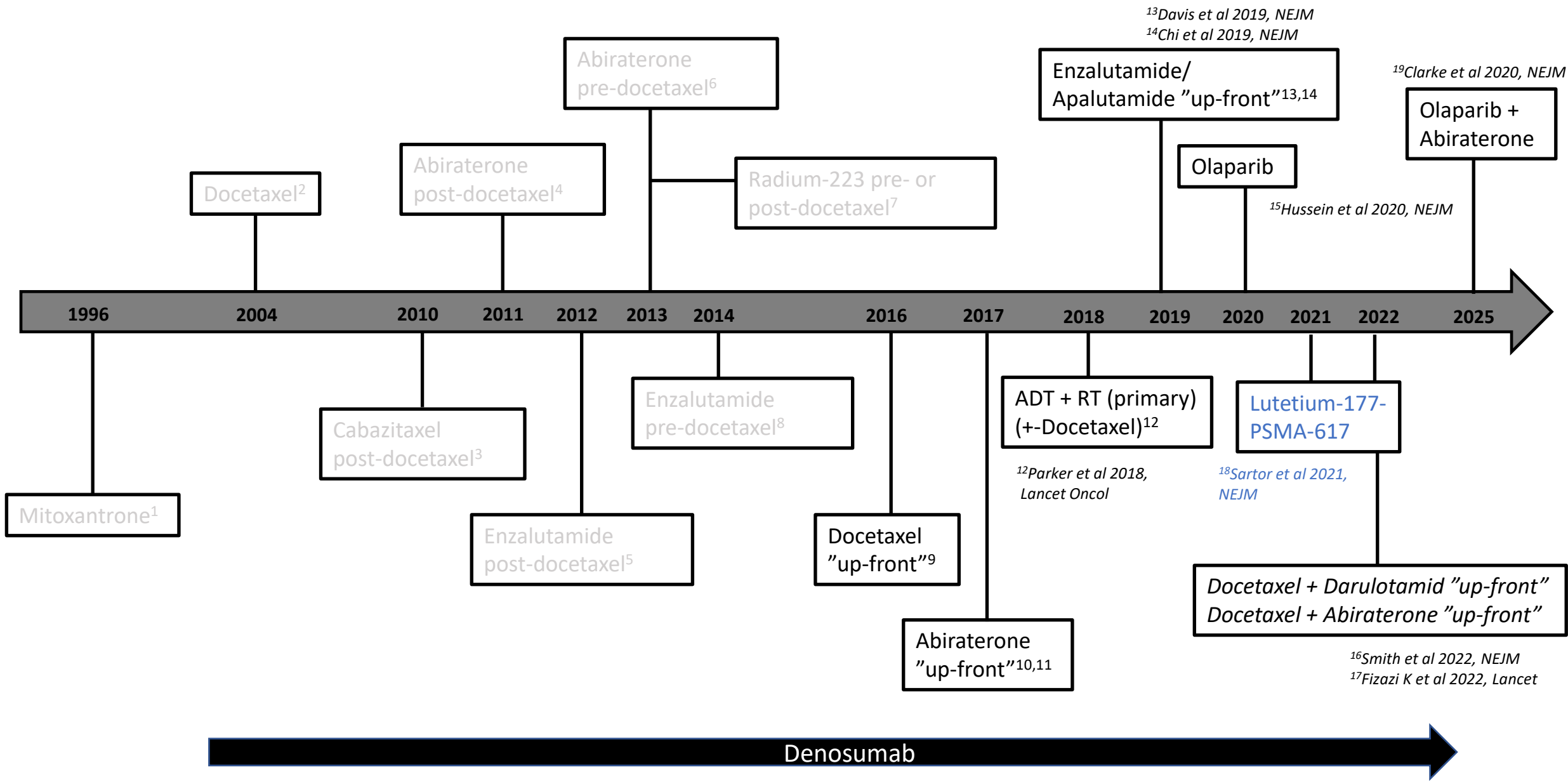
$^{177}\text{Lu}$ -PSMA-617 + SOC	551	535	506	470	425	377	332	289	236	166	112	63	36	15	5	2	0
SOC alone	280	238	203	173	155	133	117	98	73	51	33	16	6	2	0	0	0

Presented By: **Michael J. Morris**

#ASCO21 | Content of this presentation is the property of the author, licensed by ASCO. Permission required for reuse.

**2021 ASCO**  
ANNUAL MEETING

Content of this presentation is the property of the author, licensed by ASCO. Permission required for reuse.



<sup>1</sup>Tannock et al 1996, *JCO*

<sup>2</sup>Tannock et al 2004, *NEJM*

<sup>3</sup>de Bono et al 2010, *Lancet Oncol*

<sup>4</sup>de Bono et al 2011, *NEJM*

<sup>5</sup>Scher et al 2012, *NEJM*

<sup>6</sup>Ryan et al 2013, *NEJM*

<sup>7</sup>Parker et al 2013, *NEJM*

<sup>8</sup>Beer et al 2014, *NEJM*

<sup>9</sup>Vale et al 2016, *Lancet Oncol*

<sup>10</sup>Fizazi et al 2017, *NEJM*; <sup>11</sup>James et al 2017, *NEJM*;