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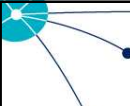
Radiotherapie
Medische Oncologie
Hematologie

Systemische behandelingen prostaatcarcinoom


Postgraduaat Iridiumkankernetwerk

Dr. Tom Van den Mooter

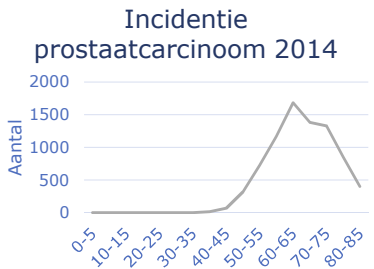
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Epidemiologie en prognose: situatie in Vlaanderen en België



Incidentie prostaatcarcinoom 2014

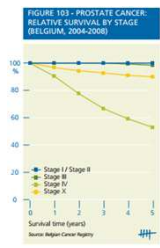


Leeftijdscategorie
Totaal aantal : 7953

4-Combined TNM stage, Belgium 2014 (Prostate Cancer)

	Stage I	Stage II	Stage III	Stage IV	Stage X	Stage NA	Total
Males (N)	2,635	1,785	1,187	922	1,418	6	7,953
Males (%)	33.1	22.4	14.9	11.6	17.8	<0.1	100

Stage IV	T4 Any T Any T	N0 N1 Any N	M0 M1 Any M	Any PSA Any PSA Any PSA	Any Gleason Any Gleason Any Gleason
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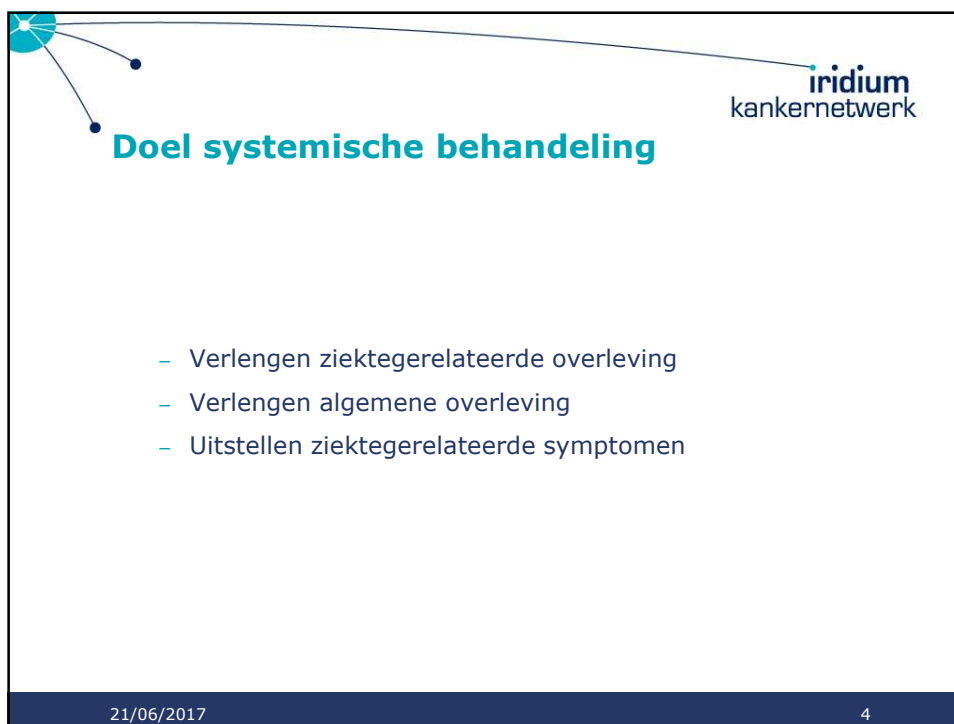
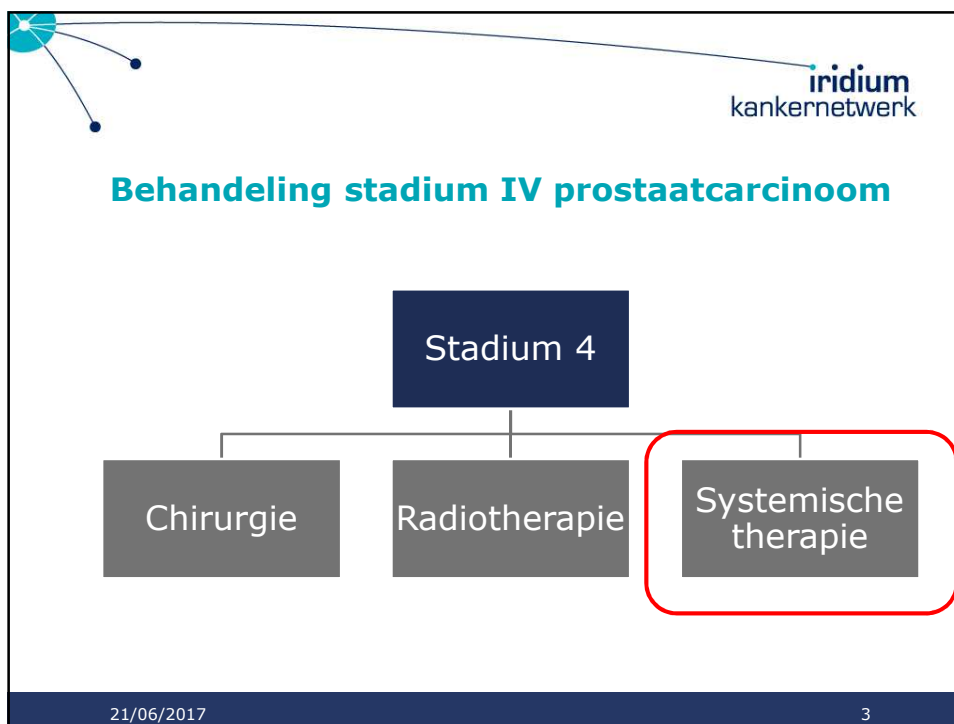


N cases	Observed Survival (%)				Relative Survival (%)				ASRS (%)
	1 year	3 year	5 year	10 year	1 year	3 year	5 year	10 year	
Belgium	42,088	95.1	86.0	77.6	98.9	96.8	95.3	93.0	
Flemish Region	31,554	93.9	84.0	75.4	97.8	94.9	93.0	89.2	

*ASRS: Age-standardized relative survival

Bron: Belgian Cancer Registry

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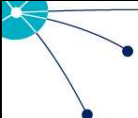


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Onderverdeling

- Castratiegevoelig prostaatcarcinoom (CSPC)
- Castratieresistent prostaatcarcinoom (CRPC)
 - Progressieve ziekte (biochemisch/radiografisch/klinisch) prostaatcancer zo effectief gecastreerd (Testosteron < 50 ng/dl; zo orchidectomie < 20ng/dl)
 - Onderverdeling:
 - Castratieresistent, hormoongevoelig
 - Castratieresistent, hormoonresistent
- Androgeen-onafhankelijke cellen!

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Evolutie behandeling prostaatcarcinoom: Voor 2004

ADT	Anti-androgenen	Prednisolone
Mitoxantrone	Ketoconazole	Oestrogenen

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Castratiegevoelig PC

Androgeen-deprivatietherapie (ADT)

- Mechanische castratie
 - Bilaterale orchidectomie
- Chemische castratie
 - LHRH-agonisten
Zoladex®, Decapeptyl®, Depo-Eligard®, Suprefact®, Gonapeptyl®, Salvacyl®
 - LHRH-antagonisten
Firmagon®

TUMOUR PROGRESSION

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Castratiegevoelig PC

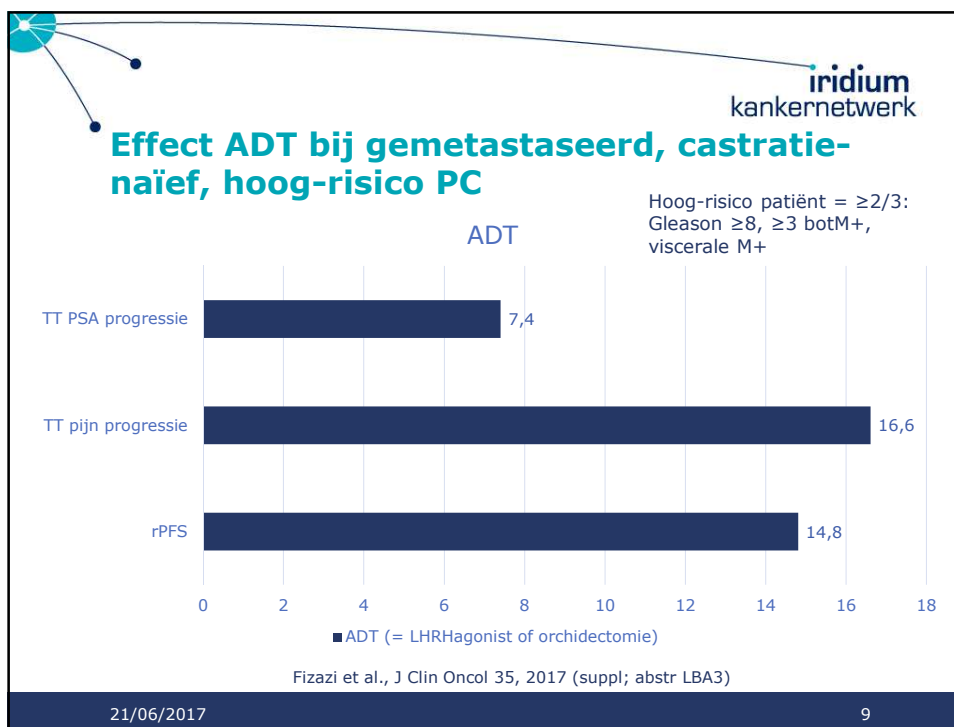
mTTTF

Treatment	mTTTF (months)
Orchidectomie	12,2
LHRH	12

■ Tijd (maanden)

Vogelzang et. al; Urology: 1995

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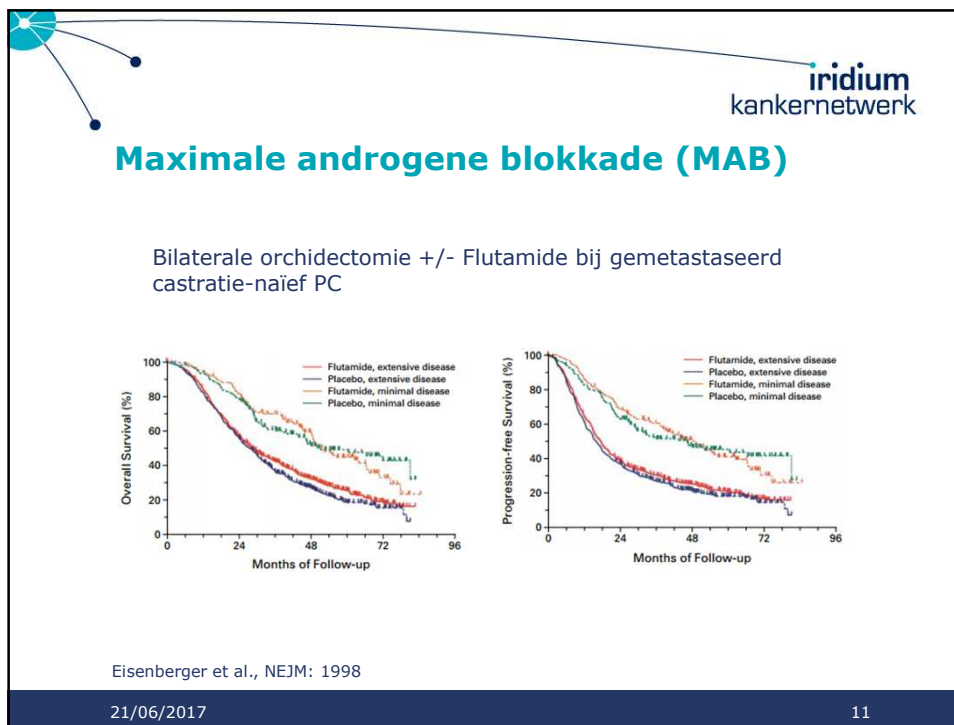
Castratieresistent, hormoongevoelig PC

- Secundaire hormonale behandeling

1. Anti-androgenen:
 - Androgeen-receptor blocker/antagonist:
 - Bicalutamide (NSAA): Casodex®, Bicalutamide Sandoz®, Bicalutamide EG®, Bicalutamide Teva®
 - Flutamide: Flutamide EG®
 - PSA daling $\geq 50\%$ in 30-50%
 - Antiandrogeen withdrawal syndrome
 - PSA daling $\geq 50\%$ in +/- 20% gedurende 3-5 m (zo reeds MAB = ADT + AA)

Bron: William K., Urology: 2002

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Castratieresistent, hormoongevoelig PC

2. Prednison (5mg 2x/d, low dose)
 - Negatieve feedbackloop
 - PSA daling $\geq 50\%$ +/- 20%
 - Respons op pijn (?)
3. Ketoconazole +/- hydrocortisone
 - Cytochrom P450i → inhibite productie androgenen bijnier
 - PSA daling $\geq 50\%$ in 20-60%
4. Oestrogenen
 - Direct toxisch effect?
 - PSA daling $\geq 50\%$ in 26-81%

ACTH

Adrenal androgens

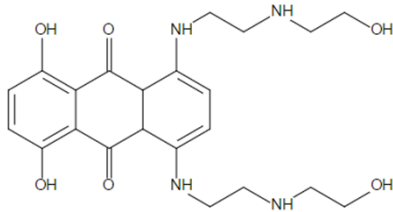
TUMOUR PROGRESSION

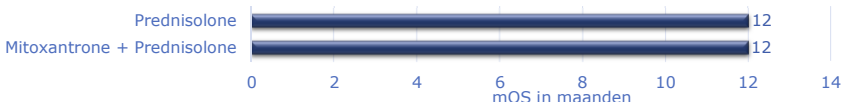
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Castratieresistent, hormoonongevoelig PC

- Mitoxantrone
 - Anthracenedione
 - PSA daling $\geq 50\%$ in 33%
 - Palliatief-effect





Treatment	mOS in maanden
Prednisolone	12
Mitoxantrone + Prednisolone	12

Tannock et al; JCO: 1996

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Evolutie behandeling prostaatcarcinoom: Voor 2004

ADT

Anti-androgenen

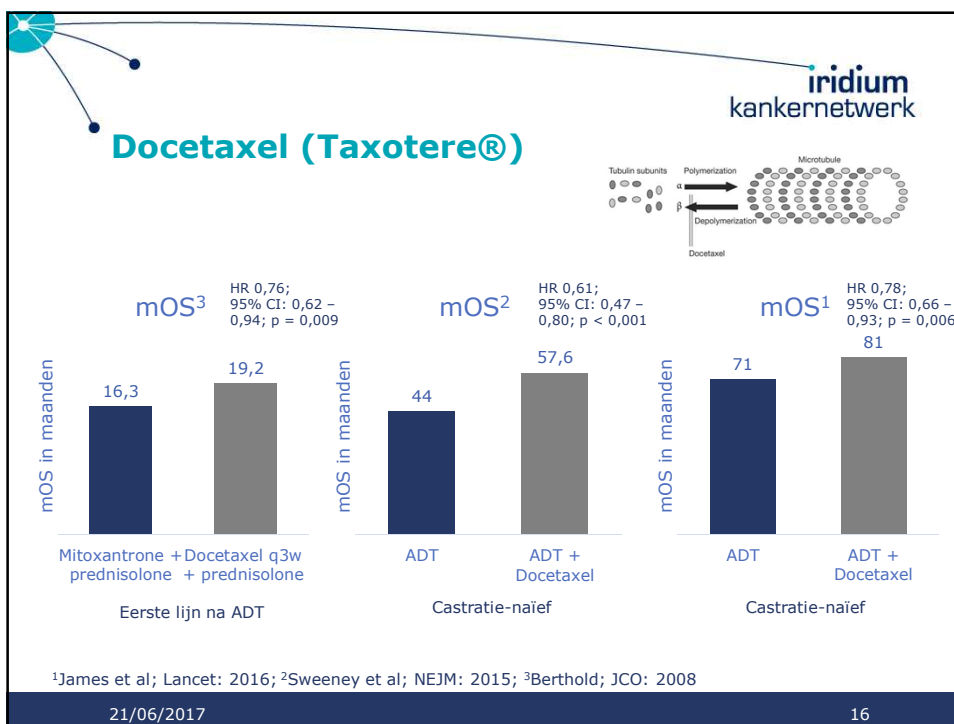
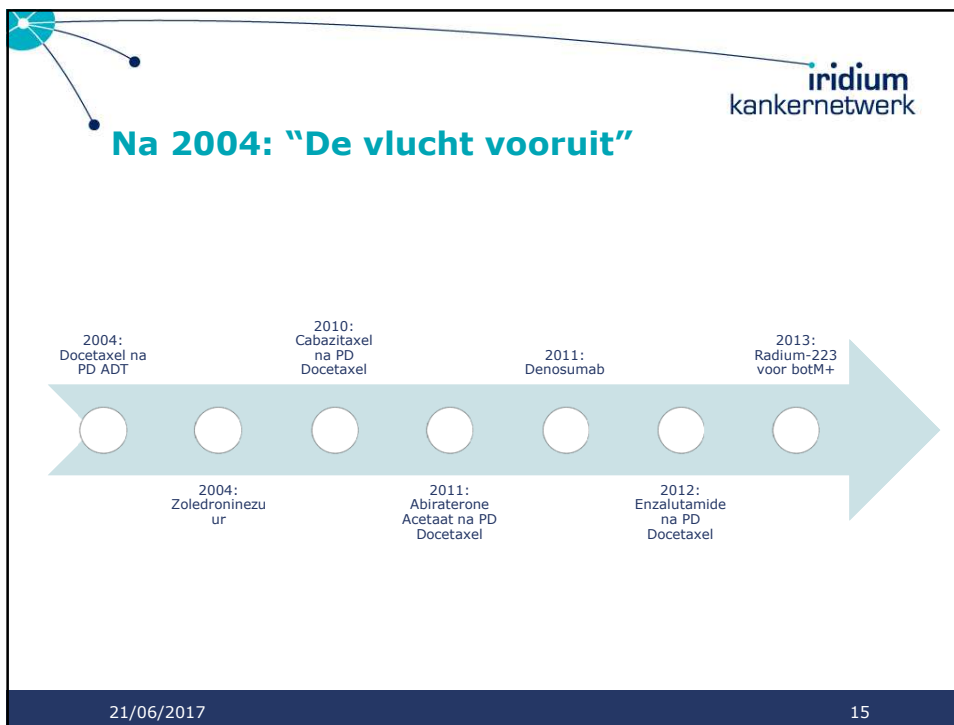
Prednisolone

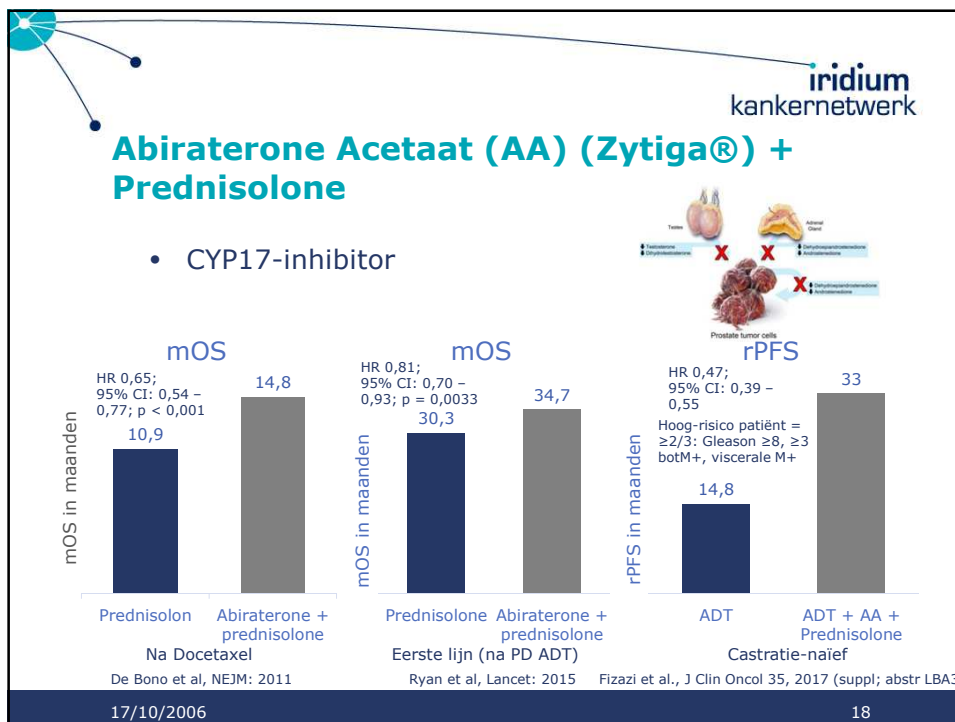
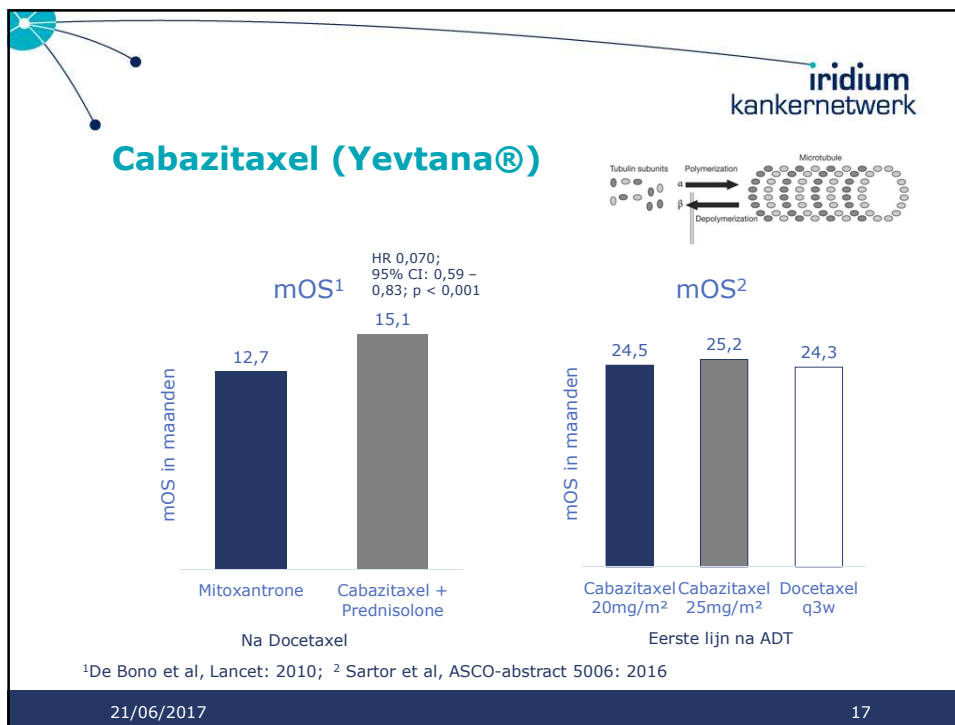
Mitoxantrone

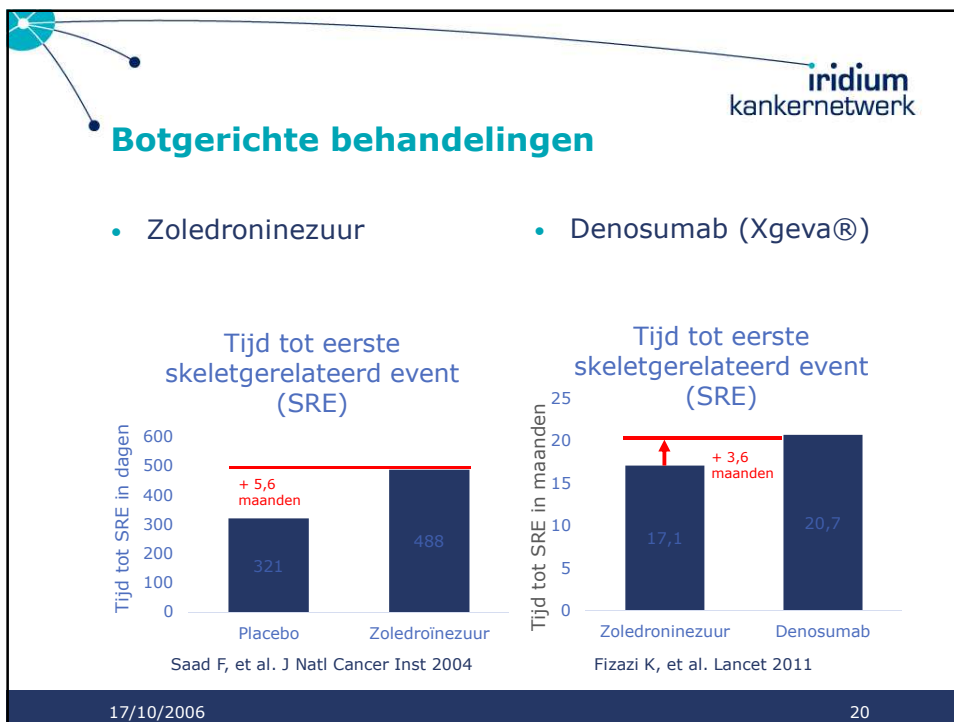
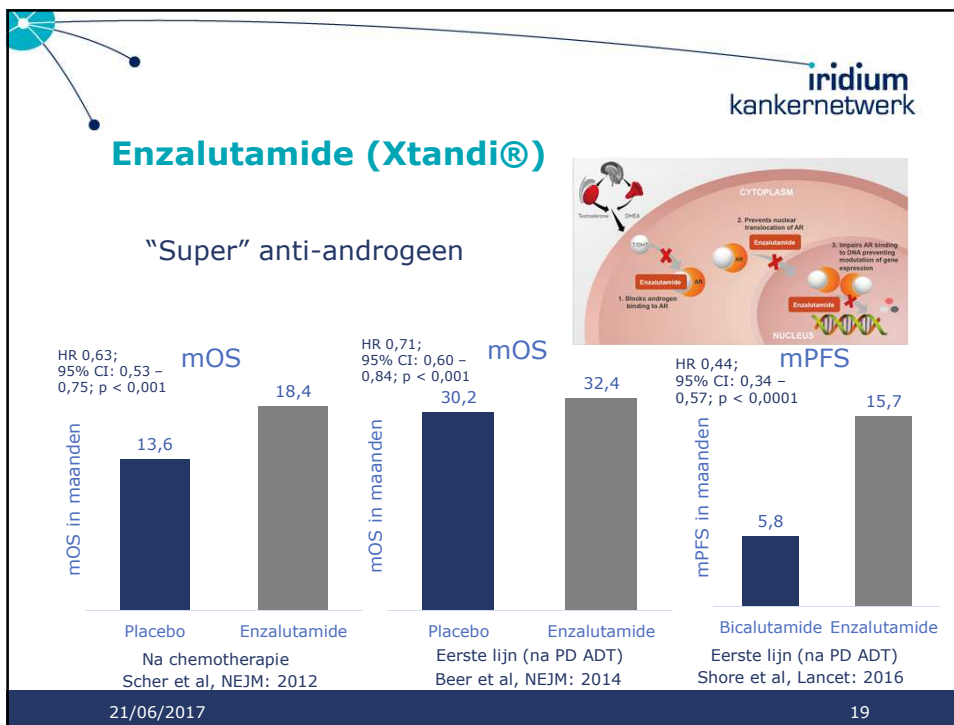
Ketoconazole

Oestrogenen

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Botspecifieke behandelingen

- Radium-223 (Xophigo®)

The diagram illustrates the interaction of beta particles and radium-223 alpha particles. Beta particles have a range of approximately 1-2 mm, affecting the bone marrow. Radium-223 alpha particles have a much shorter range of about 50-100 micrometers, targeting the tumor and the bone surface. Labels include: Range of beta particle, Bone marrow, Tumor, Bone surface, Range of radium-223 alpha particle, and Bone.

mOS

HR 0,70;
95% CI: 0,55 - 0,88; p = 0,002

Group	mOS in maanden
Radium-223 + BSOC	14
Placebo + BSOC	11,2

Tijd tot eerste SRE

HR 0,66;
95% CI: 0,52 - 0,83; p < 0,001

Group	Tijd tot SRE in maanden
Radium-223 + BSOC	15,6
Placebo + BSOC	9,8

Parker et al, NEJM: 2013

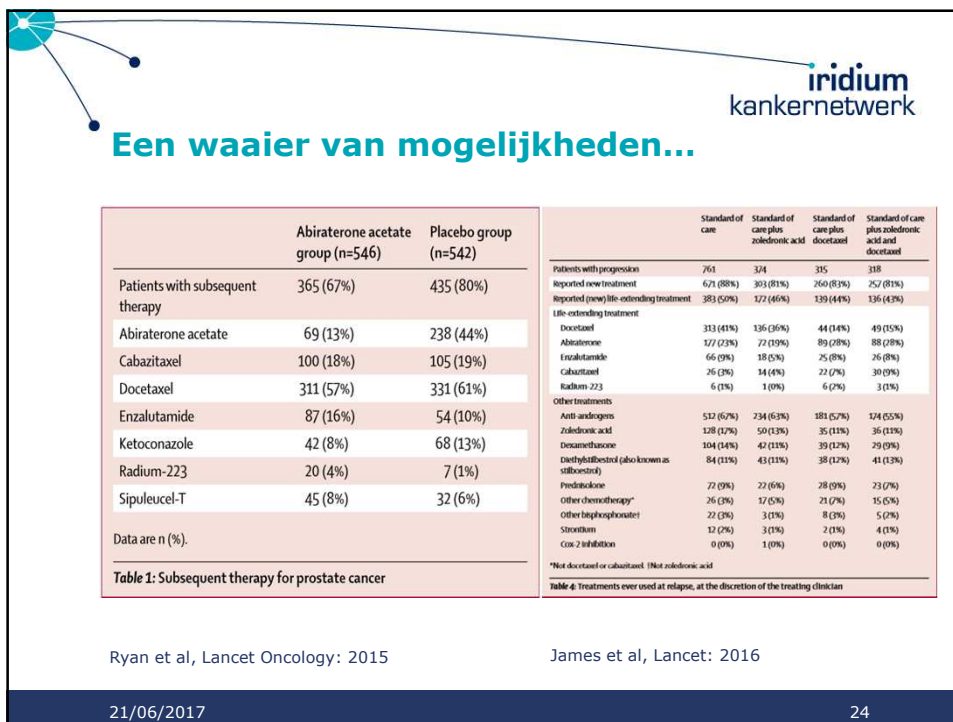
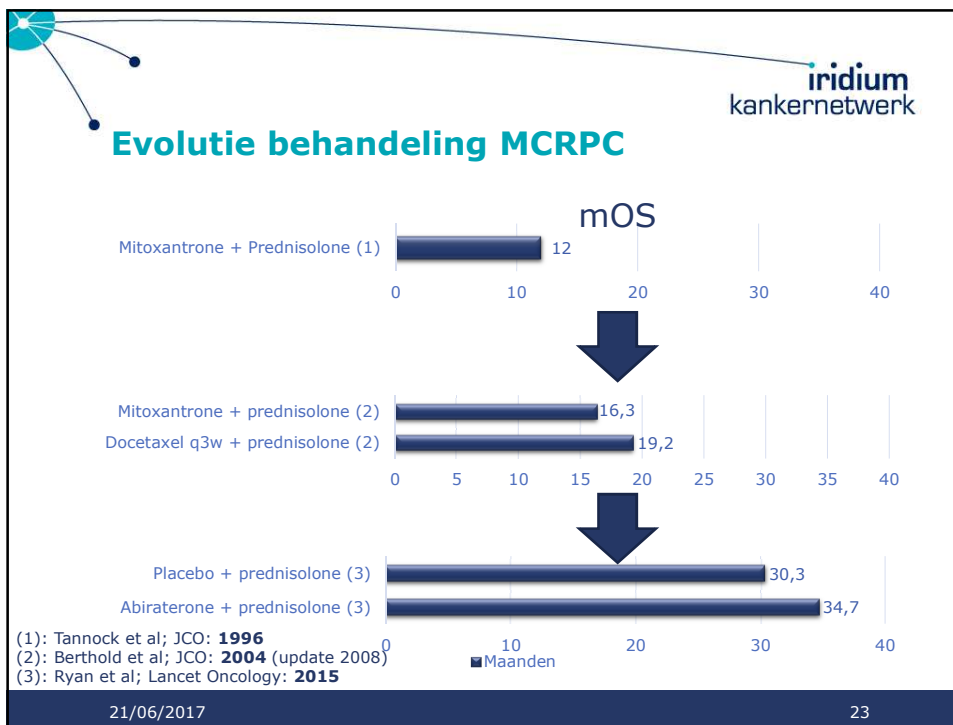
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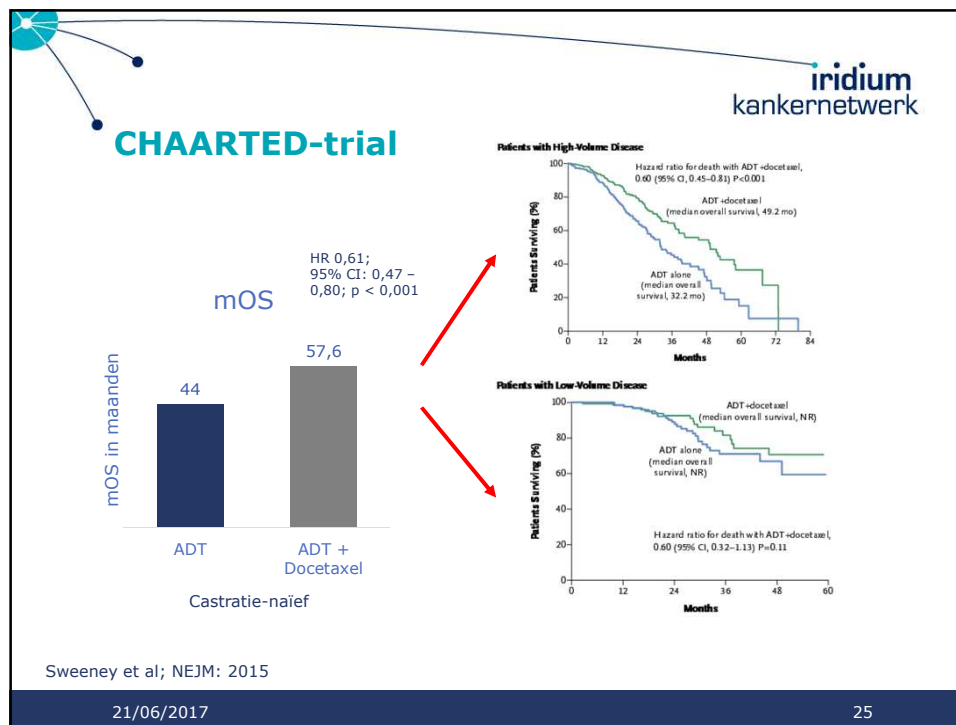
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Evolutie behandeling prostaatkarcinoom: Huidig beeld

ADT	Secundaire hormonale behandeling	Enzalutamide
Abiraterone	Radium-223	Cabazitaxel
	Docetaxel	

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De toekomst


- PEACE-1-studie: ADT +/- Abiraterone Acetaat +/- Docetaxel +/- RT MCSPC
- AR-V7-expressie:
 - Apalutamide (ARN-509): AR-antagonist
 - Darolutamide (ODM-201): AR-antagonist
- HRD:
 - PARP-inhibitoren (olaparib, rucaparib)
- PI3K/Akt/mTOR-sigtaaltransductieketen
- ...

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Vragen?

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NCCN-richtlijnen

Studies negative for distant metastases → Maintain castrate serum levels of testosterone →

- Clinical trial (preferred)
- Observation especially if PSADT ≥10 mo
- Secondary hormone therapy^m especially if PSADT <10 mo
 - ▶ Antiandrogen
 - ▶ Antiandrogen withdrawal
 - ▶ Ketoconazole ± hydrocortisone
 - ▶ Corticosteroid
 - ▶ DES or other estrogen

Visceral metastases

No →

- Abiraterone^m with prednisone (category 1)
- Docetaxel^{aa,ee} with prednisone (category 1)
- Enzalutamide^m (category 1)
- Radium-223 for symptomatic bone metastases (category 1)^{ff}
- Clinical trial
- Secondary hormone therapy^m
 - ▶ Antiandrogen
 - ▶ Antiandrogen withdrawal
 - ▶ Ketoconazole ± hydrocortisone^{gg}
 - ▶ Corticosteroid
 - ▶ DES or other estrogen

Yes →

- Docetaxel^{aa,ee} with prednisone (category 1)
- Enzalutamide^m (category 1)
- Abiraterone^m with prednisone
- Alternative chemotherapy (mitoxantrone with prednisone)^{aa}
- Clinical trial
- Secondary hormone therapy^m
 - ▶ Antiandrogen
 - ▶ Antiandrogen withdrawal
 - ▶ Ketoconazole ± hydrocortisone^{gg}
 - ▶ Corticosteroid
 - ▶ DES or other estrogen

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