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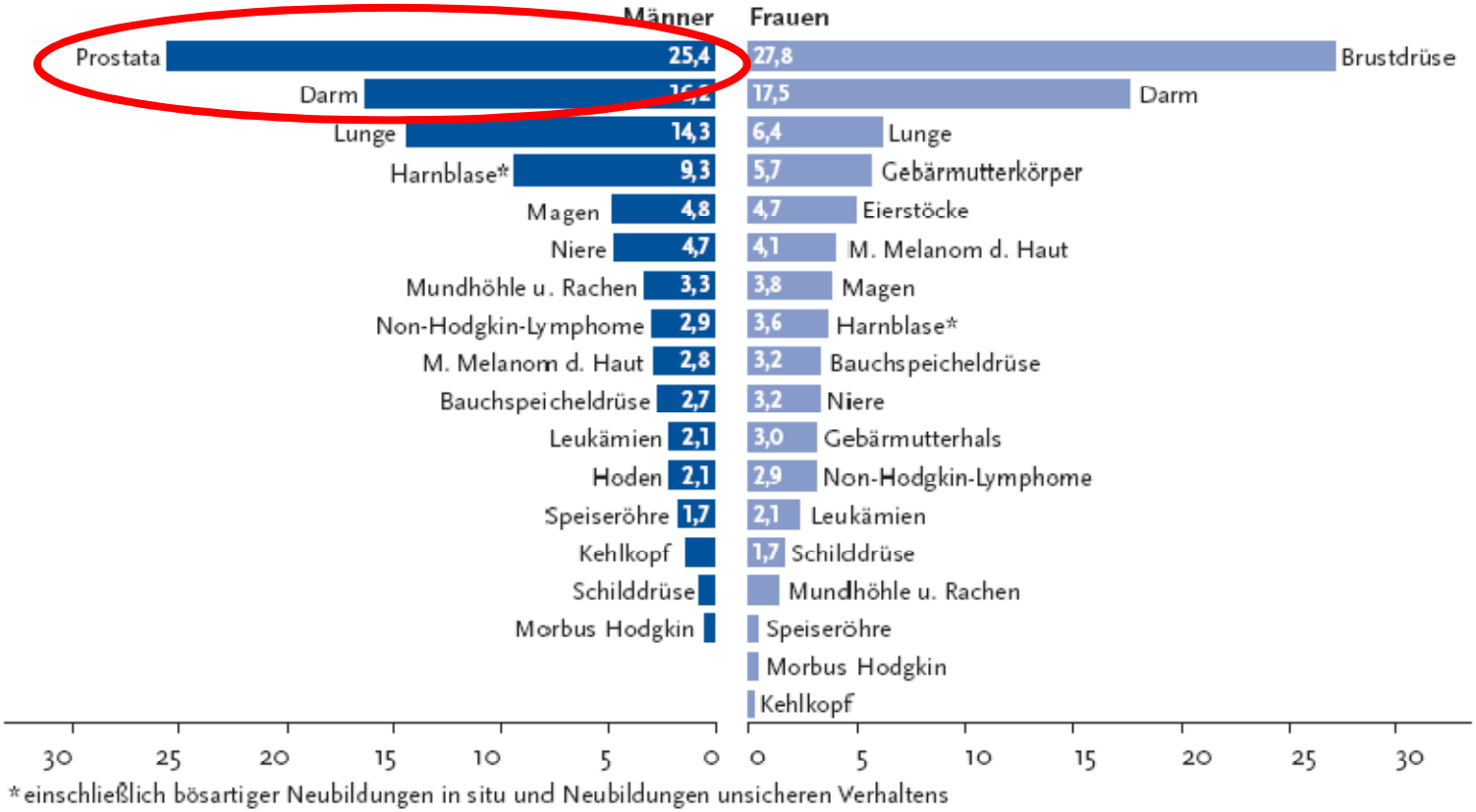
Das hormonrefraktäre Prostatakarzinom

Tumorinzidenzen

PCa häufigster Tumor des Mannes

pro Jahr ca. 58570 Neuerkrankungen

Prozentualer Anteil ausgewählter Tumorlokalisationen an allen Krebsneuerkrankungen ohne nicht-melanotischen Hautkrebs in Deutschland 2004
Quelle: Schätzung der Dachdokumentation Krebs im Robert Koch-Institut



*einschließlich bösartiger Neubildungen in situ und Neubildungen unsicheren Verhaltens

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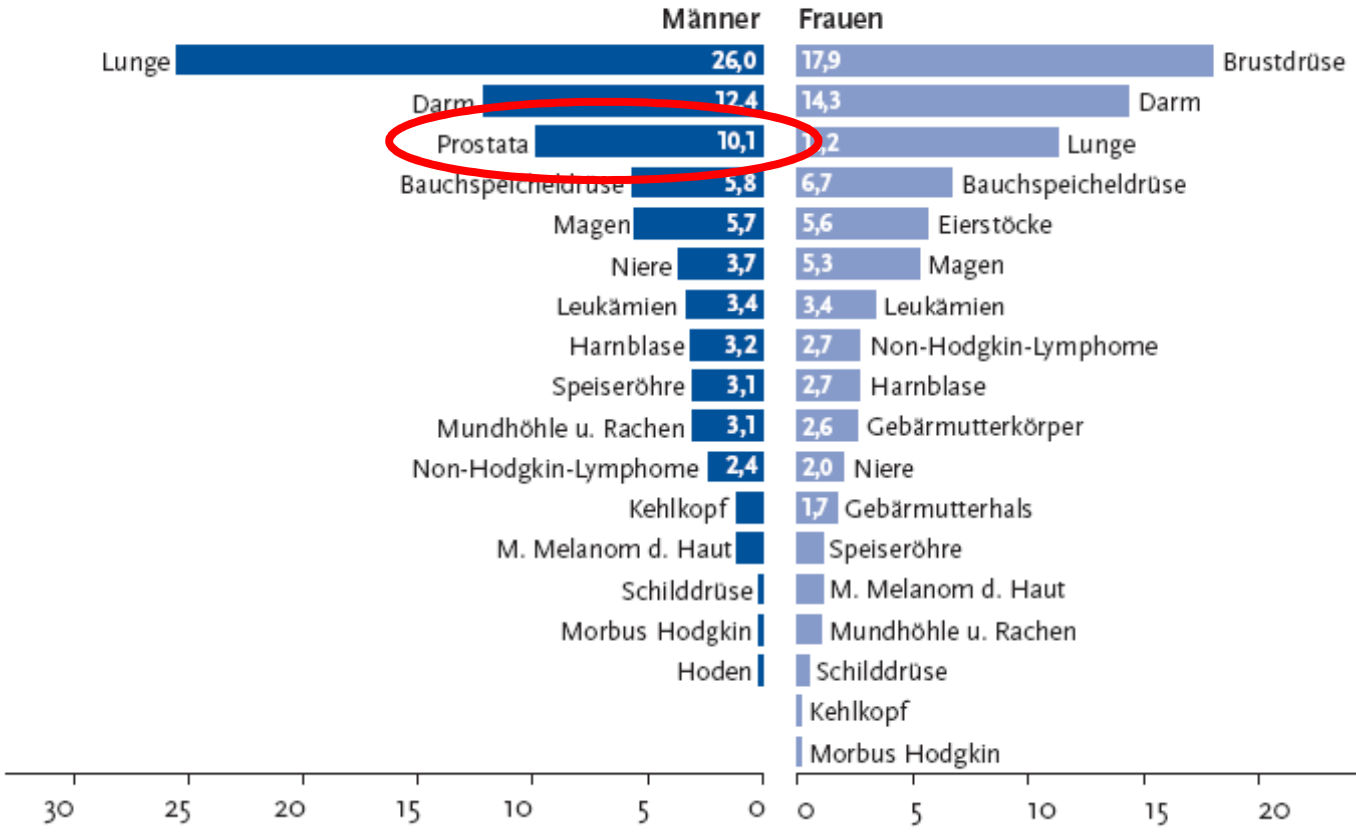
http://www.rki.de/cln_091/nn_205770/DE/Content/GBE/Gesundheitsberichterstattung/GBEDownloadsB/KID2008,templateId=raw,property=publicationFile.pdf/KID2008.pdf

Tumorsterblichkeit

11135 Todesfälle nach PCa

Prozentualer Anteil ausgewählter Tumorlokalisationen an allen Krebssterbefällen in Deutschland 2004
Quelle: Amtliche Todesursachenstatistik, Statistisches Bundesamt, Wiesbaden



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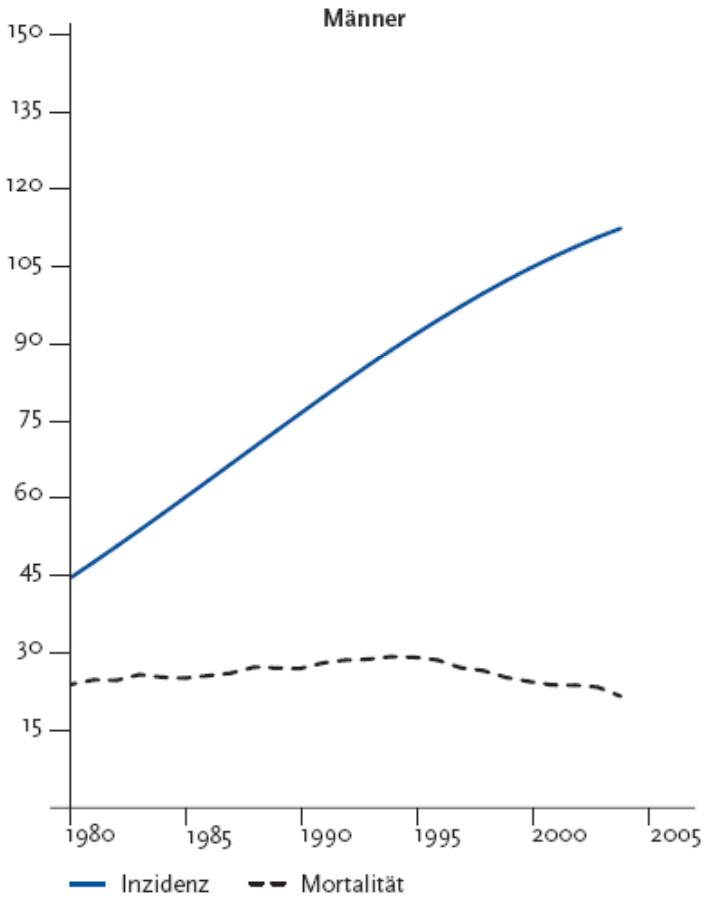
http://www.rki.de/cln_091/nn_205770/DE/Content/GBE/Gesundheitsberichterstattung/GBEDownloadsB/KID2008,templateId=raw,property=publicationFile.pdf/KID2008.pdf

Inzidenz und Mortalität des PCA

Altersstandardisierte Inzidenz und Mortalität in Deutschland 1980–2004, ICD-10 C61
Fälle pro 100.000 (Europastandard)



Mortalität leicht rückläufig

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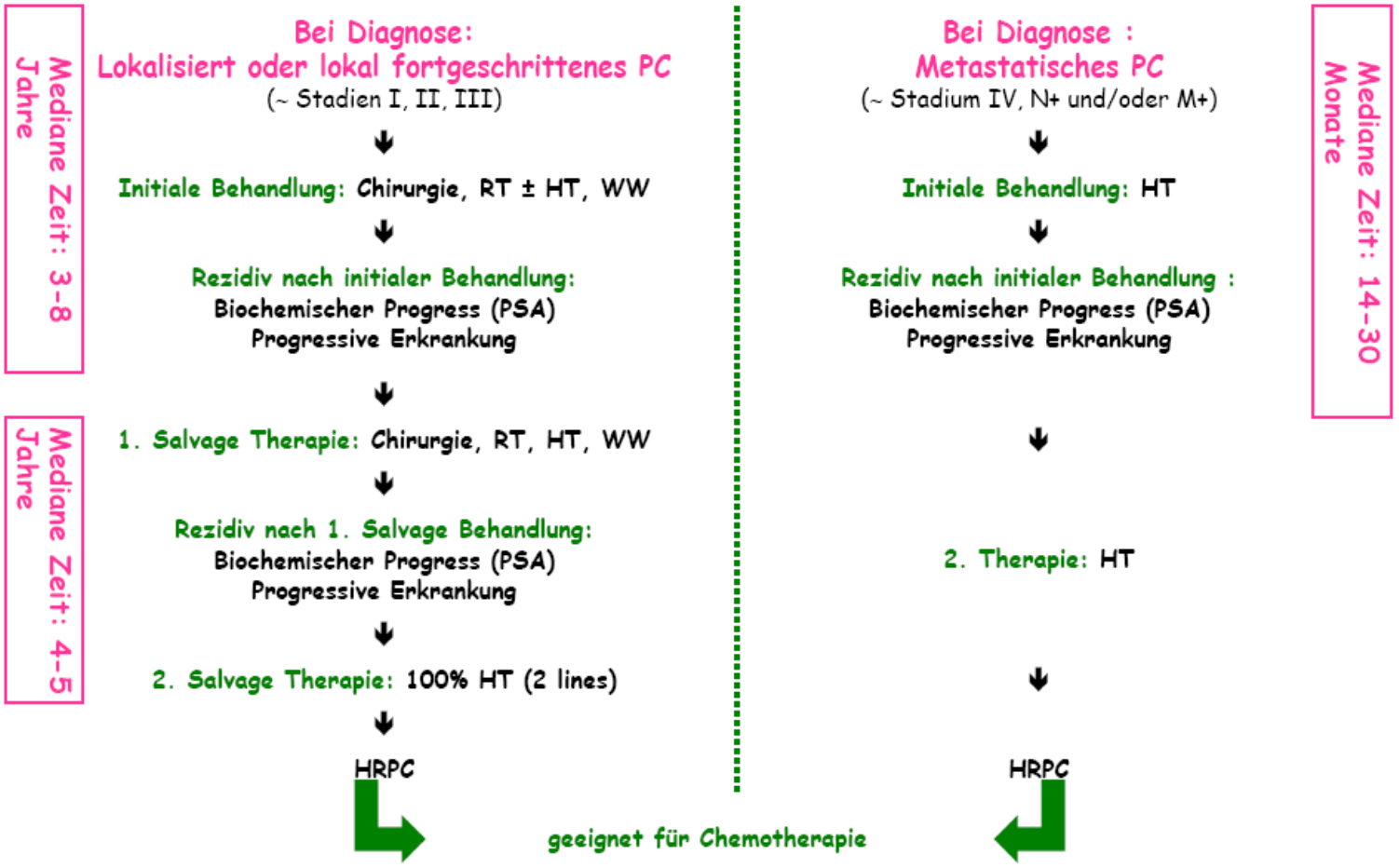
http://www.rki.de/cln_091/nn_205770/DE/Content/GBE/Gesundheitsberichterstattung/GBEDownloadsB/KID2008,templateId=raw,property=publicationFile.pdf/KID2008.pdf

Hormonrefraktäres Prostatakarzinom (HRPC)

- Definition (Expertenkonsensus)
  - Serum-Testosteron ist auf Kastrationsniveau
  - Maßnahmen der sekundären Hormonmanipulation sind ausgeschöpft
  - PSA steigt bei drei aufeinander folgenden Bestimmungen im Abstand von mindestens einer Woche an
    - unter fortgesetzter LHRH Blockade und nach Antiandrogenentzug
    - bei unterer PSA-Grenze von 0,4 ng/ml

Miller, K. et al. Aktuel. Urol. 2006; 37: 201-204

Therapie-Verlauf



HRPC: Historie

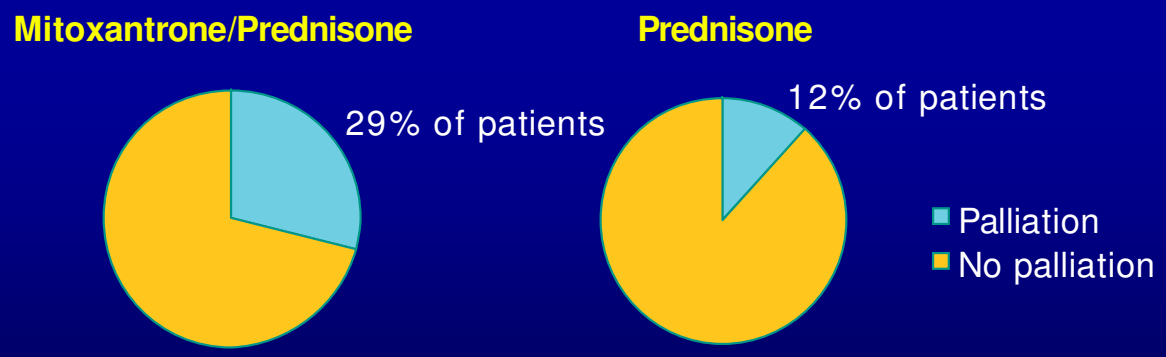
Zytostatische Therapie des HRPC

Übersichtsarbeiten	*Ansprechen*
1985: (17 Studien)	6,5 %
	M. Eisenberger, J Clin Oncol 1985
1992: (26 Studien)	8,7 %
	Yagoda & Petrylak, Cancer 1993

HRPC: Historie

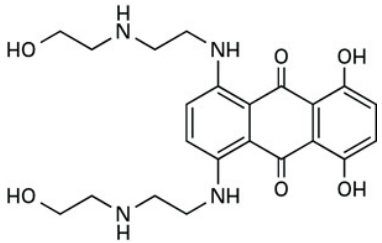
Mitoxantrone/prednisone vs prednisone in patients with symptomatic HRPC (n = 161)

- Primary endpoint: palliative pain response
- Duration of palliation: 43 weeks vs 18 weeks
- No difference in PSA or survival



Tannock et al. J Clin Oncol 1996;14:1756–1764

Mitoxantron



4.1 Anwendungsgebiete

Behandlung von Schmerzzuständen bei fortgeschrittenem, hormonresistentem Prostatakarzinom in Kombination mit niedrig dosierten Kortikosteroiden, wenn die bewährte Schmerzbehandlung nicht ausreichend oder ungeeignet ist.

- Anthracyclin
- Wirkweise
  - Interkalation der DNA
  - Hemmung der DNA- / RNA-Synthese
  - Hemmung der Topoisomerase II
  - Blockierung der Zellen in der G2 Phase
  - Radikalbildung
  - Hemmung der Angiogenese
- Präparate, z.B.:
  - Novantron® / Wyeth; Ralenova® / Wyeth
  - Mitoxantron® / GRY
  - Onkotrone® / Baxter

HRPC: Historie

Zytostatische Therapie des HRPC

Metaanalyse

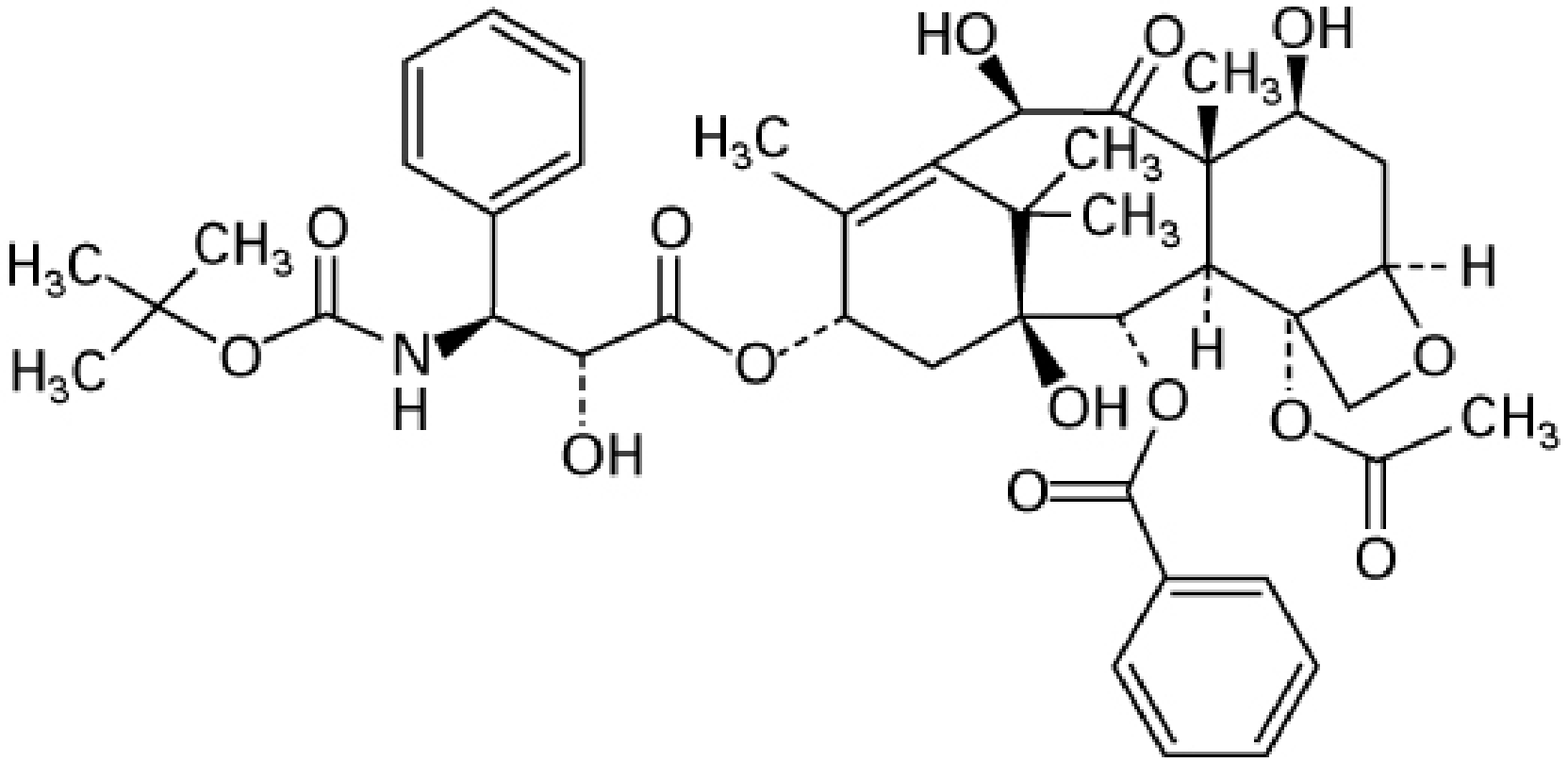
52 Studien mit 2028 Pat. im Zeitraum 1/95 - 9/00

Parameter	Range	Studien
PSA-Abfall >50%	53** - 92* %	19
Zeit bis zur Progression	2 – 12 Monate	29
Gesamtüberleben	7 – 27 Monate	21
Lebensqualität	Schmerzscore-verbesserung	4 von 8

* EMP + Docetaxel
** EMP + Paclitaxel

Casciano et al. Proc ASCO 2001 # 2428

Docetaxel: Struktur



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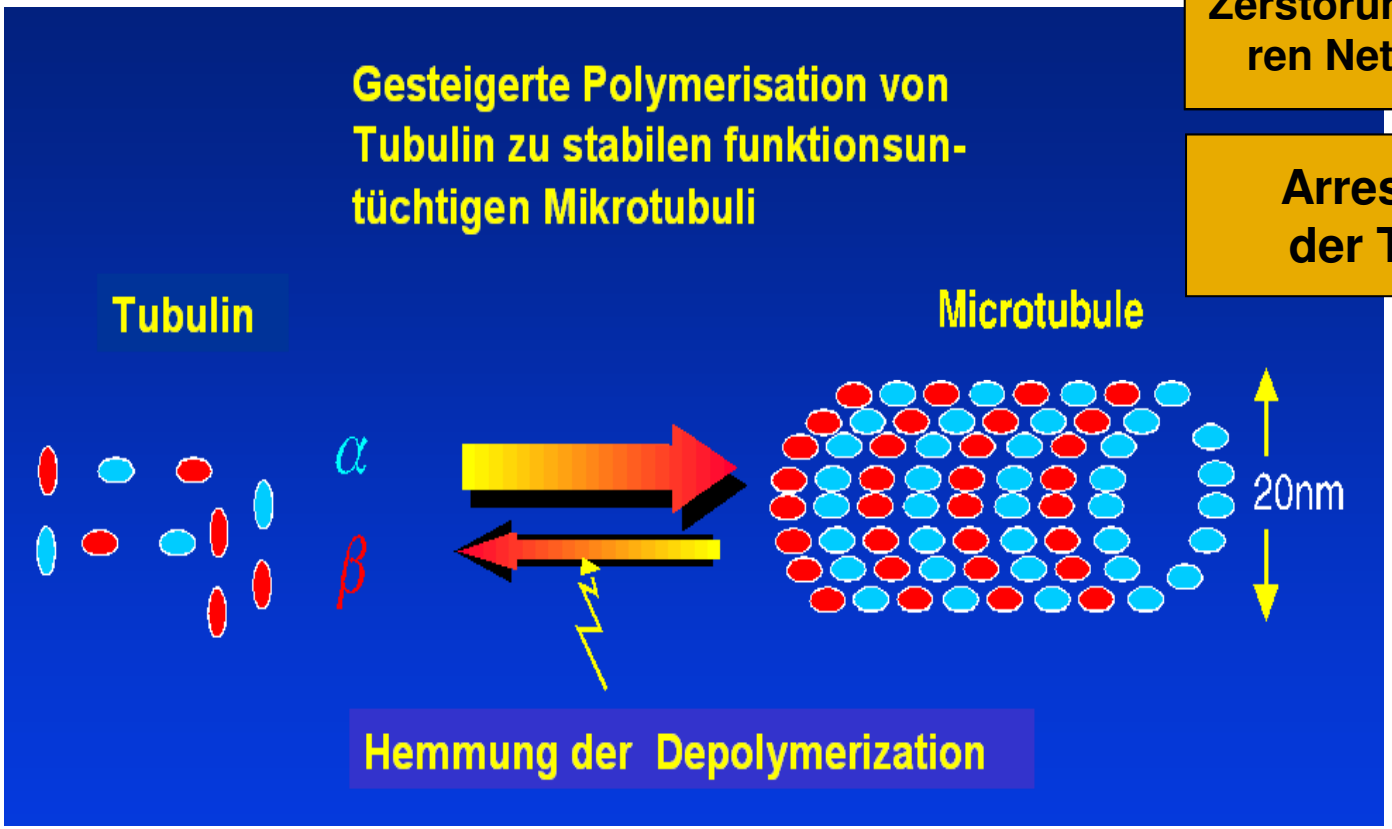
Docetaxel: Wirkweise

Abnahme des freien Tublins

Zerstörung des mikrotubulären Netzwerks der Zellen

Arrest der Zellen in der Teilungsphase



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Tax 327 Zulassungsstudie

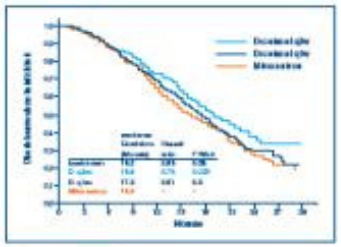
Die TAX-327-Studie: Multizentrischer Vergleich der wöchentlichen und 3-wöchentlichen Gabe von Docetaxel + Prednison mit Mitoxantron + Prednison bei Patienten mit hormonrefraktärem Prostatakarzinom.

Tannock I et al. Docetaxel plus Prednisone or Mitoxantrone plus Prednisone for Advanced Prostate Cancer. N Engl J Med 2004; 351:1502-12

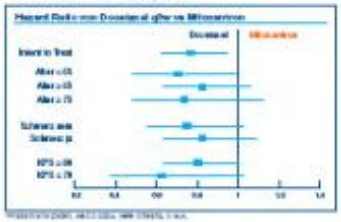
Studiendesign

Ansprechrate (sekundäres Studienziel)

Gesamtüberleben



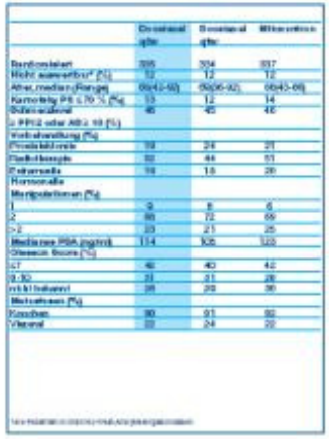
Überleben in Subgruppen*



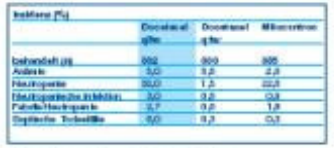
Lebensqualität

Die TAX-327-Studie: Patientencharakteristika und Nebenwirkungsprofil

Patienten-Charakteristika (n=1006)



Hämatologische Toxizität (Grade 3–4)*



Nicht-hämatologische Toxizität*

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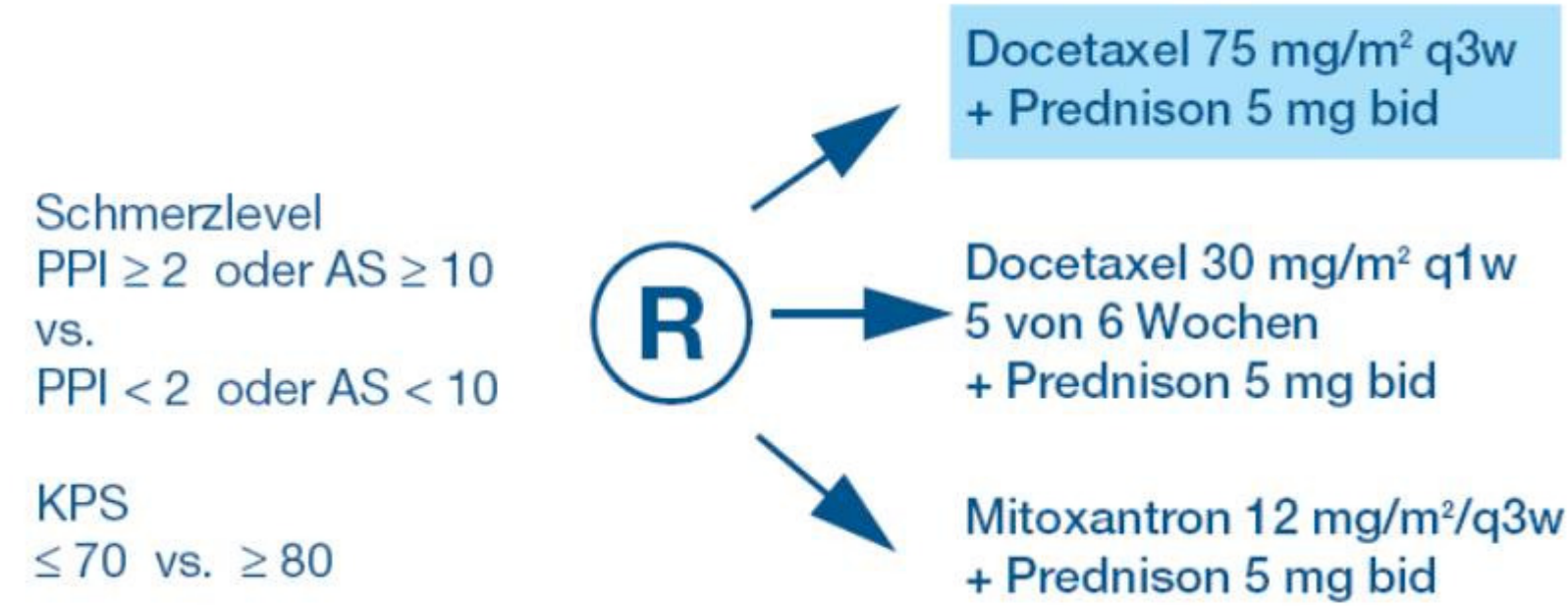
Tannock, IF et al., NEJM 2004; 351: 1502-1512

Tax 327: Design



Behandlungsdauer in allen 3 Armen = 30 Wochen

Tannock, IF et al., NEJM 2004; 351: 1502-1512

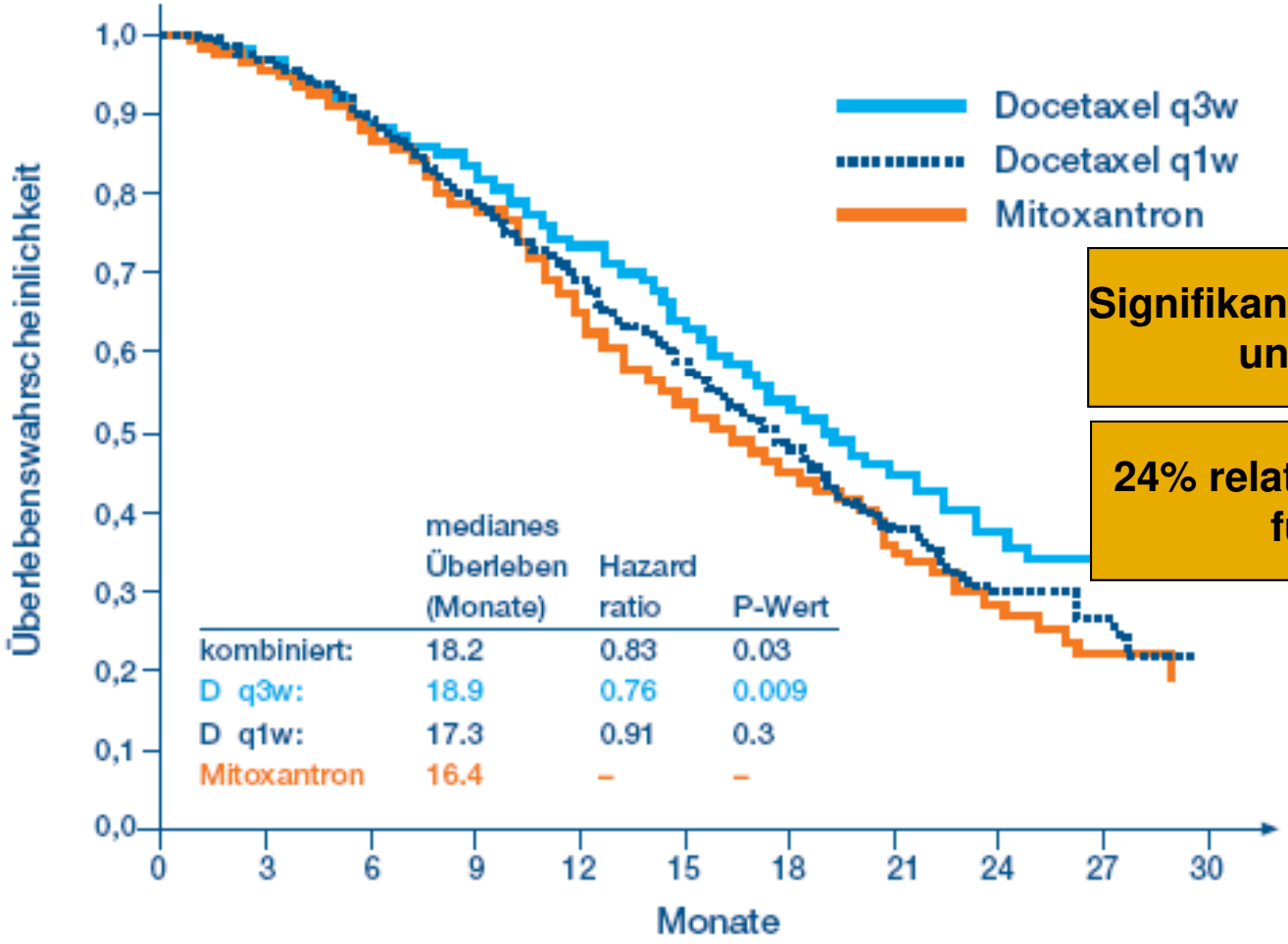
Tax 327: Einschlusskriterien

	Docetaxel q3w	Docetaxel q1w	Mitoxantron
Randomisiert	335	334	337
Nicht auswertbar* (%)	12	12	12
Alter, median (Range)	68(42-92)	69(36-92)	68(43-86)
Karnofsky PS ≤ 70 % (%)	13	12	14
Schmerzlevel ≥ PPI 2 oder AS ≥ 10 (%)	45	45	46
Vorbehandlung (%)			
Prostatektomie	19	24	21
Radiotherapie	52	44	51
Estramustin	19	18	20
Hormonelle Manipulationen (%)			
1	9	8	6
2	68	72	69
>2	23	21	25
Medianes PSA (ng/ml)	114	108	123
Gleason Score (%)			
≤7	42	40	42
8-10	31	31	28
nicht bekannt	26	29	30
Metastasen (%)			
Knochen	90	91	92
Viszeral	22	24	22

Mehr als 90% mit mindestens 2 hormonellen Therapien

Tannock, IF et al., NEJM 2004; 351: 1502-1512

Tax 327 Ergebnisse: Overall Survival



	medianes Überleben (Monate)	Hazard ratio	P-Wert
kombiniert:	18.2	0.83	0.03
D q3w:	18.9	0.76	0.009
D q1w:	17.3	0.91	0.3
Mitoxantron	16.4	–	–

Signifikant längeres Überleben unter Docetaxel

24% relative Risikoreduktion für Mortalität

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Tannock, IF et al., NEJM 2004; 351: 1502-1512

Tax 327: Sekundäre Endpunkte

	Docetaxel q3w	Docetaxel q1w	Mitoxantron
Schmerzansprechen*			
n, auswertbar	153	154	157
Ansprechrate (%)	35	31	22
P-Wert (vs. Mitoxantron)	0,01	0,08	–
PSA Ansprechen*			
n, auswertbar	291	282	300
PSA Ansprechrate (%)	45	48	32
P-Wert (vs. Mitoxantron)	0,001	<0,001	–
Tumoransprechen (objektiv)*			
n, auswertbar	141	134	137
Ansprechrate (%)	12	8	7
P-Wert (vs. Mitoxantron)	0,11	0,59	–

*nur Patienten mit Schmerzen oder PSA ≥20 oder messbarer Erkrankung zum Studienbeginn

Signifikant höhere Schmerzreduktion unter Docetaxel

Signifikant höhere PSA-Ansprechrate unter Docetaxel

Höhere Tumor-Ansprechrate unter Docetaxel

Tannock, IF et al., NEJM 2004; 351: 1502-1512

Tax 327: Hämatologische Verträglichkeit

Inzidenz (%)	Docetaxel q3w	Docetaxel q1w	Mitoxantron
behandelt (n)	332	330	335
Anämie	5,0	5,0	2,0
Neutropenie	32,0	1,5	22,0
Neutropenische Infektion	3,0	0,0	0,9
Febrile Neutropenie	2,7	0,0	1,8
Septische Todesfälle	0,0	0,3	0,3

Häufigste Grad 3/4 - Nebenwirkung: Neutropenie

Neutropenische Komplikationen selten

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Tannock, IF et al., NEJM 2004; 351: 1502-1512

Tax 327: Verträglichkeit

Inzidenz (%)

	Docetaxel q3w		Docetaxel q1w		Mitoxantron	
	alle Grade	3/4	alle Grade	3/4	alle Grade	3/4
Alopezie	65	n.a.	50	n.a.	13	n.a.
Fatigue	53	4,5	49	5,5	35	5,1
Übelkeit	41	2,7	36	2,4	36	1,5
Diarrhoe	32	2,1	34	4,8	10	1,2
Neurosensorisch	30	1,8	24	0,9	7	0,3
Nagelveränderung	30	n.a.	37	n.a.	7	n.a.
Obstipation	25	2,1	17	1,5	17	0,6
Stomatitis	20	0,9	17	0,3	8	0,0
Tränenfluß	10	0,6	21	0,3	1	0,0
Periphere Ödeme	19	0,6	12	0,6	1	0,0
Erbrechen	17	1,5	22	2,1	14	1,5
Anorexie	17	1,2	21	0,3	14	0,3
Dyspnoe	15	2,7	14	1,5	9	0,6
Nasenbluten	6	0,3	17	0,6	2	0,0

n.a. = nicht anwendbar

Tannock, IF et al., NEJM 2004; 351: 1502-1512

Tax 327: Lebensqualität

Lebensqualität unter Docetaxel signifikant besser

FACT-P Score im Vergleich zum Studienbeginn (> 16 Punkte)

	Docetaxel q3w	Docetaxel q1w	Mitoxantron
auswertbare Patienten	**278**	**270**	**267**
Ansprechen (%)	22	23	13
(95% CI)	(17–27)	(18–28)	(9-18)
P-Wert*	0,009	0,005	

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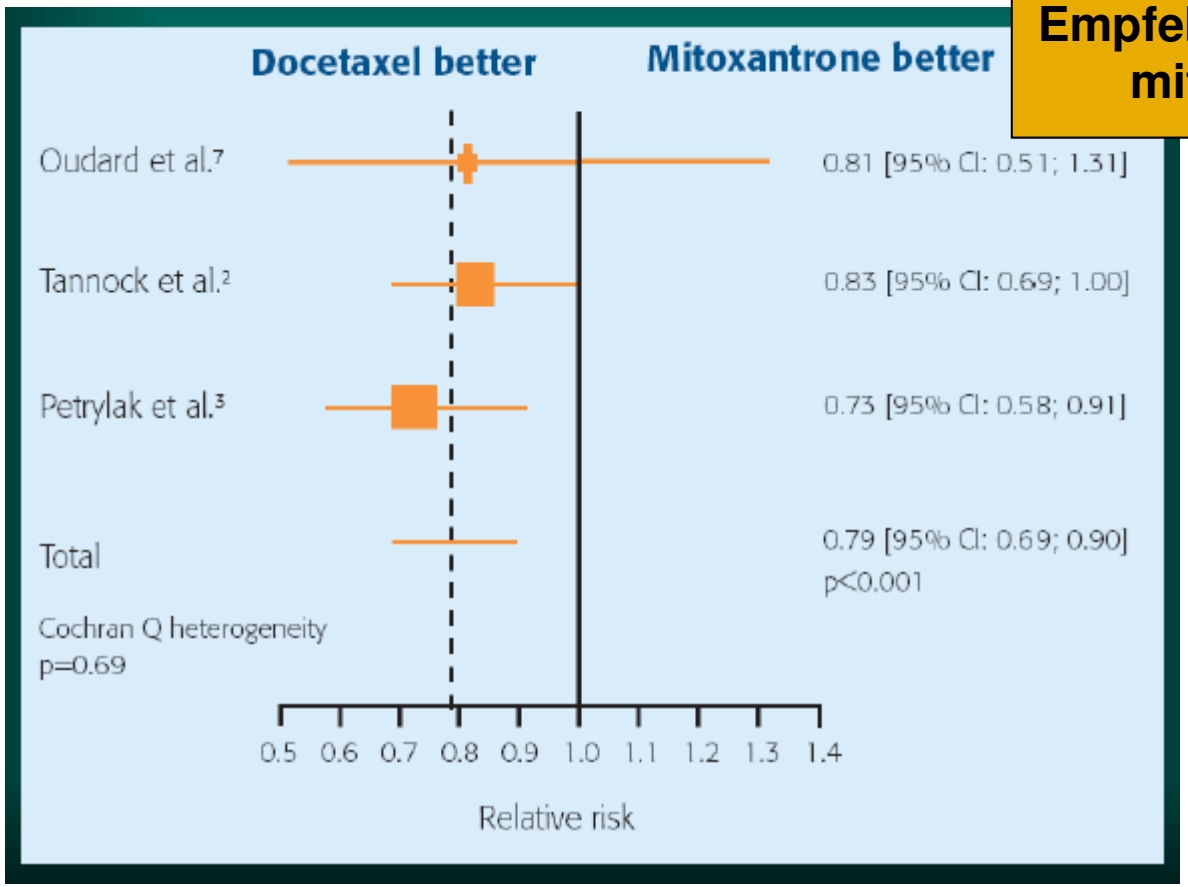
Tannock, IF et al., NEJM 2004; 351: 1502-1512

Docetaxel bei HRPC

TAX 327 Ergebnisse reproduzierbar

Empfehlung von Docetaxel mit Evidenzgrad 1A



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Oudard ASCO 2005; #4634

Docetaxel in den Leitlinien: ASCO

Major Guideline Recommendations and Qualifying Statements

The CCO guideline recommendations for nonhormonal therapy in men with castration-resistant (ie, hormone-refractory) prostate cancer are as follows, and are taken verbatim from the CCO guideline:

- For men with clinical or biochemical evidence of progression and evidence of metastases, treatment with docetaxel 75 mg/m^2 administered intravenously every 3 weeks with 5 mg oral prednisone twice daily should be offered to improve overall survival, disease control, symptom palliation, and quality of life.
- Alternative therapies that have not demonstrated improvement in overall survival but can provide disease control, palliation, and improve quality of life include weekly docetaxel plus prednisone, and mitoxantrone plus prednisone (or hydrocortisone).

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Basch, EM et al. JCO 2007; 25: 5313-5318

Docetaxel in den Leitlinien: ASCO (2)

The CCO guideline also included the following qualifying statements, which are taken verbatim from the CCO guideline:

- Docetaxel-based chemotherapy is the only treatment that has demonstrated an overall survival benefit in men with hormone-refractory prostate cancer.
- The timing of docetaxel therapy in men with evidence of metastases but without symptoms should be discussed with patients and individualized based on their clinical status and preferences.
- In the largest clinical trials reviewed for this guideline, the men enrolled continued on gonadal androgen suppression and discontinued the use of antiandrogens. These maneuvers are recommended for men with hormone-refractory prostate cancer who receive chemotherapy.
- Men with hormone-refractory prostate cancer should have symptom control optimized.
- Use of estramustine in combination with other cytotoxic agents is not recommended due to the increased risk of clinically important toxicities without evidence of improved survival or palliation.

Basch, EM et al. JCO 2007; 25: 5313-5318

Docetaxel in den Leitlinien: EAU

17.12 Guidelines and recommendations for cytotoxic therapy in HRPC

Guidelines and recommendations	GR
• Cytotoxic therapy should only be used to treat non-metastatic HRPC in clinical trials	
• In patients with a PSA rise only, two consecutive increases of PSA serum levels above a previous reference level should be documented	B
• Prior to treatment, PSA serum levels should be > 5 2 ng/mL to assure correct interpretation of therapeutic efficacy	B
• Potential benefits of cytotoxic therapy and expected side-effects should be discussed with each individual patient	C
• In patients with metastatic HRPCA, and who are candidates for cytotoxic therapy, docetaxel at 75 mg/m^2 every 3 weeks has shown a significant survival benefit	A
• In patients with symptomatic osseous metastases due to HRPCA, either docetaxel or mitoxantrone with prednisone or hydrocortisone are viable therapeutic options	A
• Second-line docetaxel should be considered in previously responding patients to docetaxel Otherwise, treatment is tailored to the individual patient	B

GR = grade of recommendation

Heidenreich A, et al., EAU Guidelines on Prostate Cancer, http://www.uroweb.org/fileadmin/tx_eauguidelines/2009/Full/Prostate_Cancer.pdf

Docetaxel in den Leitlinien

clinical recommendations

Annals of Oncology 18 (Supplement 2): ii36–ii37, 2007
doi:10.1093/annonc/mdm028

Prostate cancer: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

metastatic disease

- Androgen suppression using bilateral orchiectomy or an LHRH agonist should be first-line treatment.
- Short-course antiandrogen should be used to prevent disease flare on starting an LHRH agonist.
- Patients with castration-refractory disease should have continued androgen suppression.
- Patients with castration-refractory disease should receive second-line hormonal therapy (e.g. antiandrogen, corticosteroid) and be considered for third-line (e.g. oestrogen).
- Docetaxel using a three-weekly schedule should be considered for symptomatic, castration-refractory disease [II, A].
- External beam radiotherapy should be offered for patients with painful bone metastases from castration-refractory disease (fractioning 1 × 8 Gy or 10 × 3 Gy may be used with equal pain-reducing efficacy) [II, A].
- Radioisotope therapy with strontium-89 may be considered for patients with painful bone metastases from castration-refractory disease [II, A].
- Intravenous bisphosphonates (e.g. pamidronate) should be considered for patients with bone pain resistant to palliative radiotherapy and conventional analgesics [II, A].
- Patients with castration-refractory disease should be managed in collaboration with dedicated palliative care services.

Interdisziplinäre S3 Leitlinien: Therapie des Androgen-unabhängigen CRPC

6.32	Patienten mit symptomatischer progredienter Erkrankung unter medikamentöser Kastration und in gutem Allgemeinzustand sollte die Gabe einer zytostatischen Therapie mit Docetaxel 75 mg/m^2 Körperoberfläche alle drei Wochen in Kombination mit Prednisolon 5 mg zweimal täglich angeboten werden. *Empfehlungsgrad B, LoE 1+* *Gesamtabstimmung: 96 %* **Literatur:** [539-541]	**B**

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http://www.aezq.de/edocs/pdf/leitlinien/s3-leitlinie-prostatakarzinom-konsultationsfassung

Interdisziplinäre S3 Leitlinien: Therapie des Androgen-unabhängigen CRPC

	Empfehlungen/Statements	Empfehlungs-grad
6.27	Patienten mit asymptomatischer progredienter Erkrankung unter Androgendeprivation kann eine Chemotherapie angeboten werden bei • raschem PSA-Anstieg (PSAD < 3 Monate); • Progression in der Bildgebung; • PSA-Anstieg und Therapiewunsch. *Empfehlungsgrad 0, Expertenkonsens* *Gesamtabstimmung: 80 %* **Literatur:** [538]	0
6.28	Vor Entscheidung über eine Chemotherapie sollen Patienten mit asymptomatischer progredienter Erkrankung unter Androgendeprivation über folgende Inhalte aufgeklärt werden: • es handelt sich um eine palliative Therapiemaßnahme; • die Chemotherapie ist mit Nebenwirkungen verbunden; • eine Verbesserung des Überlebensvorteils bei frühzeitigem Beginn der Chemotherapie im asymptomatischen Stadium gegenüber einem Therapiebeginn bei Symptomen ist nicht erwiesen. *Empfehlungsgrad A, Expertenkonsens* *Gesamtabstimmung: 75 %*	A

http://www.aezq.de/edocs/pdf/leitlinien/s3-leitlinie-prostatakarzinom-konsultationsfassung

Therapie-Empfehlungen

4.2 Dosierung, Art und Dauer der Anwendung

Prostatakarzinom

Die empfohlene Dosierung von Docetaxel beträgt 75 mg/m². Es werden zweimal täglich 5 mg Prednison oder Prednisolon oral kontinuierlich gegeben (siehe auch Abschnitt 5.1).

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Therapie-Empfehlungen

5. PHARMAKOLOGISCHE EIGEN-SCHAFTEN

5.1 Pharmakodynamische Eigenschaften

Vor dem Hintergrund der Tatsache, dass TAXOTERE bei wöchentlicher Gabe ein etwas besseres Sicherheitsprofil zeigte als bei Gabe alle 3 Wochen, ist es möglich, dass bestimmte Patienten von der wöchentlichen Gabe einen Nutzen haben.

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Fachinformationen Taxotere® 20/ mg/1ml, Taxotere® 80 mg/4ml Konzentrat zur Herstellung einer Infusionslösung

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Tax 327 update

Berthold, DR et al. JCO 2008; 26: 242-245

Tax 327 update

- 557 von 1006 Patienten zum Zeitpunkt der Primäranalyse verstorben
- 840 von 1006 Patienten zum Zeitpunkt des Updates Prostate ASCO 2007 verstorben
- 867 von 1006 Patienten zum Zeitpunkt des Updates ASCO 2007 verstorben

Berthold, DR et al. JCO 2008; 26: 242-245

Wirksamkeit der Tax Behandlung

Table 1. Survival of Men Treated With D3P, D1P, or MP: Initial and Updated Data

Data	D3P (n = 335)	D1P (n = 334)	MP (n = 337)
Original data, 2003			
Patients who died			
Nc.	166	190	201
%	50	57	60
Survival time, months			
Median	18.9	17.4	16.5
Range	17.0-21.2	15.7-19.0	14.4-18.6
Hazard ratio	0.76	0.91	
95% CI	0.62 to 0.94	0.75 to 1.11	
P	.009	.36	
Updated data, 2006-2007			
Patients who died			
Nc.	285	285	297
%	85.1	85.3	88.1
Survival time, months			
Median	19.2	17.8	16.3
Range	17.5-21.3	16.2-19.2	14.3-17.9
Hazard ratio	0.79	0.87	
95% CI	0.67 to 0.93	0.74 to 1.02	
P	.004	.086	
Survival > 3 years			
3-year survival rate, %	18.6	16.8	13.5

Abbreviations: D3P, docetaxel administered every 3 weeks plus prednisone; D1P, weekly docetaxel plus prednisone; MP, mitoxantrone plus prednisone.

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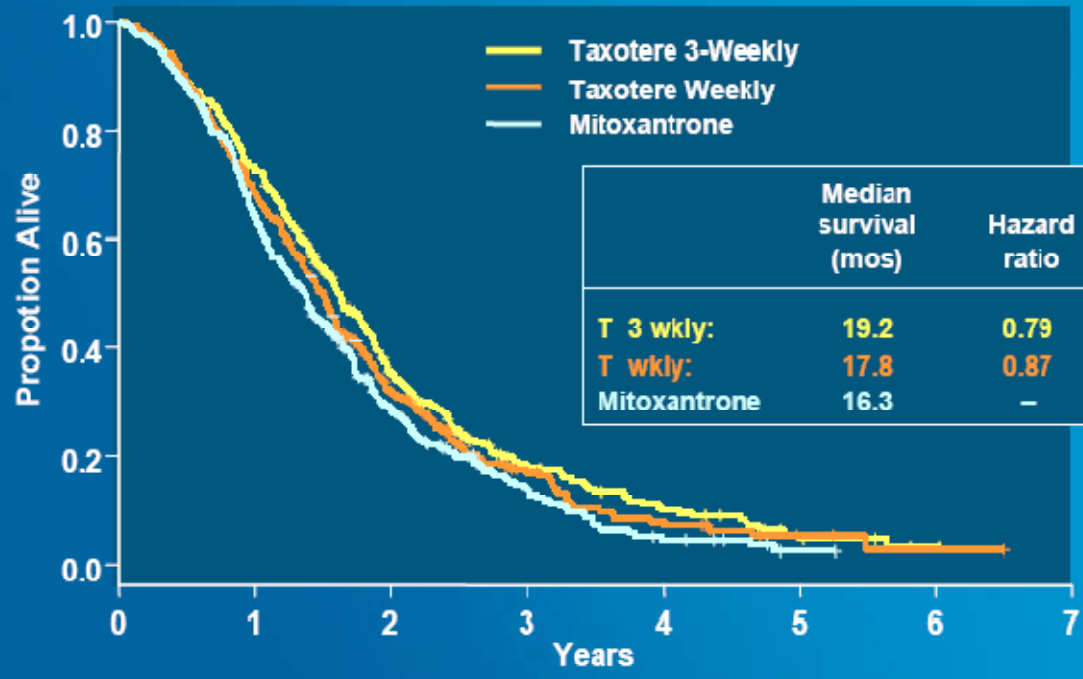
Berthold, DR et al. JCO 2008; 26: 242-245

Tax 327 update

TAX 327 3-yr Updated Survival Analysis

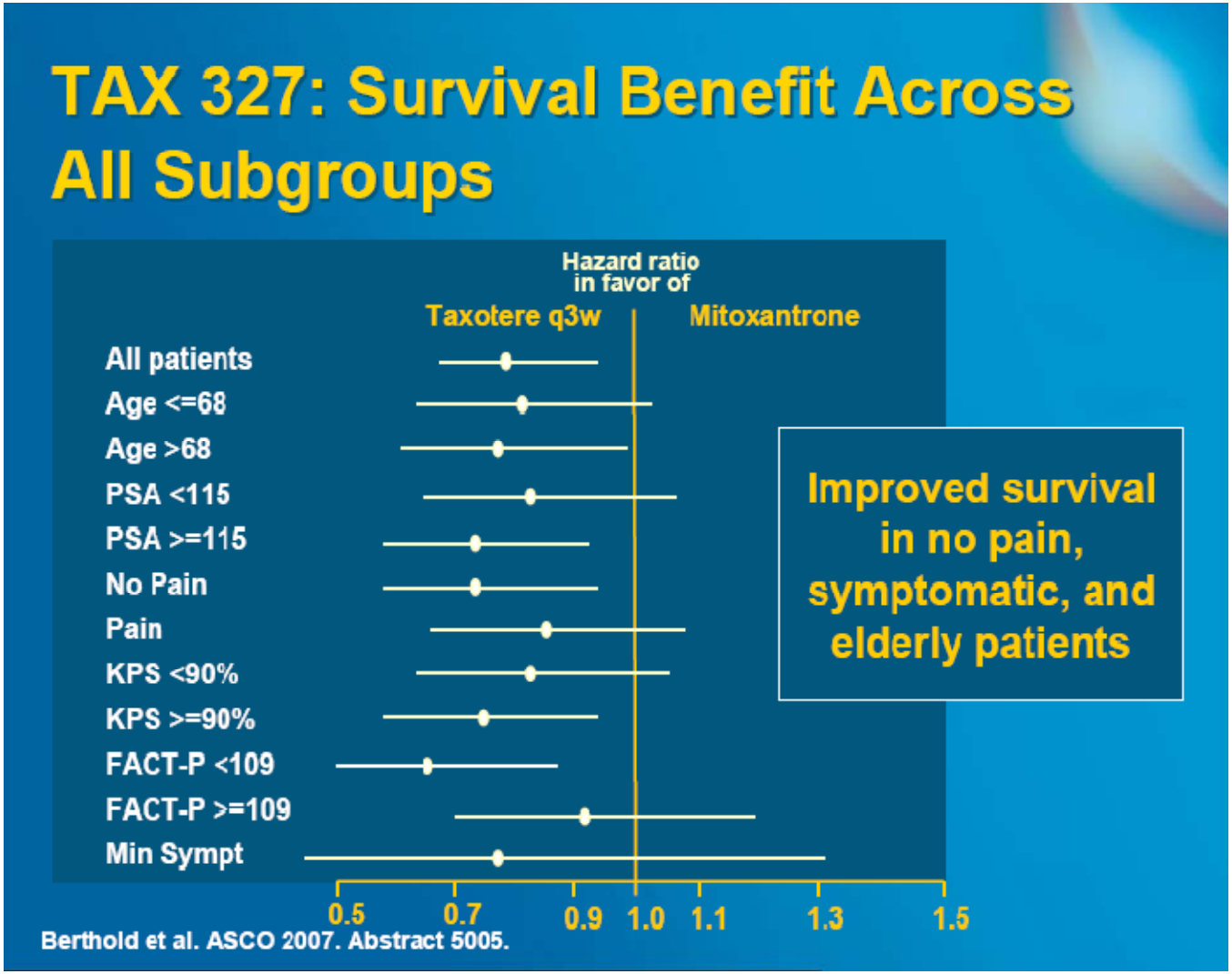


	Median survival (mos)	Hazard ratio	P-value
T 3 wkly:	19.2	0.79	0.004
T wkly:	17.8	0.87	0.09
Mitoxantrone	16.3	–	-

Significantly longer survival with 1st line Taxotere than with mitoxantrone, representing a 21% reduction in risk of mortality (HR=.79)

Berthold et al. ASCO 2007. Abstract 5005.

Tax 327 update



Tax 327 update: Zusammenfassung

- Update bestätigt und erhärtet Primäranalyse
- 19,3 Monate vs. 16,3 Monate mOS für Tax q3w vs. Mitoxantron
- 3 Monate Differenz in allen Subgruppen
- HR für Mortalität 0,79

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Zusatzanalysen aus der Tax 327 Datenbank

PSA als Surrogat

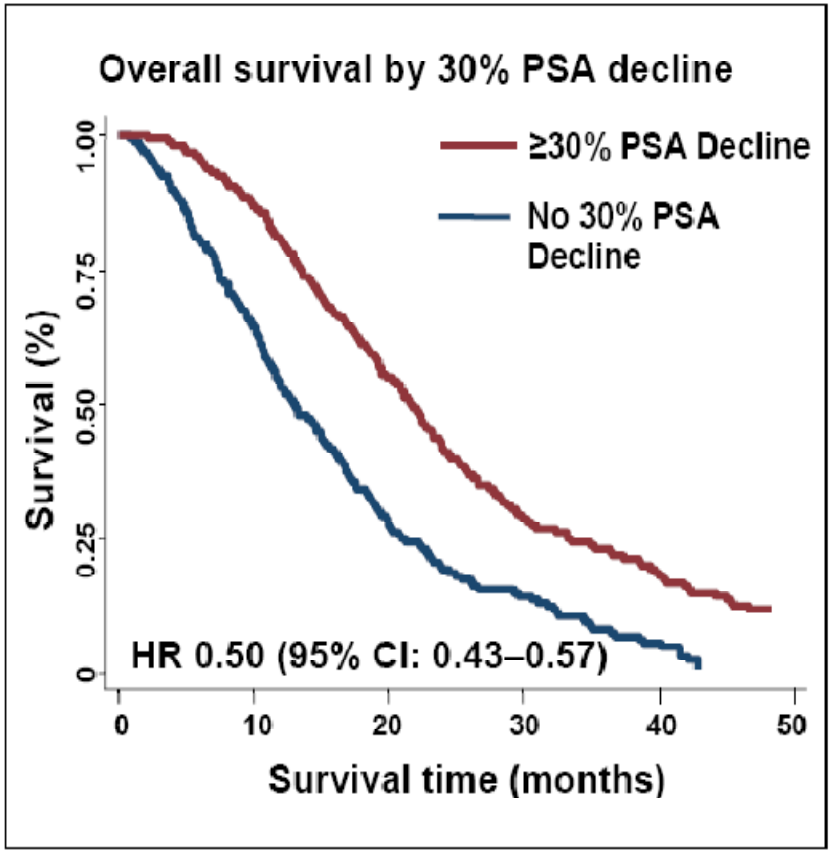

Figure 3. Overall survival in TAX327 according to 30% PSA decline status within the first 3 months of treatment initiation (updated November 2006).

- The adjusted HR for q3w DP lost significance after adjustment for 30% PSA decline.
- Prentice criteria were fulfilled for 3-month PSA declines of ≥10–70%.
- A ≥30% 3-month decline in the serum PSA was prognostic and occurred in 65%, 67%, and 44% of subjects randomized to q3w DP, q1w DP, and q3w MP, respectively.

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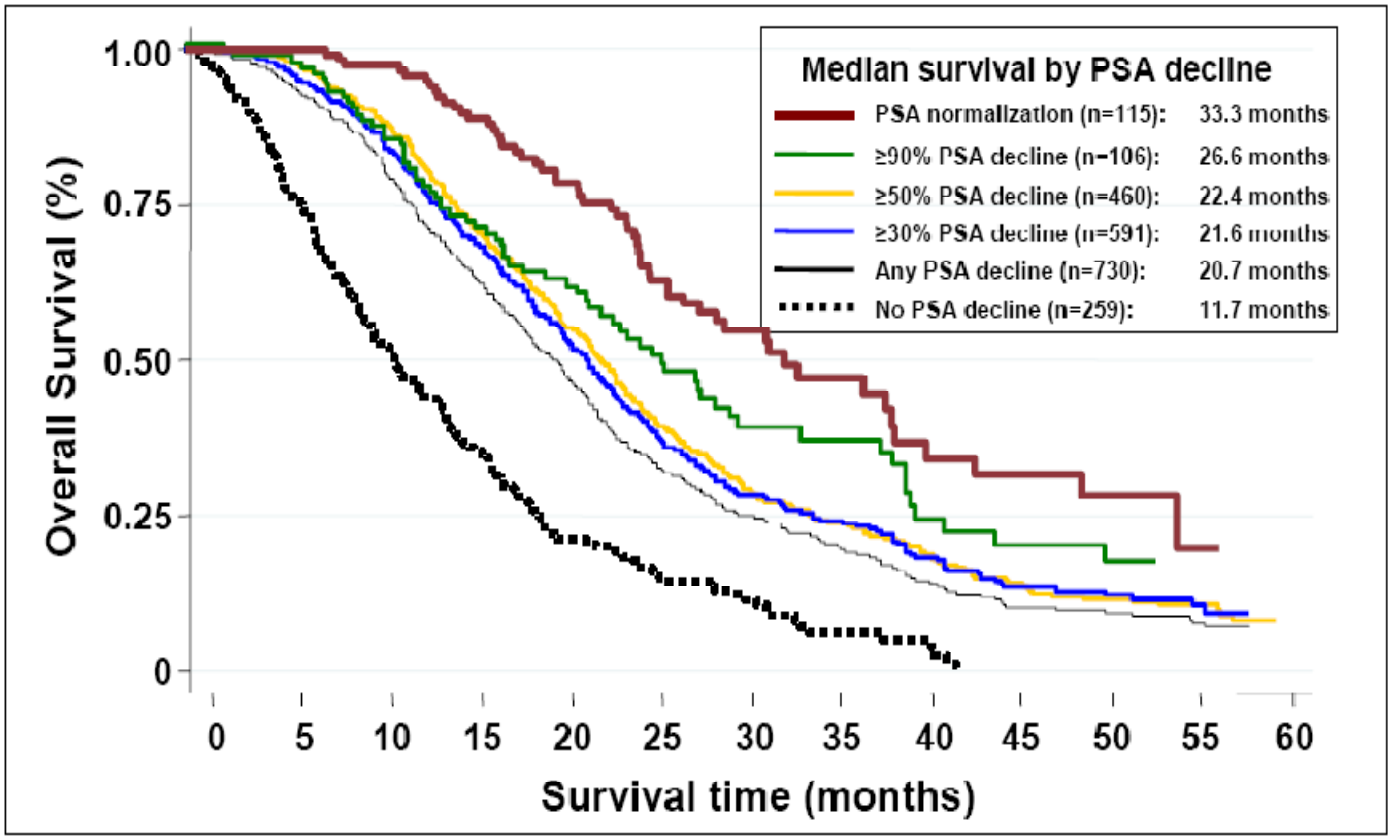
Armstrong, AJ Prostate ASCO 2007 #148

mOS nach PSA Response



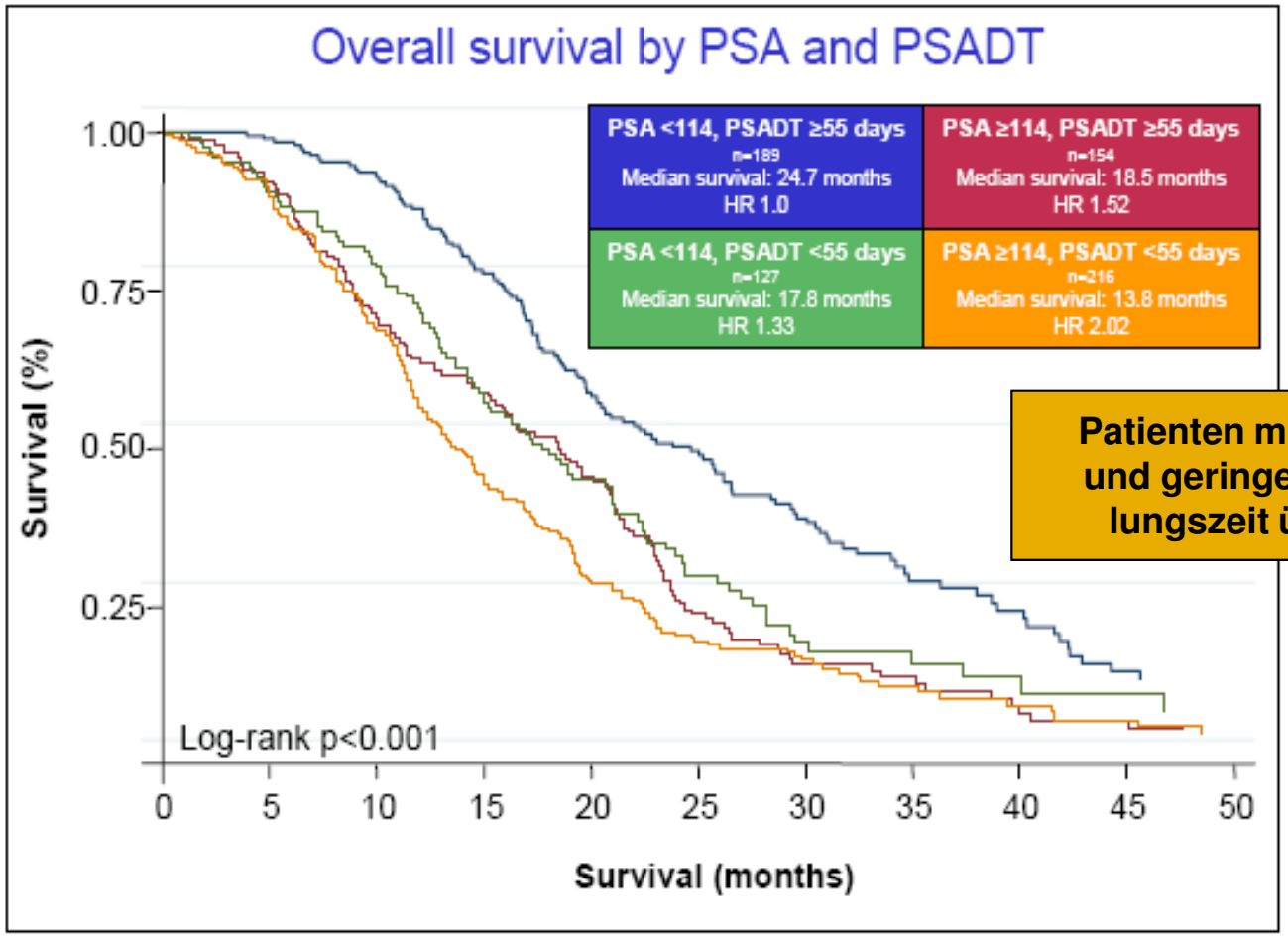
Armstrong, AJ Prostate ASCO 2007 #148

Unabhängige Prognosefaktoren für mOS

Variable	Multivariate HR	95% CI	p-value
Liver metastases	1.64	1.07–2.50	0.023
Number of metastatic sites (>2 vs ≤2)	1.58	1.19–2.09	0.001
Pain at baseline	1.46	1.21–1.76	<0.0001
Karnofsky performance status (≤70 vs ≥80)	1.42	1.08–1.85	0.011
Progression type: Measurable disease Bone scan progression	 1.40 1.28	 1.13–1.76 1.05–1.55	 0.002 0.014
Baseline PSADT (<55 days vs. ≥55 days)	1.20	1.001–1.44	0.048
Baseline log PSA (for every unit rise in log(PSA) in ng/mL)	1.17	1.10–1.24	<0.0001
Tumor grade: (Gleason ≥8 or WHO 3–4 vs Gleason ≤7 or WHO 2–3)	1.18	0.98–1.41	0.076
Alkaline phosphatase (per log unit rise, IU/L)	1.26	1.14–1.38	<0.001
Hemoglobin (per unit rise, g/dL)	0.91	0.85–0.97	0.006

HR = hazard ratio for overall survival; 95% CI = 95% confidence interval;
PSADT = prostate-specific antigen doubling time

Armstrong, AJ Prostate ASCO 2007 #222



Patienten mit geringerem PSA und geringerer PSA-Verdopplungszeit überleben länger

Figure 2. Overall survival according to baseline prostate-specific antigen doubling time (PSADT) (in days) and PSA (in ng/mL) (n=686, 518 events). Reference group is PSA <114 ng/mL, PSADT ≥55 days.

- Test for interaction of PSA and PSADT was nonsignificant (p=0.18).
- The concordance index for this bivariate model was 0.62.

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Unabhängige Prognosefaktoren für mOS

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HR = hazard ratio for overall survival; 95% CI = 95% confidence interval;
PSADT = prostate-specific antigen doubling time

Armstrong, AJ Prostate ASCO 2007 #222

Schmerz als Surrogat

Schmerzresponse korrelliert mit Überleben

	Pain response (n=135)	No pain response (n=331)
Median survival, months (95% CI)	18.6 (16.4–20.3)	12.5 (11.3–14.3)

Table 2. Pain response

- Pain response carried prognostic information among 466 evaluable patients (HR for OS 0.60; 95% CI: 0.48–0.75).
- The PTE associated with pain response was 0.64 (95% C: 0.22–1.0).

Armstrong, AJ Prostate ASCO 2007 #148

Post-Progression Survival

Mitoxantron Weiterbehandlung ohne Effekt

Patienten profitieren von Weiterbehandlung mit Tax trotz Progress

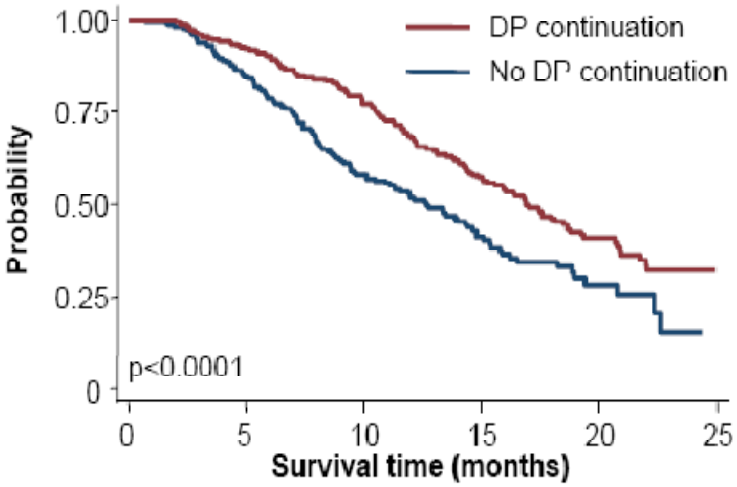


Figure 1. Overall post-progression survival among docetaxel–prednisone (DP)-treated subjects (combined groups) according to continuation of protocol therapy (n=486) (see Table 2).

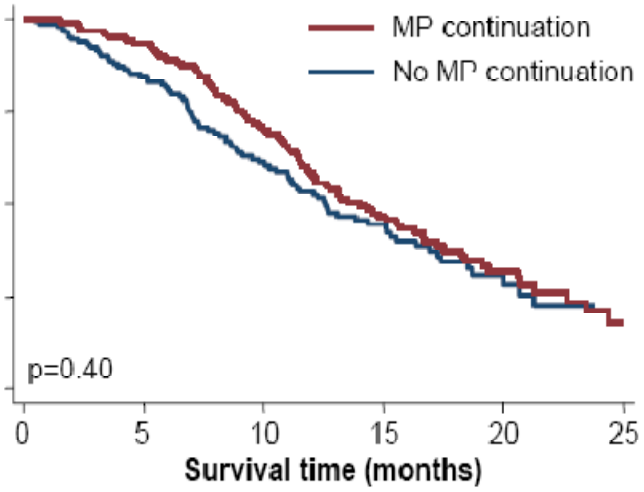
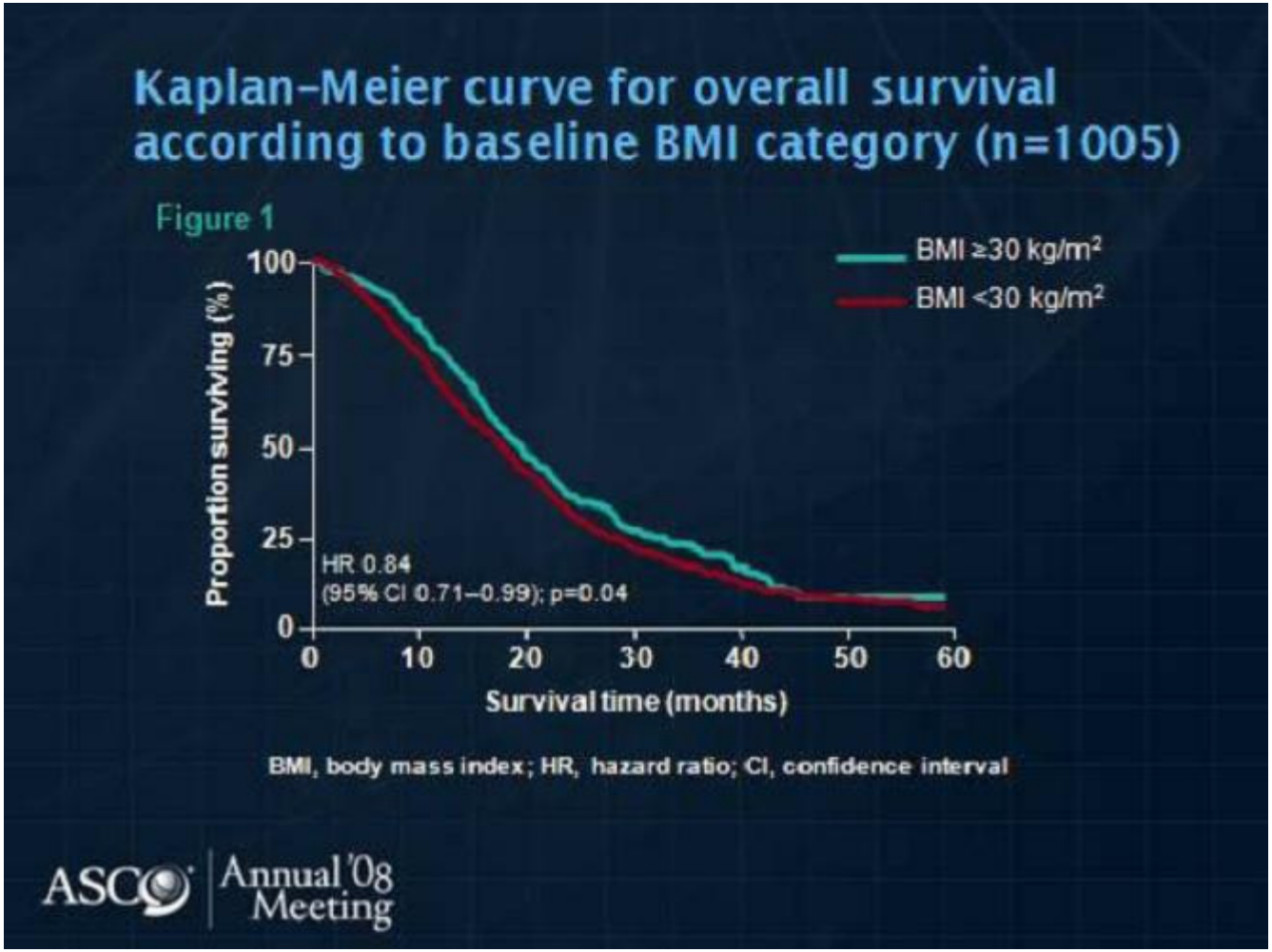


Figure 2. Overall post-progression survival among mitoxantrone–prednisone (MP)-treated subjects according to continuation of protocol therapy (n=265) (see Table 2).

Armstrong, AJ Prostate ASCO 2007 #223

BMI = Risikofaktor?



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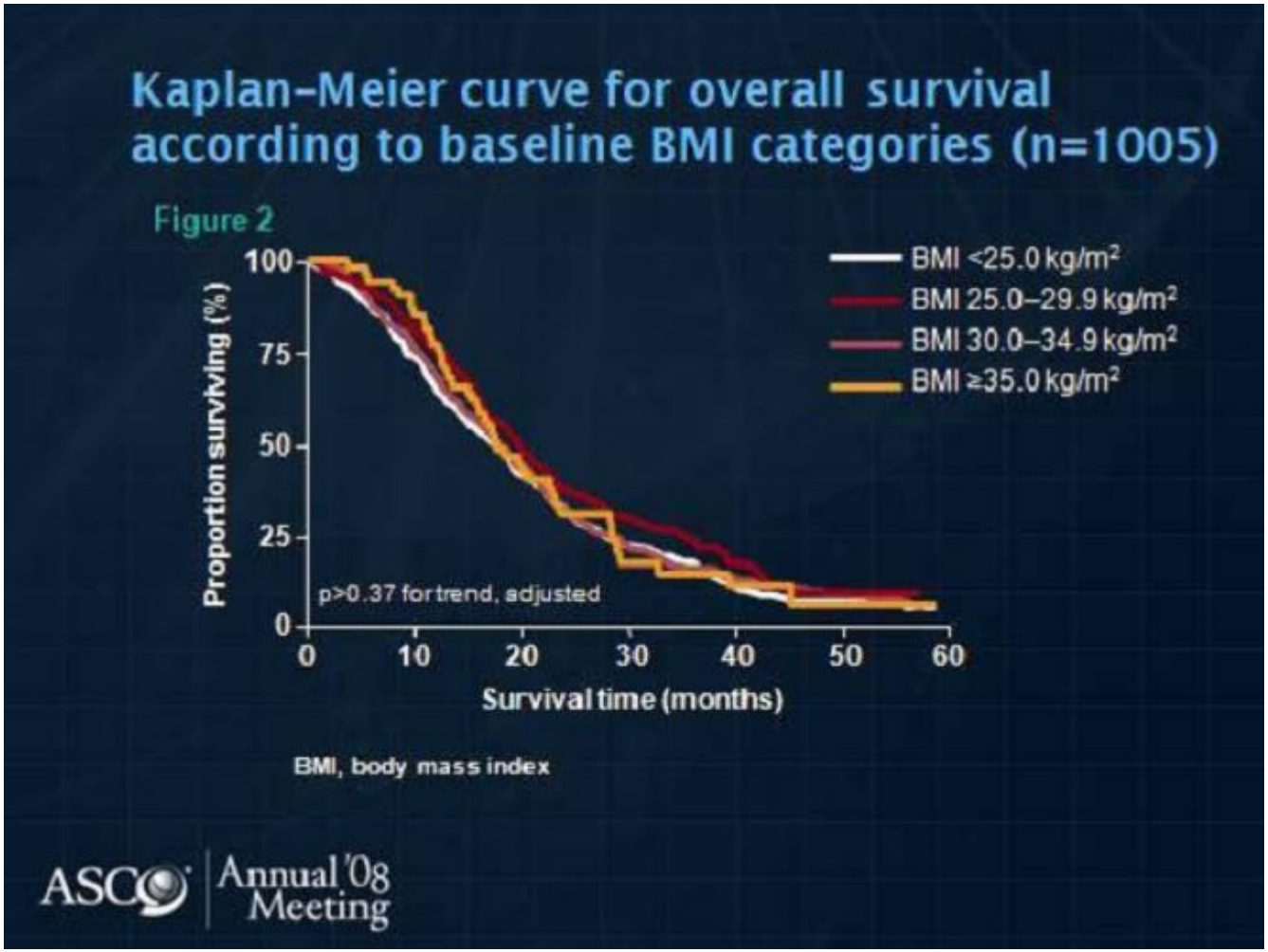
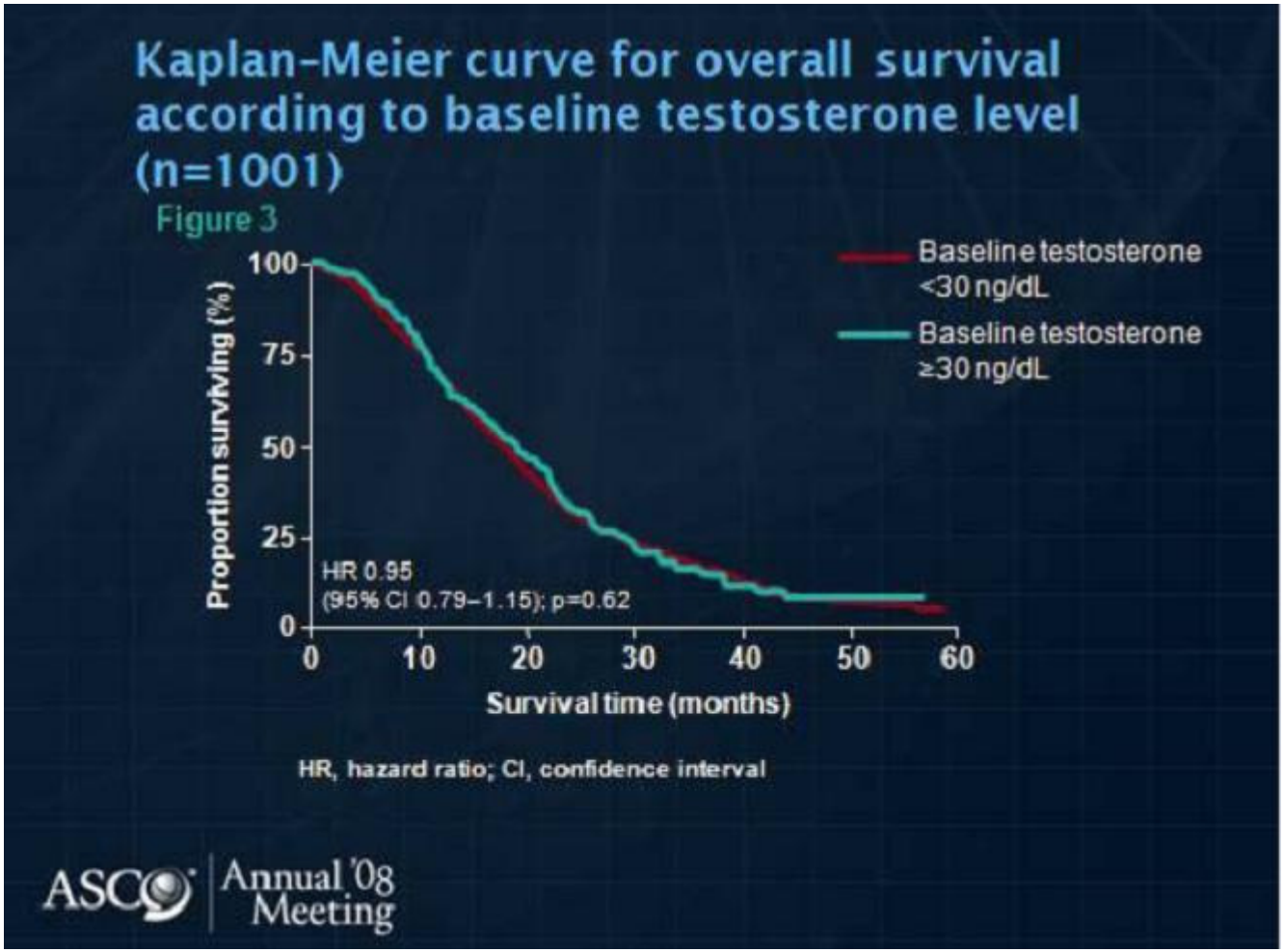
Armstrong, AJ ASCO 2008 #5074

BMI = Risikofaktor?



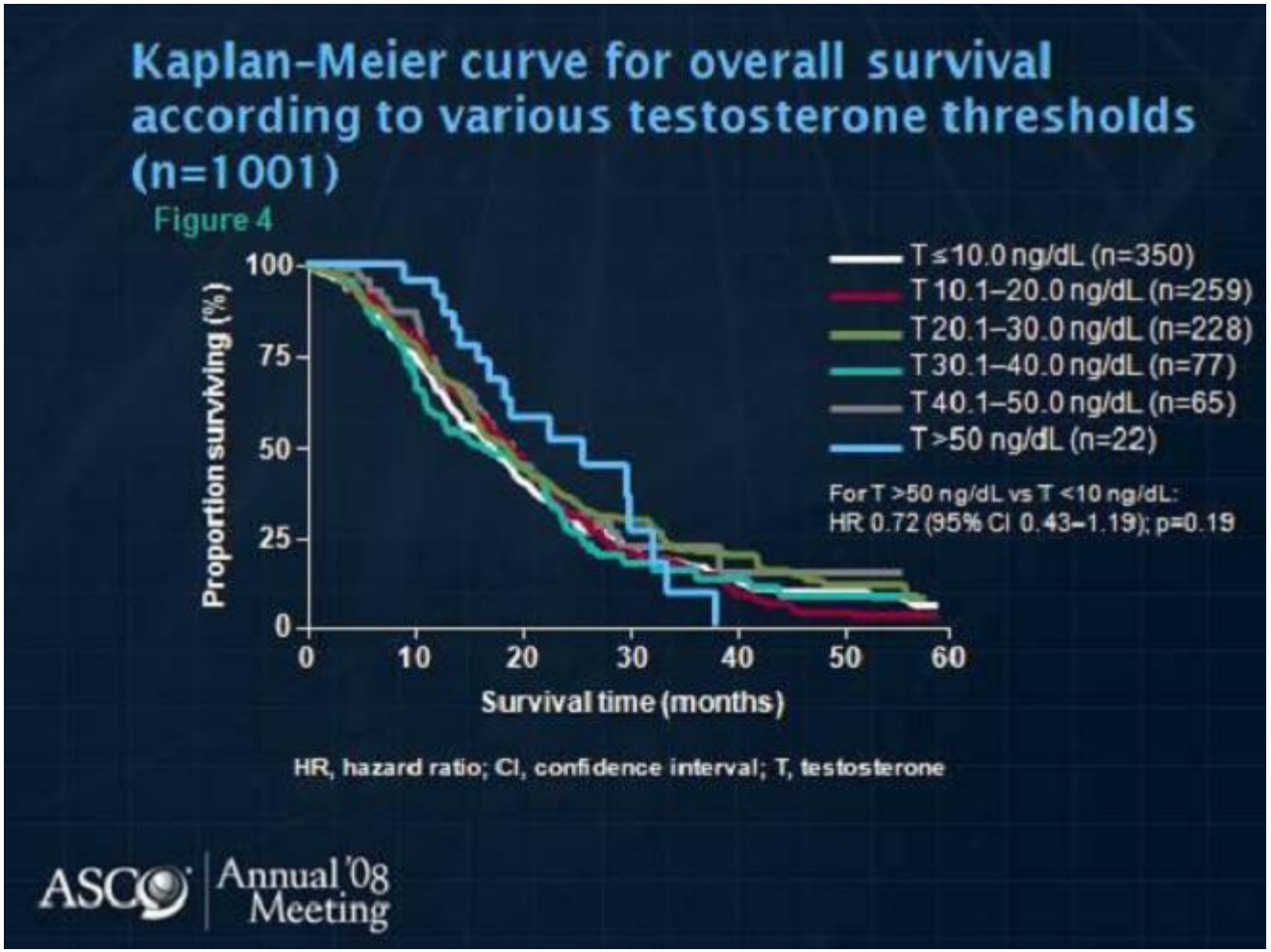
Armstrong, AJ ASCO 2008 #5074

Testosteron = Risikofaktor?



Armstrong, AJ ASCO 2008 #5074

Testosteron = Risikofaktor?



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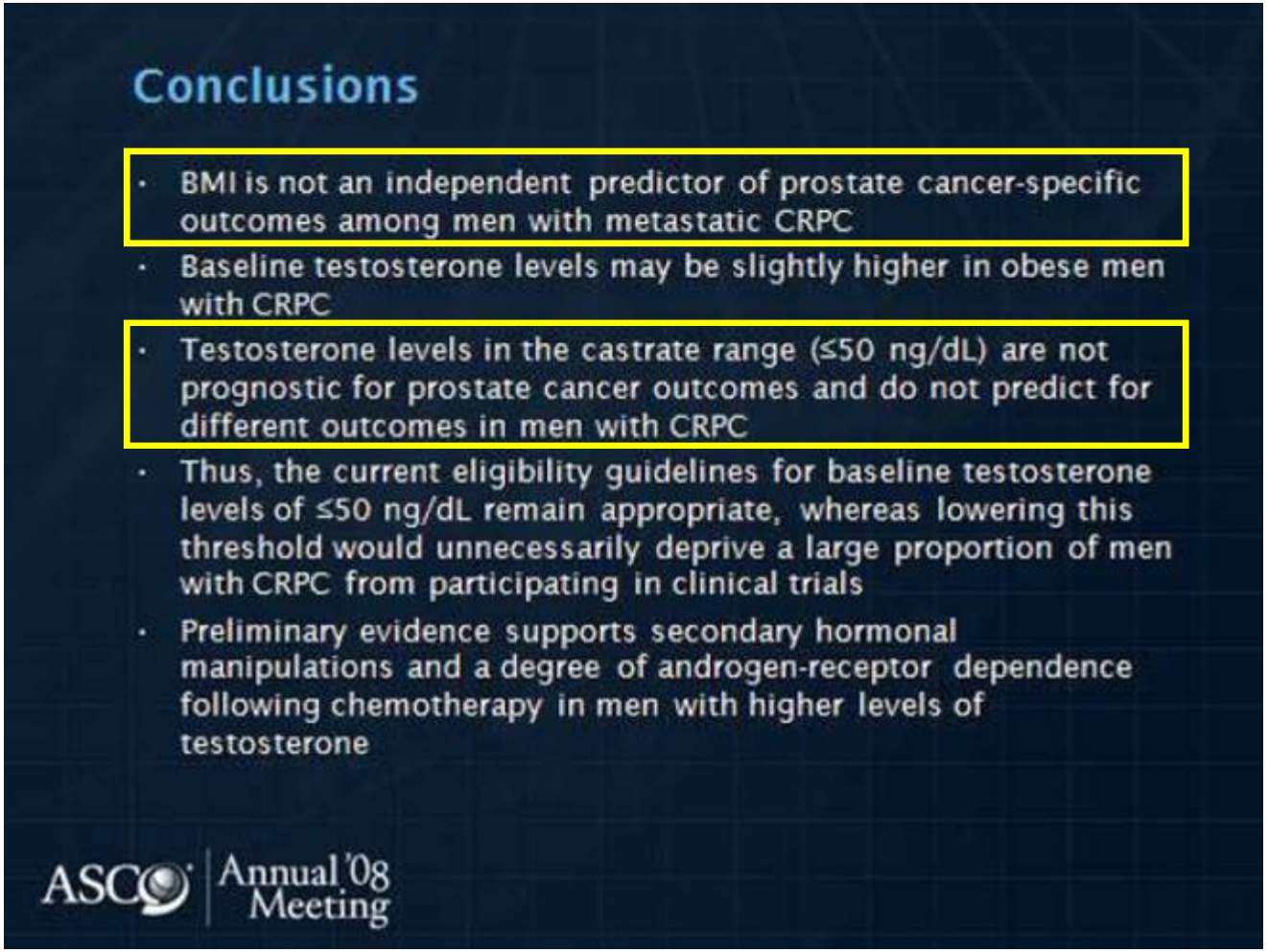
Einfluss BMI / Serum Testosteron auf Outcome



Armstrong, AJ ASCO 2008 #5074

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Besondere Patientengruppen

Der asymptomatische Patient

Der ältere Patient

Der asymptomatische Patient

Es ist derzeit unklar, ob hormonrefraktäre Patienten, die keine Symptome aufweisen und keine erkennbaren Metastasen haben, von einer frühen Chemotherapie profitieren.

Trends in den Subgruppenanalysen der TAX-327-Studie [3] und der SWOG 9916 – [4] Studie legen einen früheren Therapiebeginn aber nahe.

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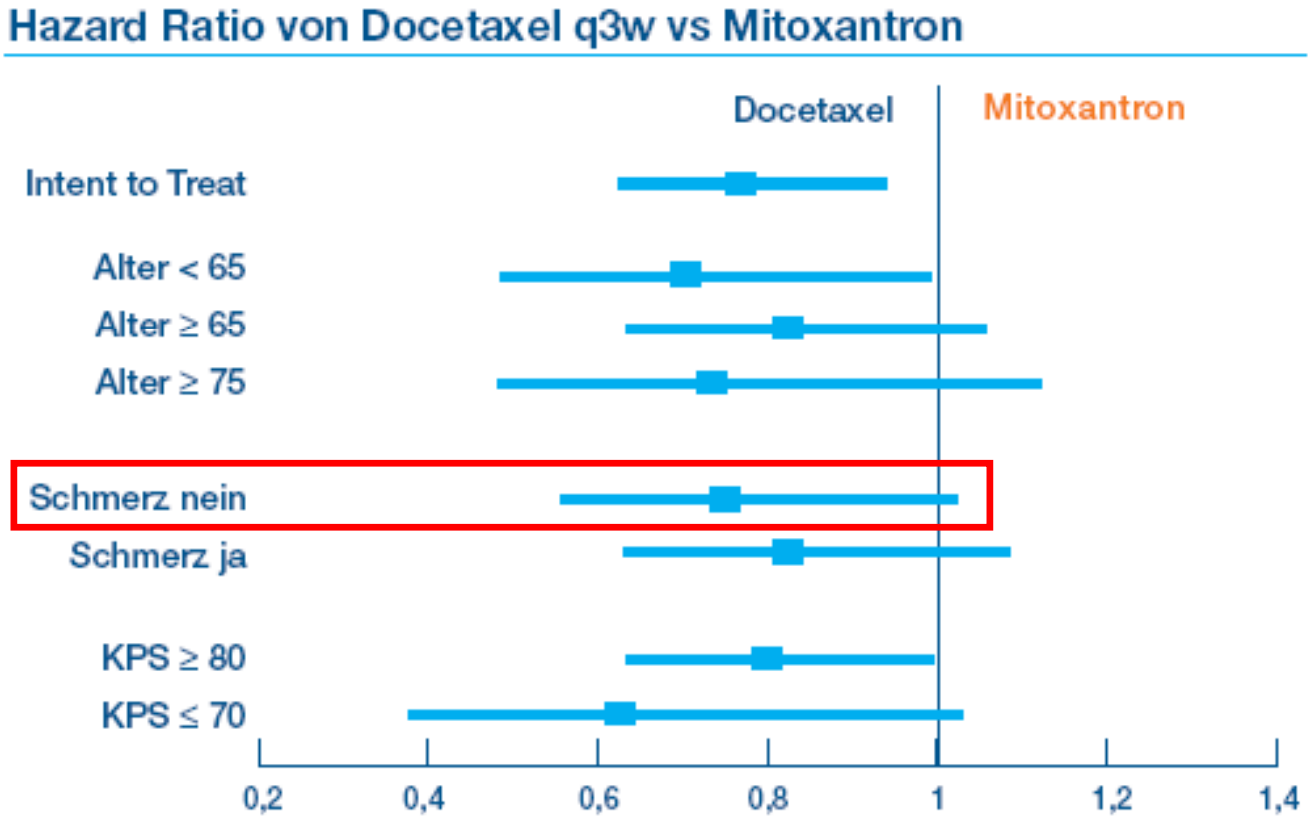
Miller, K. et al. Aktuel. Urol. 2006; 37: 201-204

Der asymptomatische Patient

in TAX 327 Trend für asymptomatische Patienten



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de Wit, R et al. Ann Oncol 2004; 15 (Suppl.3): Abstr.4

Der asymptomatische Patient

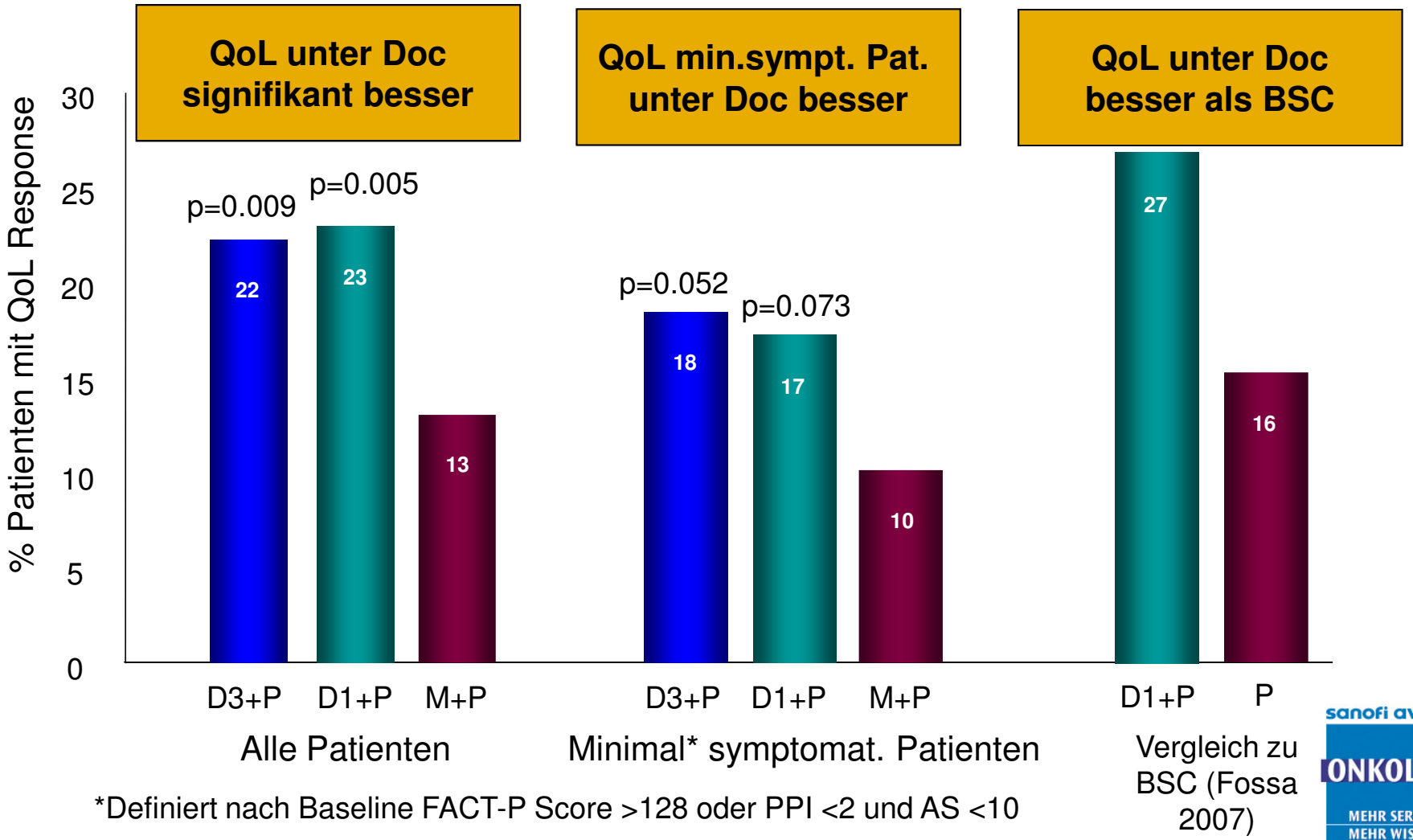
	Docetaxel q3w	Docetaxel q1w	Mitoxantron
Randomisiert	335	334	337
Nicht auswertbar* (%)	12	12	12
Alter, median (Range)	68(42-92)	69(36-92)	68(43-86)
Karnofsky PS ≤ 70 % (%)	13	12	14
Schmerzlevel ≥ PPI 2 oder AS ≥ 10 (%)	45	45	46
Vorbehandlung (%)			
Prostatektomie	19	24	21
Radiotherapie	52	44	51
Estramustin	19	18	20
Hormonelle Manipulationen (%)			
1	9	8	6
2	68	72	69
>2	23	21	25
Medianes PSA (ng/ml)	114	108	123
Gleason Score (%)			
≤7	42	40	42
8-10	31	31	28
nicht bekannt	26	29	30
Metastasen (%)			
Knochen	90	91	92
Viszeral	22	24	22

ca. 50 % asymptomatische Patienten in TAX 327

mindestens 90 % der Tax 327 Patienten metastasiert

Tannock, IF et al. NEJM 2004; 351: 1502-1512

Der asymptomatische Patient



*Definiert nach Baseline FACT-P Score >128 oder PPI <2 und AS <10

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Pond, G.R. et al. ASCO 2006, #4557

PSA, PSA-DT als prognostische Marker

Table 2. Overall survival according to PSA doubling time

Survival parameter	PSA-DT <45 days (n = 125)	PSA-DT ≥45 days (n = 125)
Deaths, n (%)	86 (69)	88 (70)
OS (months)		
Median (95% CI)	16.5 (12.5–20.5)	26.4 (20.3–32.4)
1-year OS, % (95% CI)	62 (53–70)	80 (72–87)
2-year OS, % (95% CI)	32 (23–41)	55 (45–64)
3-year OS, % (95% CI)	22 (14–30)	33 (24–43)

n, number of patients; PSA-DT,prostate-specific antigen doubling time; OS, overall survival; CI, confidence interval.

Oudard, S et al. Ann. Oncol. 2007; 18: 1828-1833

Start Chemotherapy Earlier

Retrospective study: 145 pts treated in 1 single centre in France

	Minim.-No Pain (n:79)	Mild Pain (n:41)	Moderate-Severe Pain (n:25)
Median OS	21.4 mo [16-26.8]	15.0 mo [8.2-21.8]	13.1 mo [9.8-16.5]
PSA DT ≥ 45 d	32.4 mo	18.4 mo	16.1 mo
PSA DT < 45 d	16.5 mo	11.2 mo	8.3 mo
1-yr OS	75%	56%	52%
2-yr OS	43%	20%	20%
3-yr OS	29%	11%	4%

- Results indicate the use of Taxotere before bone pain appears
- OS benefit is higher in minimal- to no-pain patients with longer PSADT
- The author recommends not to delay the interval between the evidence of HRPC and the start of chemotherapy

Oudard et al. ASCO 2007. Abstract 5149.

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Asymptomatisch vs. symptomatisch: UK experience

Real Life konsistent mit Studie bzgl. OS

Comparison with TAX 327 study

	TAX 327	4 centre analysis n = 170
Age (median)	68 (42-92)	71 (48-88)
Gleason score (median)	7	8
PSA (median)	114	115
Evaluable response	12%	51.6%
> 50% PSA response with Docetaxel	45%	45.2%
Overall survival (months)	18.9	18.02

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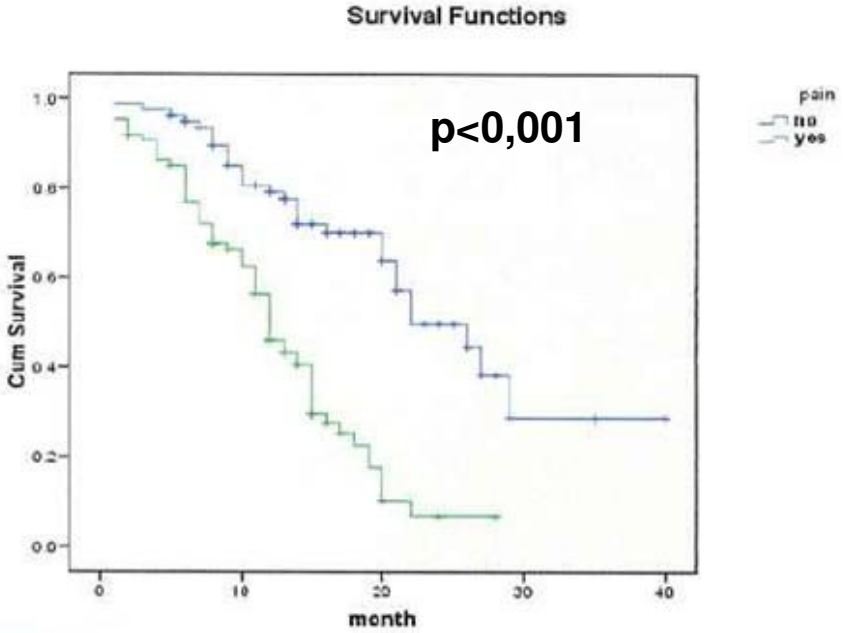
Bahl, A. et al. #224, GUCS Orlando 2009

Asymptomatisch vs. symptomatisch: UK experience

asympt. Patienten leben doppelt so lange verglichen mit sympt. Pat.

Overall survival in groups with or without pain



	n = 90 Pain	n = 80 No Pain
> 50% PSA response	32.9%	66.2%
Median survival (months)	13.75	27.5

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Bahl, A. et al. #224, GUCS Orlando 2009

Der asymptomatische Patient: Optimaler Beginn der Chemotherapie?

EUROPEAN JOURNAL OF CANCER 44 (2008) 1193–1197

available at www.sciencedirect.com

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journal homepage: www.ejconline.com

Current Perspective

When to start cytotoxic therapy in asymptomatic patients with hormone refractory prostate cancer?

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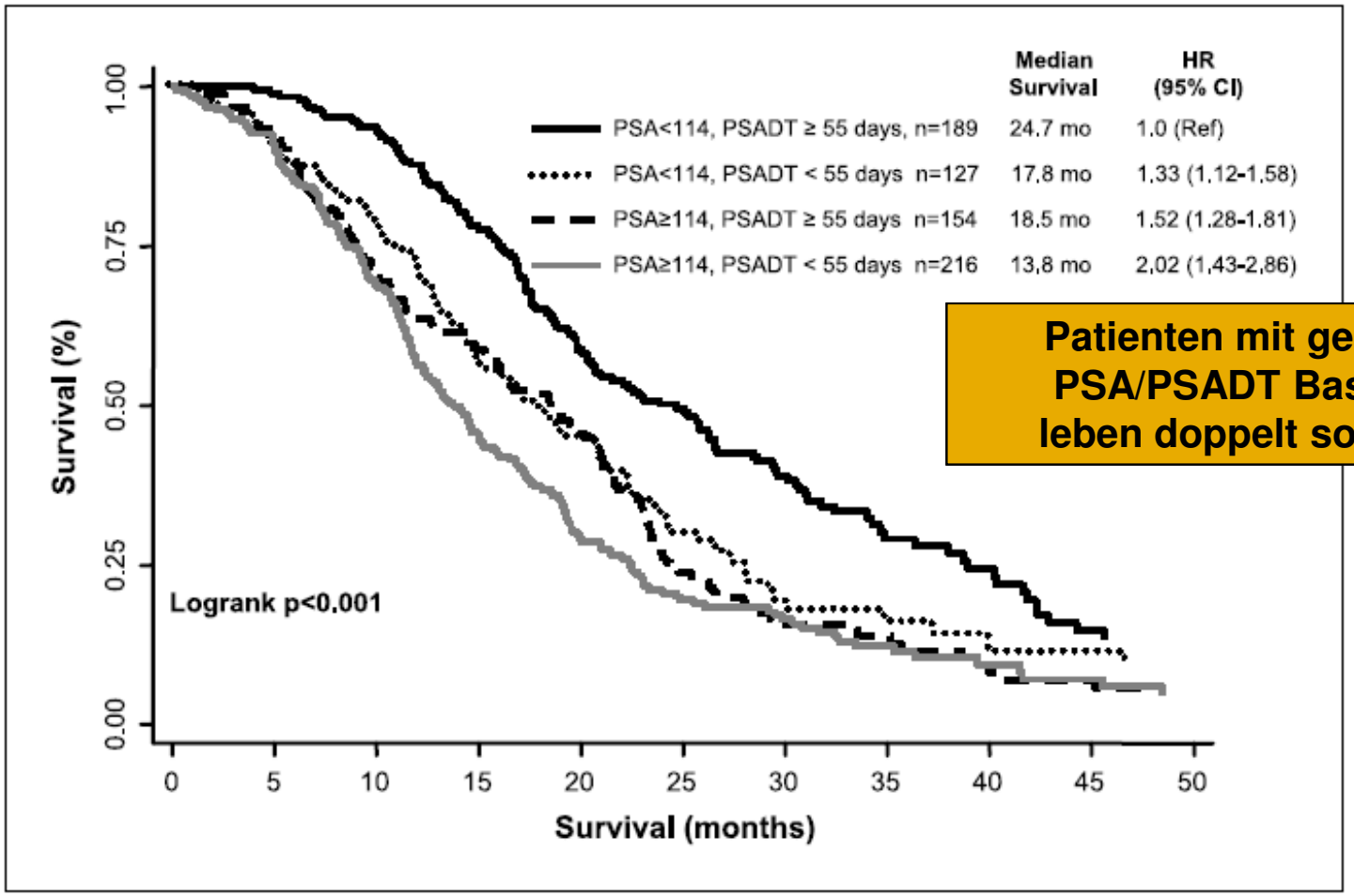
Cytotoxic therapy
Docetaxel
Timing

ABSTRACT

Until the publication of two pivotal trials, there were no treatment options available that did prolong the overall survival in men with hormone refractory prostate cancer (HRPC). Currently, docetaxel-based cytotoxic treatment is considered as a standard of care in all the patients with progressive metastatic HRPC. The use of this treatment regimen renders an equal survival benefit in all the subgroups of patients; however, there is a substantial difference in the overall survival between the subgroups. This review addresses the optimal timing of the cytotoxic treatment in asymptomatic patients with HRPC.

PSA, PSADT als prognostische Marker



Patienten mit geringer PSA/PSADT Baseline leben doppelt so lange

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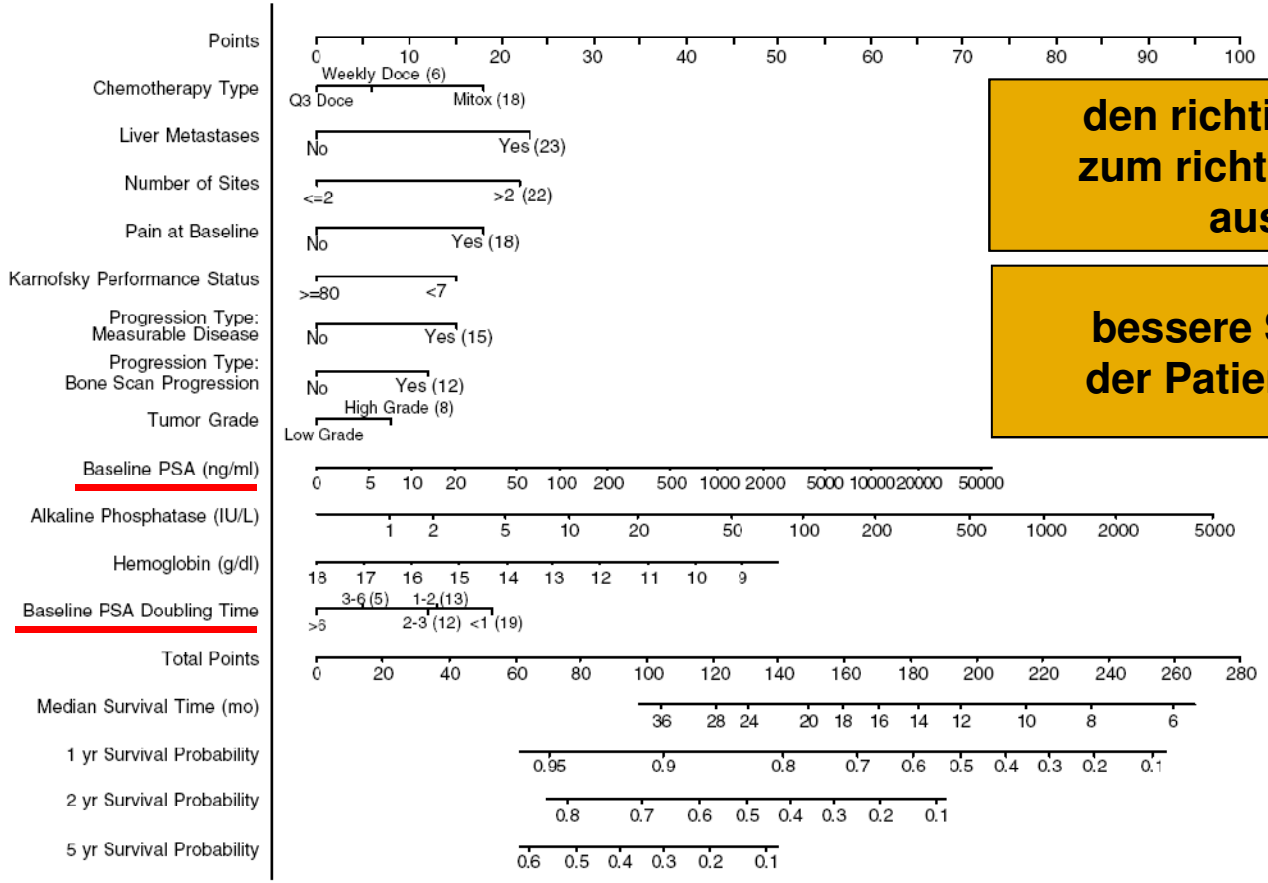
Armstrong, AJ et al. Clin. Cancer Res. 2007; 13: 6396-6403

Helfen Nomogramme?



den richtigen Patienten zum richtigen Zeitpunkt auswählen

bessere Stratifizierung der Patienten möglich?

Fig. 2 – Nomogram for survival of patients with progressive HRPC. Instructions for physician: Locate the liver metastasis axis. Draw a straight line upward to the points axis to determine how many points towards survival the patient receives for the presence or absence of liver metastases. Repeat this process for each predictor variable and sum the points for each predictor. Locate this sum on the total points axis. Draw a straight line downward from the total points axis to identify the predicted median survival and the predicted 1-year, 2-year and 5-year overall survival probabilities. Reprinted from Berthold et al.[4] with permission from the American Society of Clinical Oncology.

Hamberg, P et al. Eur.J.Cancer 2008; 44: 1193-1197

Der asymptomatische Patient

Kardinalfrage nach Metastasierung, nicht nach Symptomatik !

Konsens besteht, dass eine Chemotherapie mit Docetaxel begonnen werden soll bei Patienten

- mit Progression, wenn diese mit einer klinischen Symptomatik (Schmerzen etc.) verbunden ist.
- die asymptomatisch sind, aber
  - einen schnellen PSA-Anstieg haben (PSA-Verdopplungszeit [PSAdt] unter 3 Monaten), auch wenn in bildgebenden Verfahren der Nachweis einer Progression (noch) nicht geführt werden kann.
  - in bildgebenden Untersuchungen eine Progression nachgewiesen wurde.
- für die 1. und 2. nicht zutreffen, die jedoch bei nachgewiesenem PSA-Anstieg den dringenden Wunsch nach einer Therapie äußern.

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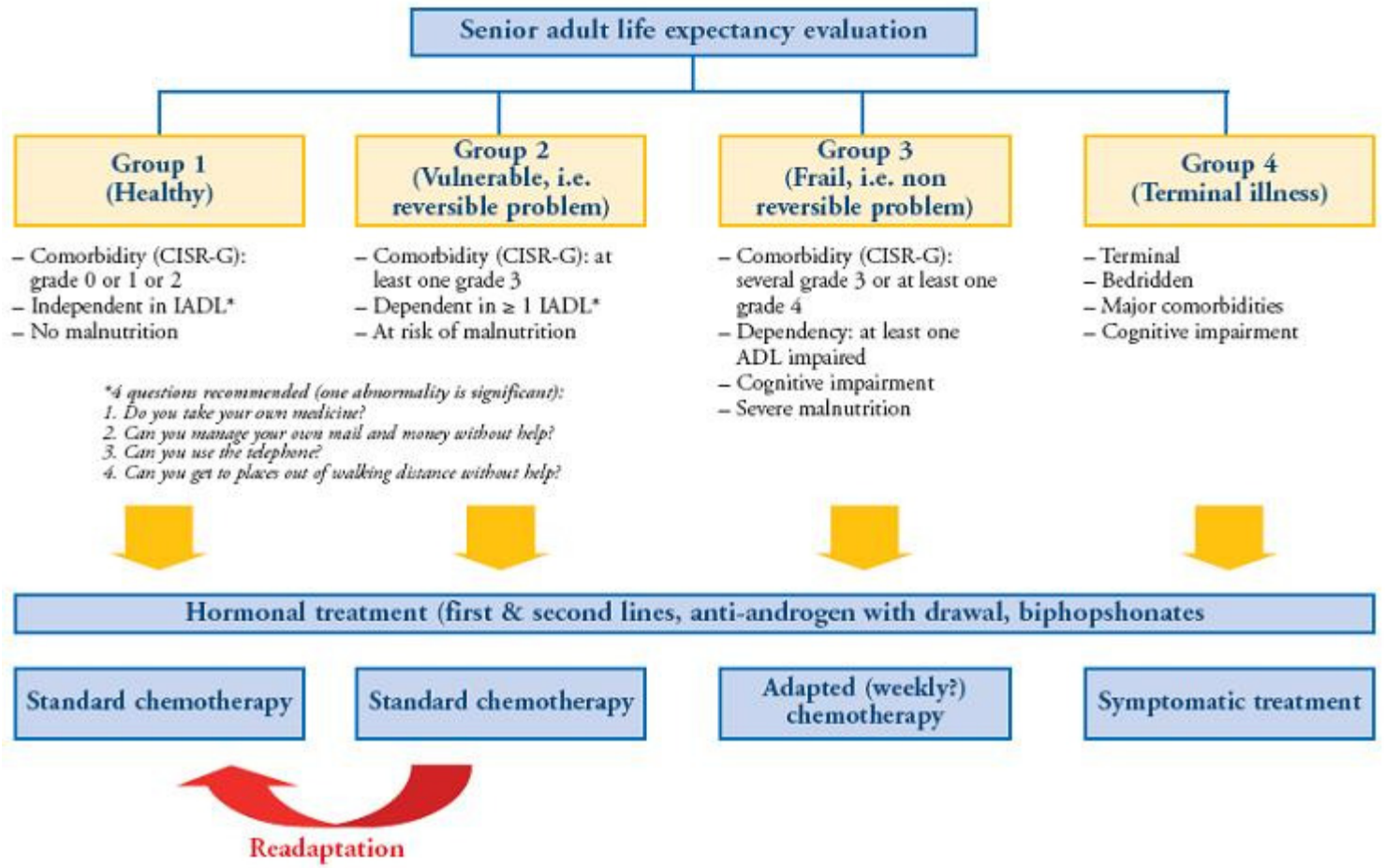
Miller, K. et al. Aktuel. Urol. 2006; 37: 201-204

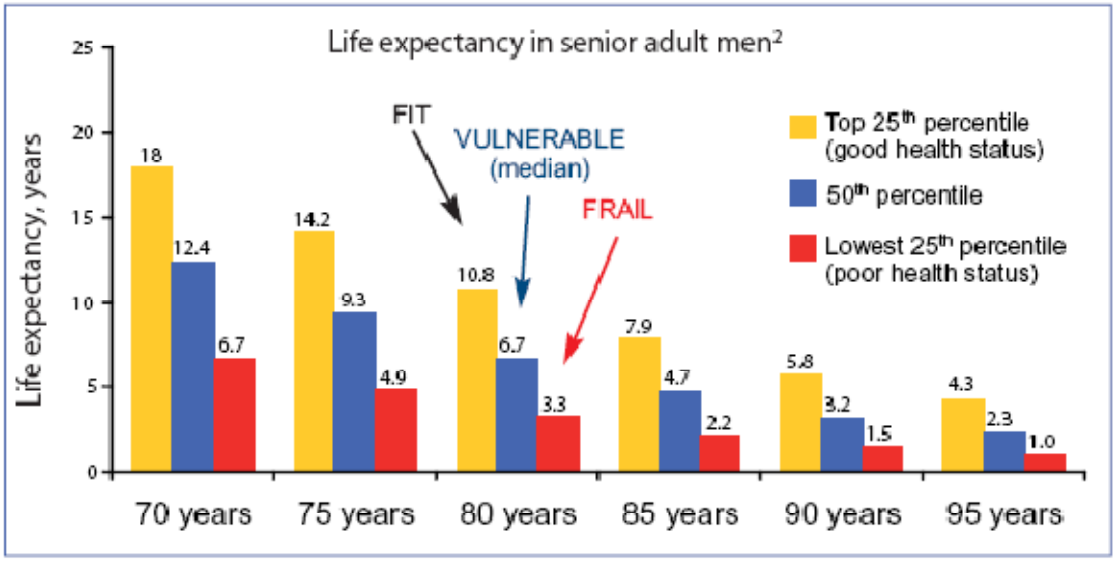
Der ältere Patient: SIOG - Leitlinien



Droz, JP et al. Critical Reviews in Oncology/Haematology 2010;73:68-91

Der ältere Patient: SIOG - Leitlinien

LIFE EXPECTANCY IN SENIOR ADULTS: A LARGE VARIABILITY REFLECTING HEALTH STATUS VARIABILITY



The 50th percentile represents the median life expectancy for each age class.

For a given age, a proportion of men in the top 25th percentile have a good health status (FIT patients) and may have a longer life expectancy than men who are 5, 10 or even 15 years younger but are in the lowest 25th percentile (FRAILpatients)[2].

Droz, JP et al. Critical Reviews in Oncology/Haematology 2010;73:68-91

Der ältere Patient: SIOG - Leitlinien

COMORBIDITY: A KEY PREDICTOR OF LIFE EXPECTANCY

Charlson comorbidity index[3]

COMORBIDITY	PRESENT	POINTS
Myocardial infarct		1
Congestive heart failure		1
Peripheral vascular disease		1
Cerebrovascular disease (except hemiplegia)		1
Dementia		1
Chronic pulmonary disease		1
Connective tissue disease		1
Ulcer disease		1
Mild liver disease		1
Diabetes (without complications)		1
Diabetes with end organ damage		2
Hemiplegia		2
Moderate or severe renal disease		2
2nd solid tumor (non metastatic)		2
Leukemia		2
Lymphoma, multiple myeloma…		2
Moderate or severe liver disease		3
2nd metastatic solid tumor		6
AIDS		6
TOTAL POINTS		

CISR-G[7]

	Score
HEART	
VASCULAR	
HAEMATOPOIETIC	
RESPIRATORY	
EYES, EARS, NOSE, THROAT & LARYNX	
UPPER GI	
LOWER GI	
LIVER	
RENAL	
GENITOURINARY	
MUSCULOSKELETAL/INTEGUMENT	
NEUROLOGICAL	
ENDOCRINE/METABOLIC & BREAST	
PSYCHIATRIC ILLNESS	
TOTAL NUMBER OF CATEGORIES ENDORSED	
TOTAL SCORE	
Severity index (total score / total number of categories endorsed)	
Number of categories at level 3 severity	
Number of categories at level 4 severity	

RATING STRATEGY: 0= no problem; 1= Current mild problem or past significant problem; 2= Moderate disability or morbidity/ requires "first line" therapy; 3= Severe/constant significant disability/ uncontrollable chronic problems; 4= Extremely severe/immediate treatment required/end organ failure/severe impairment in function

Droz, JP et al. Critical Reviews in Oncology/Haematology 2010;73:68-91

Der ältere Patient: SIOG - Leitlinien

EVALUATION OF DEPENDENCE STATUS IN SENIOR ADULTS

IADL[9]

One abnormality is significant:

1. Can you use the telephone? [3] without help; [2] with some help; [1] completely unable to use the telephone
2. Can you get to places out of walking distances? [3] without help; [2] with some help; [1] completely unable to travel unless special arrangements are made
3. Can you go shopping for groceries or food without help? [3] without help; [2] with some help; [1] completely unable to do any shopping
4. Can you prepare your own meals or use a microwave? [3] without help; [2] with some help; [1] completely unable to prepare any meals
5. Can you do your own housework (vacuum, dust, do dishes) or any handwork (use hammer, screwdriver, lawnmower) [3] without help; [2] with some help; [1] completely unable to do any housework or handyman work
6. Can you do your own laundry or take it to cleaners? [3] without help; [2] with some help; [1] completely unable to do any laundry/go to cleaners
7. Do you take your own medicine (or could you take it)? [3] without help (in the right doses at the right time); [2] with some help (take medicine if someone prepares it for you or reminds you to take it); [1] completely unable to take your own medicine
8. Can you manage your own money and mail? [3] without help; [2] with some help; [1] completely unable to handle your money and mail

ADL[8]

One abnormality is significant:

1. Bathing: Independent (assistance only in bathing a single part (as back or disabled extremity) or bathes self completely) Dependent (assistance in bathing more than one part of body; assistance in getting in or out of tub or does not bathe self)
2. Dressing: Independent (gets clothes from closets and drawers; puts on clothes, outer garments, braces; manages fasteners; act on tying shoes is excluded) Dependent (does not dress self or remains partly undressed)
3. Going to toilet Independent (gets to toilet; gets on and off toilet; arranges clothes; cleans organs of excretion) Dependent (uses bedpan or commode or receives assistance in getting to and using toilet)
4. Transfer Independent (moves in and out of bed independently and moves in and out of chair independently) Dependent (assistance in moving in or out of bed and/or chair; does not perform one or more transfers)
5. Continence Independent (urination and defecation entirely self-controlled) Dependent (partial or total incontinence in urination or defecation; partial or total control by enemas, catheters, or regulated use of urinals and/or pedpans)
6. Feeding Independent (gets food from plate or its equivalent into mouth) Dependent (assitance in act of feeding; does not eat at all or parenteral feeding)

Droz, JP et al. Critical Reviews in Oncology/Haematology 2010;73:68-91

Der ältere Patient: SIOG - Leitlinien

SPECIAL CONSIDERATIONS FOR SENIOR ADULTS

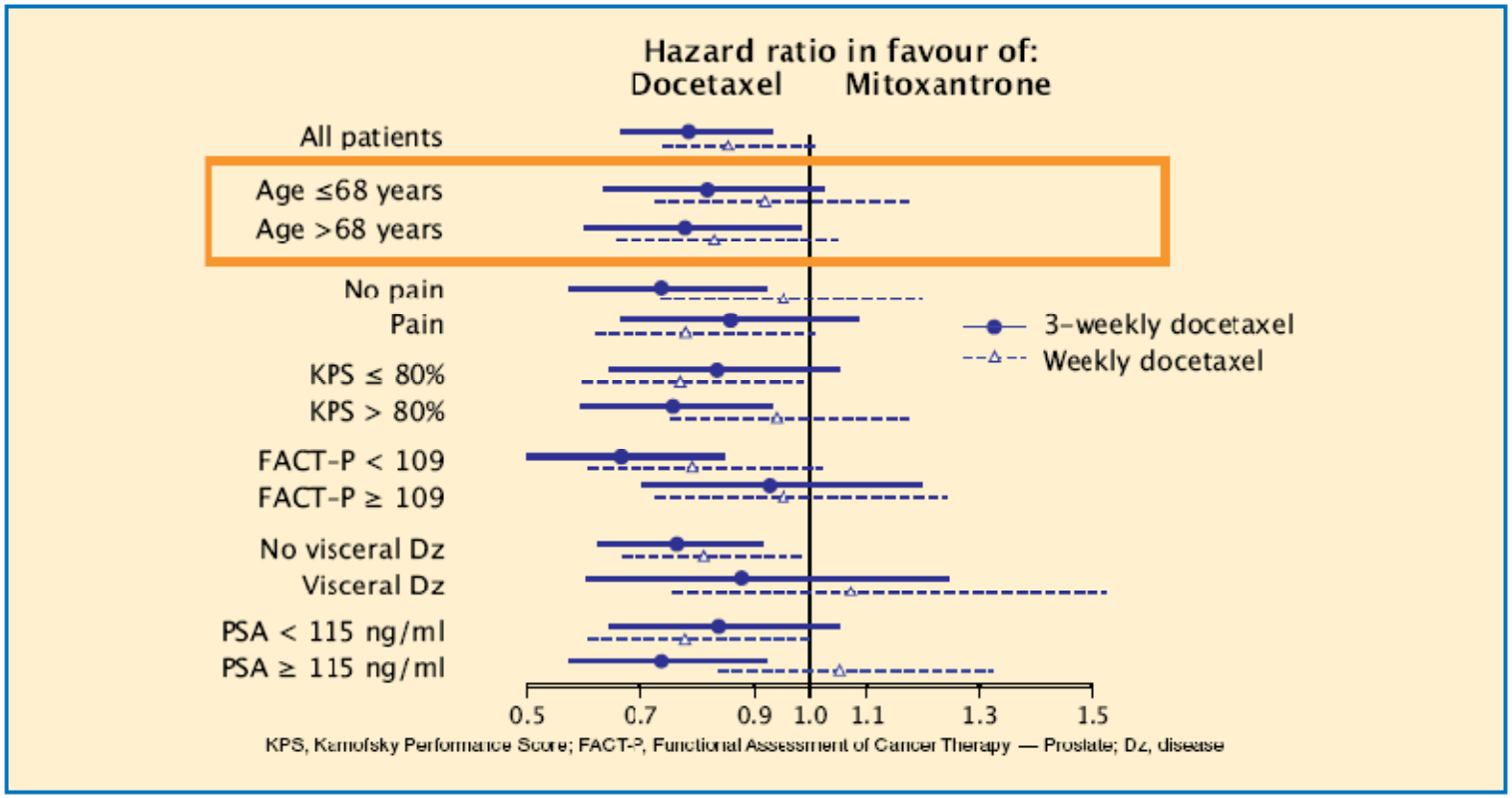
Chemotherapy in senior adults

- In metastatic HRPC, chemotherapy with docetaxel (75 mg/m2 q3w) is the standard[10]. It shows the same efficacy and an acceptable tolerability in healthy senior adults as in younger patients (Figure)[17-18].
- The tolerability of docetaxel q3w has not been specifically studied in vulnerable and frail senior adults. Several clinical trials suggest that weekly docetaxel shows a low incidence of myelosuppression (table)[19-21]. The place of weekly docetaxel in vulnerable and frail patients should be further evaluated.
- Palliative treatments include palliative surgery, radiopharmaceutics, radiotherapy, medical treatments for pain and symptoms.

Droz, JP et al. Critical Reviews in Oncology/Haematology 2010;73:68-91

Der ältere Patient: SIOG - Leitlinien

TAX 327 forest plot: docetaxel shows the same efficacy in healthy senior adults as in younger patients[18]



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Droz, JP et al. Critical Reviews in Oncology/Haematology 2010;73:68-91

Der ältere Patient

HR für cut-off 75 Jahre 0,80

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Docetaxel Every 3 Wk	Weekly Docetaxel	Mitoxantrone Every 3 Wk
No. randomized	335	334	337
Ineligible (%)	12	12	12
Age			
Median (yr)	68	69	68
Range (yr)	42–92	36–92	43–86
≥75 Yr (%)	20	21	20

Tannock, IF et al. NEJM 2004; 351: 1502-1512

Der ältere Patient: SIOG - Leitlinien

Weekly docetaxel shows the same efficacy and acceptable tolerability in senior adults as in younger patients[21]

		< 70 years (n=34)	≥70 years (n=52)
ECOG performance :	– 0	17.6%	23.1%
	– 1	55.9%	50%
	– 2	23.5%	26.9%
	– 3	2.9%	0%
Overall survival, median [95% CI], weeks		45 [36-54]	33 [13-54]
Grade 3-4 adverse events :	– Anemia	8.8%	5.8%
	– Neutropenia	2.9%	3.8%
	– Thrombocytopenia	2.9%	1.9%

No significant difference for all parameters

Droz, JP et al. Critical Reviews in Oncology/Haematology 2010;73:68-91

Gepoolte Daten zweier Phase II Studien

Patient Characteristics	All Patients (N = 86)	Patients < 70 Years of Age (n = 34)	Patients ≥ 70 Years of Age (n = 52)	P Value*
Median PSA, ng/mL (Range)	129.5 (0-2737)	82.9 (0.6-1502)	159.0 (0-2737)	0.04
Median Alkaline Phosphatase, U/L (Range)	168 (20-2573)	145 (20-859)	181 (23-2574)	0.27
Median Hemoglobin, g/dL (Range)	12.2 (6.8-19.5)	12.4 (6.8-19.5)	11.6 (8.3-14.8)	0.05
ECOG Performance Status				
0	20.9%	17.6%	23.1%	
1	52.3%	55.9%	50.0%	0.56
2	25.6%	23.5%	26.9%	
3	1.2%	2.9%	0	

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Beer, TM et al. Clin Prostate Cancer 2003; 2: 167-172

Gepoolte Daten zweier Phase II Studien

Response unabhängig vom Alter!

Table 2 | Univariate Analysis of Principal Efficacy Measures by Age

Outcome Variable	All Patients (N = 86)	Patients < 70 Years of Age (n = 34)	Patients ≥ 70 Years of Age (n = 52)	P Value*
PSA Response Rate (95% CI)	44% (33%-55%)	40% (23%-57%)	47% (33%-61%)	0.54
Measurable Disease Response Rate (n = 16; 95% CI)	31% (7%-55%)	33% (0-66%)	29% (0-65%)	0.84
Median Time to Progression (95% CI)	21 Weeks (19-23)	19 Weeks (16-22)	23 Weeks (20-26)	0.30
Median Overall Survival (95% CI)	42 Weeks (29-54)	45 Weeks (36-54)	33 Weeks (13-54)	0.98

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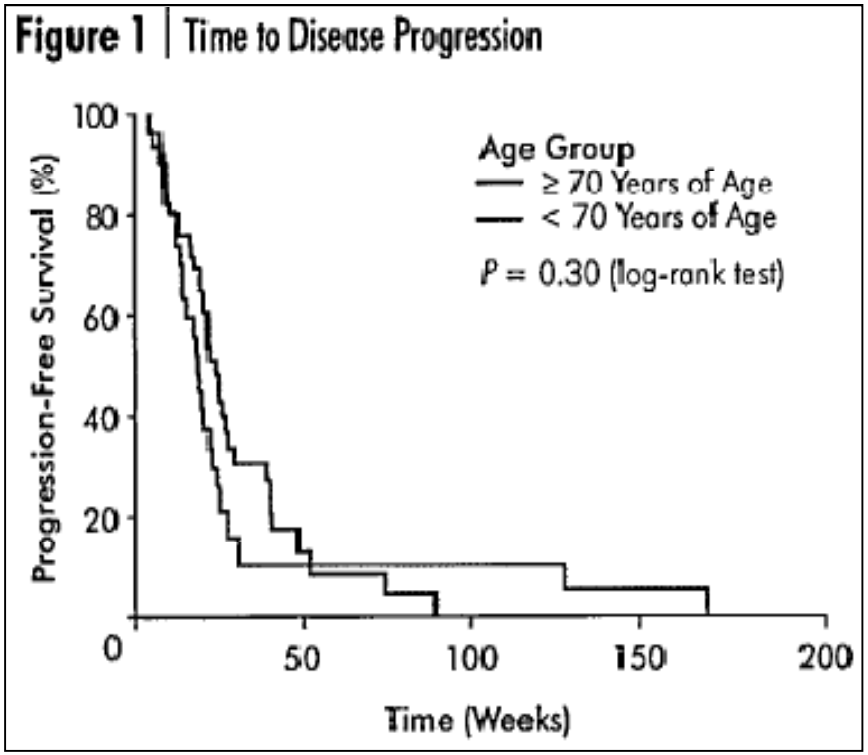
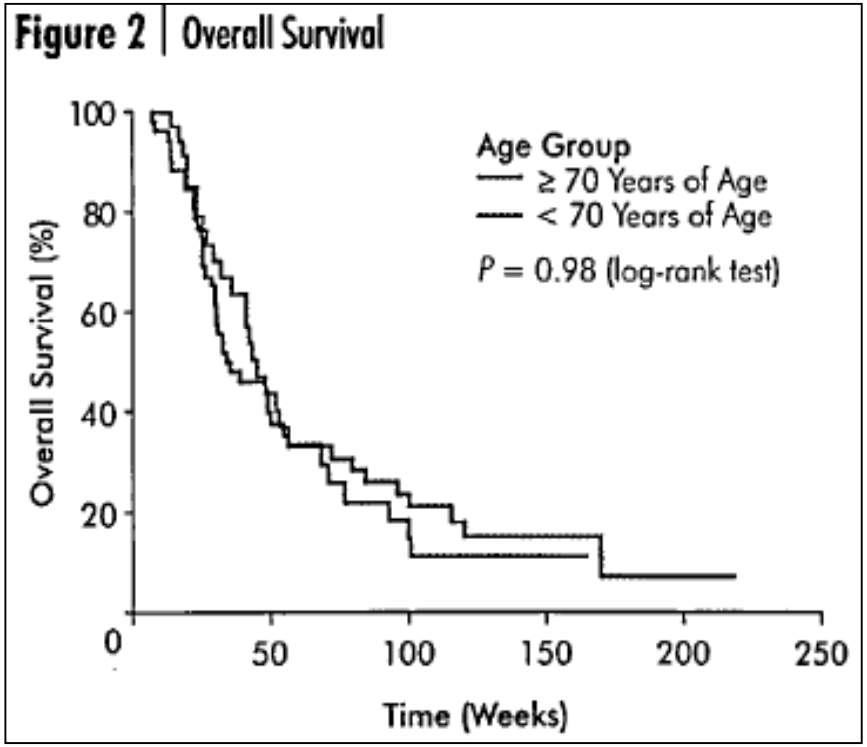
Gepoolte Daten zweier Phase II Studien

Response unabhängig vom Alter!





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Beer, TM et al. Clin Prostate Cancer 2003; 2: 167-172

Gepoolte Daten zweier Phase II Studien

keine erhöhte Tox bei älteren Patienten

Table 3 | Toxicity Summary

Outcome Variable	All Patients (N = 86)	Patients < 70 Years of Age (n = 34)	Patients ≥ 70 Years of Age (n = 52)	*P* Value*
Incidence of Grade ≥ 3 Hematologic Toxicity (95% CI)	14 (7-21)	12 (5-19)	15 (7-23)	0.64
Incidence of Grade ≥ 3 Nonhematologic Toxicity (95% CI)	41 (31-51)	32 (22-52)	46 (35-57)	0.20
Toxicity Events per Patient (95% CI)				
Grade 2 hematologic toxicity	0.16 (0.06-0.26)	0.24 (0.07-0.41)	0.12 (0-0.25)	0.26
Grade ≥ 3 hematologic toxicity	0.17 (0.07-0.27)	0.18 (0-0.36)	0.17 (0.05-0.29)	0.97
Grade 2 nonhematologic toxicity	1.17 (0.84-1.50)	0.88 (0.44-1.32)	1.37 (0.92-1.82)	0.16
Grade ≥ 3 nonhematologic toxicity	0.83 (0.55-1.11)	0.59 (0.26-0.92)	0.98 (0.58-1.38)	0.18

Beer, TM et al. Clin Prostate Cancer 2003; 2: 167-172

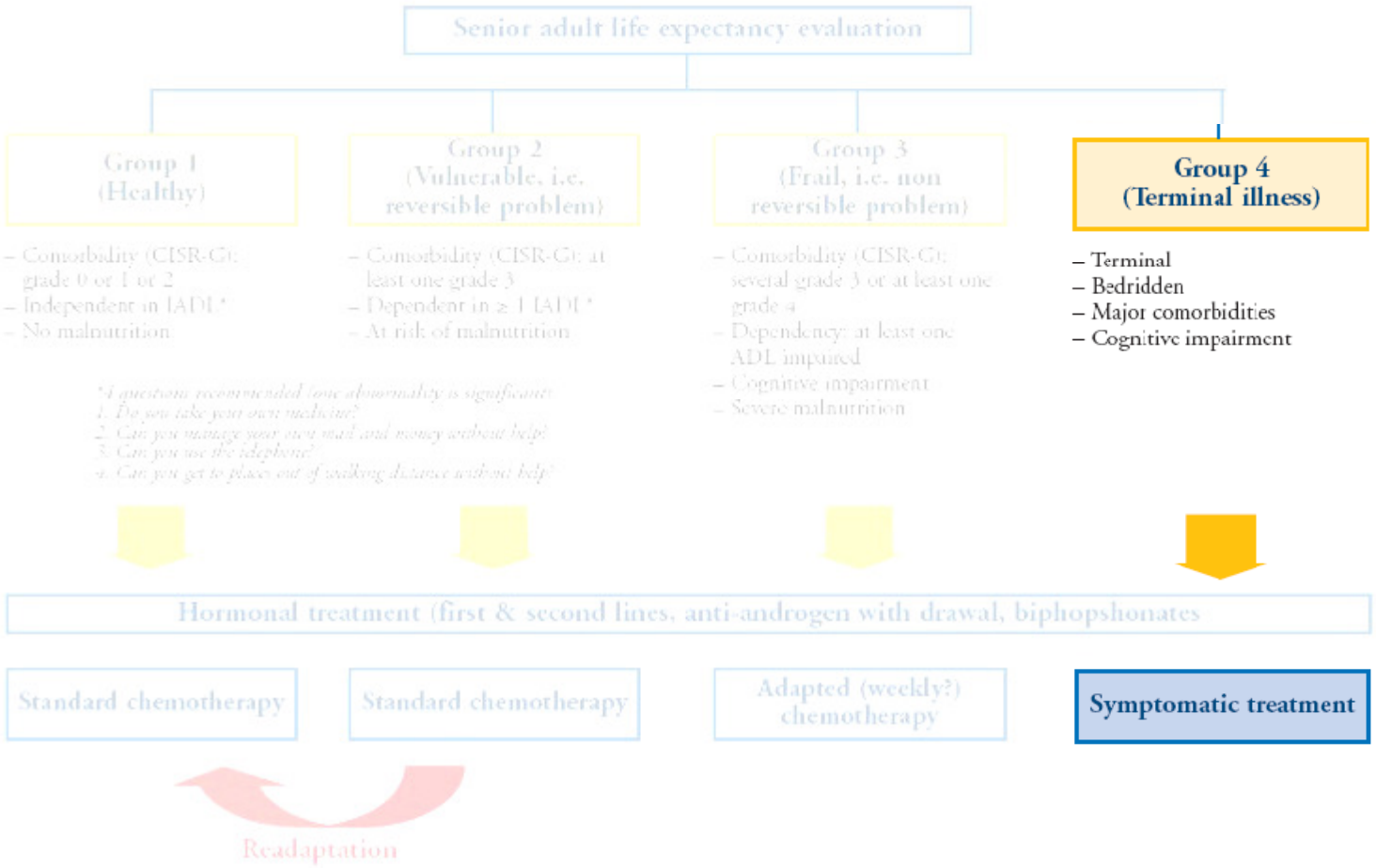
Der ältere Patient: SIOG - Leitlinien

SIOG PRACTICAL RECOMMENDATIONS FOR MANAGEMENT OF PROSTATE CANCER IN SENIOR ADULTS

- The urological approach is fundamentally the same in senior adults with prostate cancer as in younger patients.
- Internationally accepted guidelines are used. In this discussion, EAU guidelines[10] have been developed, but other guidelines such as the NCCN guidelines[16] are also valid, as well as national scientifically established guidelines.
- Treatment decisions should be based on evaluation of patient "health status" which permits evaluation of an individual's risk of death from other causes than prostate cancer (i.e. individual life expectancy).
- Evaluation of "health status" requires a standard clinical examination and is performed in a few minutes. It is based on the evaluation of:
  - comorbidities (CISR-G grading)
  - dependence status (IADL and ADL)
  - nutritional status
  - presence of a clinically evident cognitive impairment, depression and/or repeated delirium.
- Patients dhould be treated according to their health status:
  - **"Fit"** or **"healthy"** senior adults should receive the same treatment as younger patients
  - **"Vulnerable"** patients (i.e. reversible impairment) should receive standard treatment after readaptation
  - **"Frail"** patients (i.e. non-reversible impairement) should receive adapted treatment
  - **"too sick"** patients are candidates for symptomatic treatments.

Droz, JP et al. Critical Reviews in Oncology/Haematology 2010;73:68-91

Der ältere Patient: SIOG - Leitlinien



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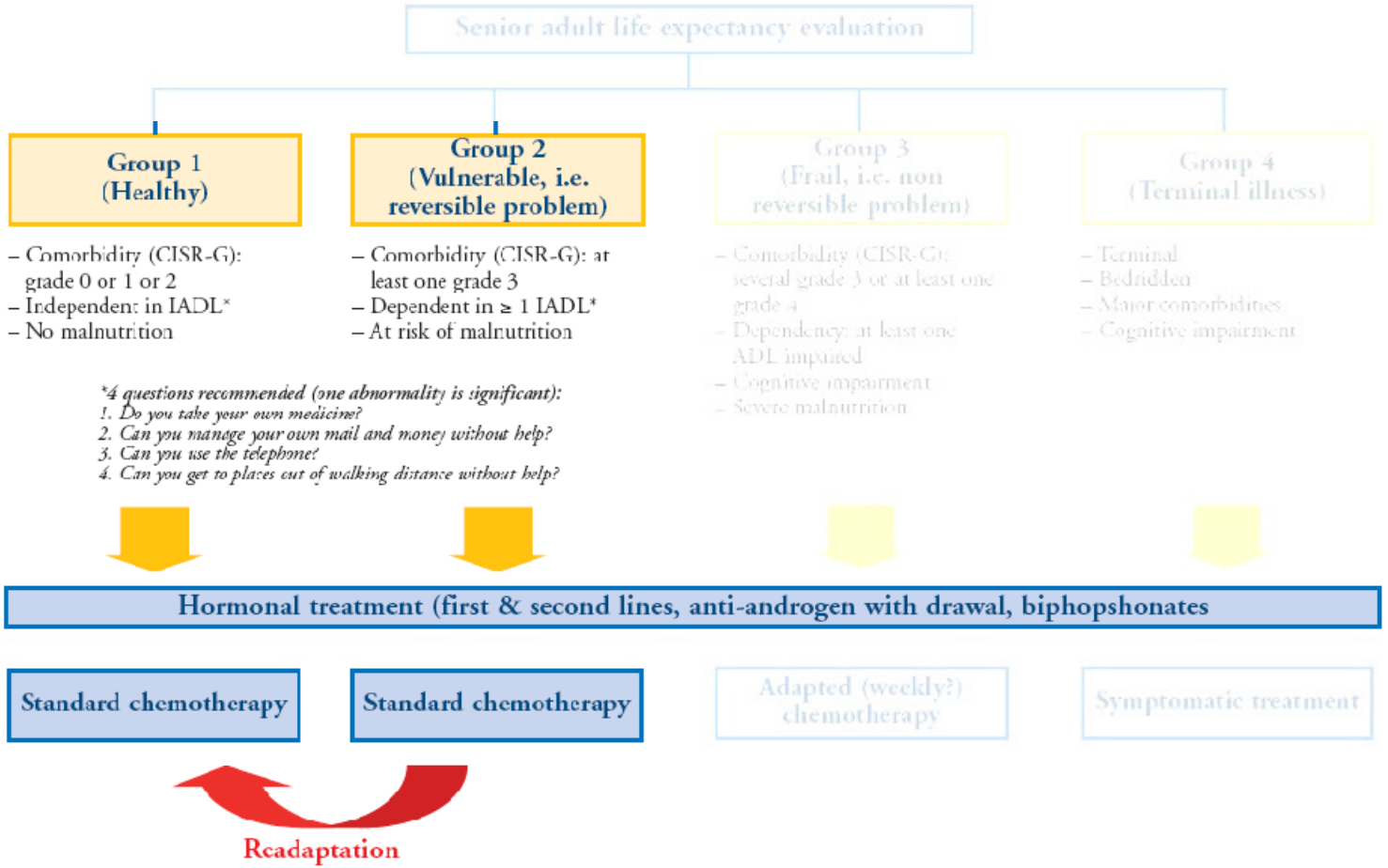
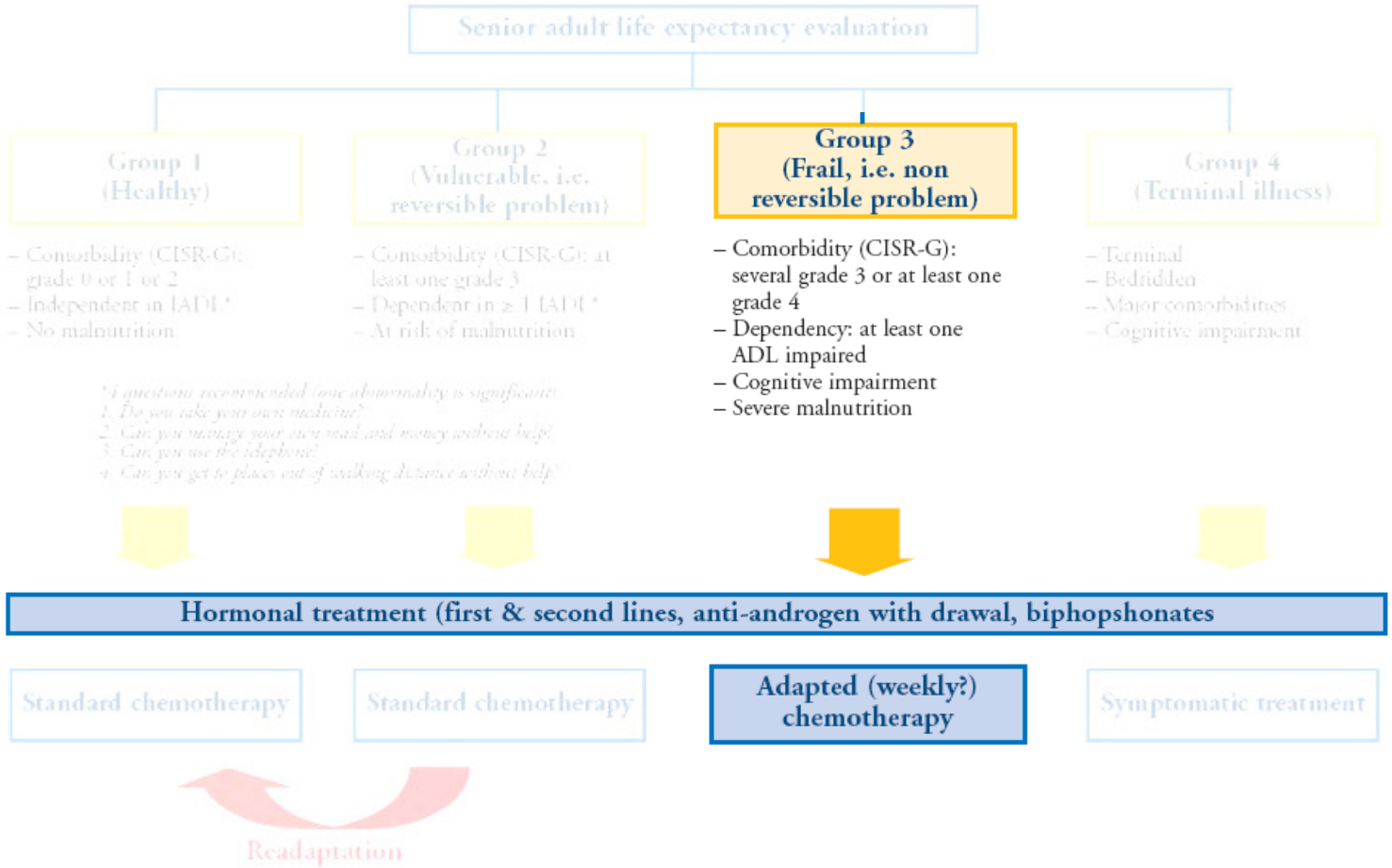
Droz, JP et al. Critical Reviews in Oncology/Haematology 2010;73:68-91

Der ältere Patient: SIOG - Leitlinien



Droz, JP et al. Critical Reviews in Oncology/Haematology 2010;73:68-91

Der ältere Patient: SIOG - Leitlinien



Droz, JP et al. Critical Reviews in Oncology/Haematology 2010;73:68-91

Der ältere Patient

retrospektive Analyse der Daten von 175 älteren Patienten aus 9 franz. KH (2000-2003)

Table 2 – Patterns of docetaxel-based treatment ($n = 175$)

	No. patients	%	Median number of cycles (range)
SR ($n = 95$)			
Docetaxel 75 mg/m^2 every 3 wk	68	71.5	6 (1–10)
Docetaxel 70 mg/m^2 every 3 wk	27	28.5	6 (1–9)
AR ($n = 80$)			
Docetaxel 30–35 mg/m^2 weekly for 6 of every 8 wk	27	33.8	2 (1–4)
Docetaxel 35 mg/m^2 weekly for 2 of every 3 wk	26	32.5	6 (2–18)
Docetaxel 50–60 mg/m^2 every 3 wk	9	11.2	5 (1–10)
Docetaxel 30–35 mg/m^2 weekly for 3 of every 4 wk	7	8.7	3 (1–4)
Docetaxel 30–35 mg/m^2 weekly for 5 of every 6 wk	6	7.5	3 (1–5)
Docetaxel 30–35 mg/m^2 weekly for 4 of every 5 wk	5	6.3	2 (1–4)

AR, adapted regimen; SR, standard regimen.

Italiano, A. et al Eur. Urol. (2008), doi:10.1016/j.eururo.2008.07.078

Der ältere Patient

Therapieabbruch wegen Tox häufiger in AR vs. SR (30% vs. 8%, p=0,0005)

Table 1 – Patient characteristics (n = 175)

	AR (n = 80)	SR (n = 95)
Age at diagnosis, years		
Median	78	77
Mean	78.9	77.9
≥80 yr (%)	41.2*	25.3*
ECOG PS (%)		
≤1	72.5	86.3
≥2	27.5*	13.7*
Comorbidities		
Median number	1	1
Range	0–2	0–4
PSA (ng/ml)		
Median	102	113
Range	0.04–2179	0.04–37 200
Pain (%)		
Daily consumption of analgesics (overall)	62.5*	42.1*
Daily consumption of narcotic analgesics	37.5	36.8
Daily consumption of non-narcotic analgesics	15.0	5.3
Extent of disease (%)		
Bone metastases	83.7	80.0
Visceral metastases	33.7	22.1
Measurable lesions	62.5	49.5
Evidence of progression at entry (%)		
PSA	81.2	77.9
Measurable/nonmeasurable lesions	67.5	62.1

AR, adapted regimen; SR, standard regimen; ECOG, Eastern Cooperative Oncology Group; PS, performance status; PSA, prostate-specific antigen.
* $p < 0.05$ for the comparison between the two groups.

Table 3 – Grade 3–4 adverse events (%)

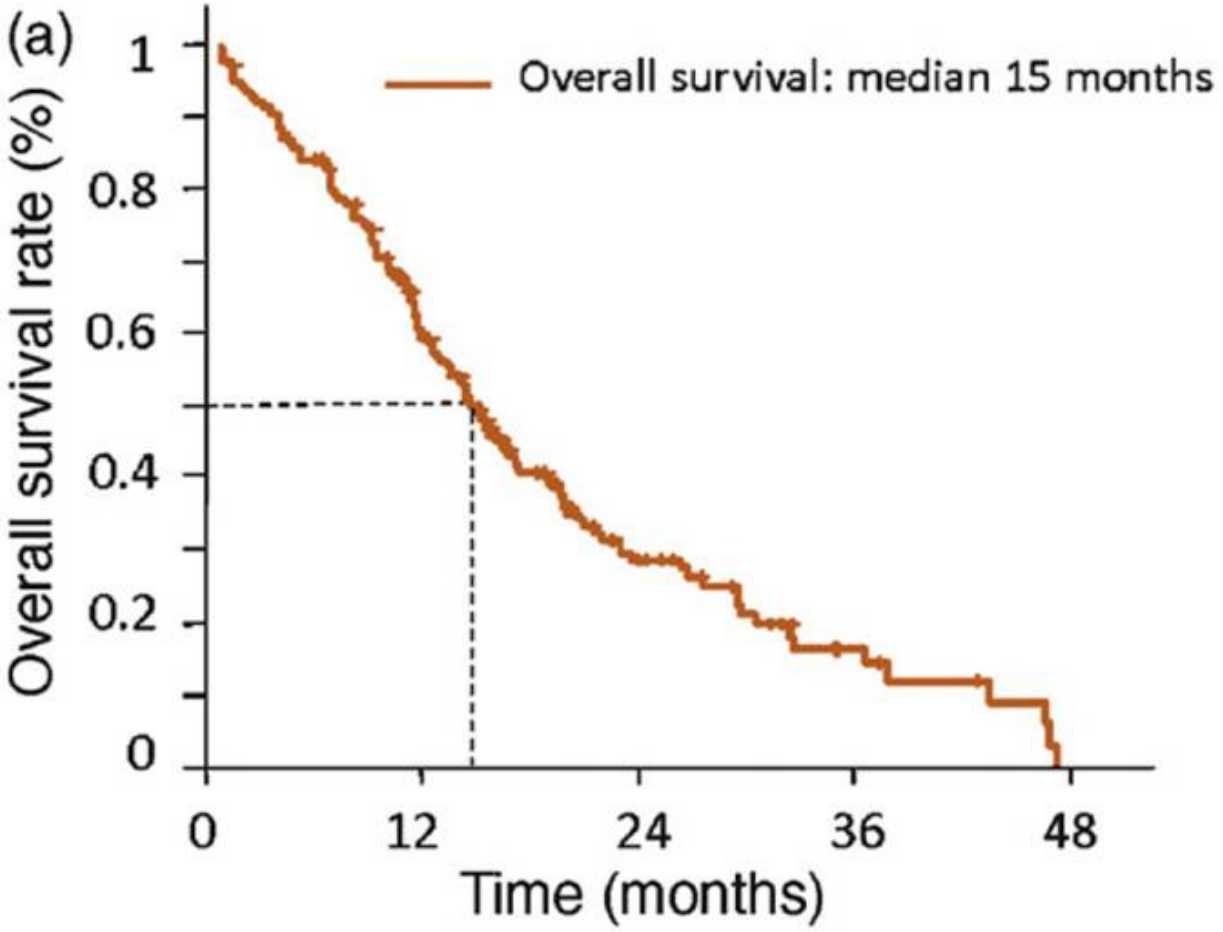
	AR (n = 80)	SR (n = 95)	p value*
Anaemia	5.0	6.0	0.96
Thrombocytopenia	2.5	2.0	0.77
Neutropenia	5.0	25.0	0.0004
Febrile neutropenia	1.0	9.5	0.02
Fatigue	20.0	6.0	0.01
Nausea, vomiting	1.0	2.0	0.94
Diarrhoea	9.0	4.0	0.30
Nail changes	4.0	2.0	0.74
Sensory neuropathy	2.5	2.0	0.77
Anorexia	2.5	1.0	0.85
Stomatitis	2.5	0.0	0.40
Dyspnoea	1.0	0.0	0.88
Peripheral oedema	1.0	0.0	0.88
Rash/desquamation	5.0	0.0	0.09
Cholestasis	1.0	0.0	0.88
≥1 AE	52.5	40.0	0.13
≥1 nonhaematologic AE	40.0	15.8	0.0006
Treatment-related death	2.5	2.0	0.77

AE, adverse event; AR, adapted regimen; SR, standard regimen.
* p values are for the comparison of the percentage of patients with grade 3 or 4 AEs in each treatment group.

Italiano, A. et al Eur. Urol. (2008), doi:10.1016/j.eururo.2008.07.078

Der ältere Patient

OS_{AR} vs. OS_{SR} vergleichbar

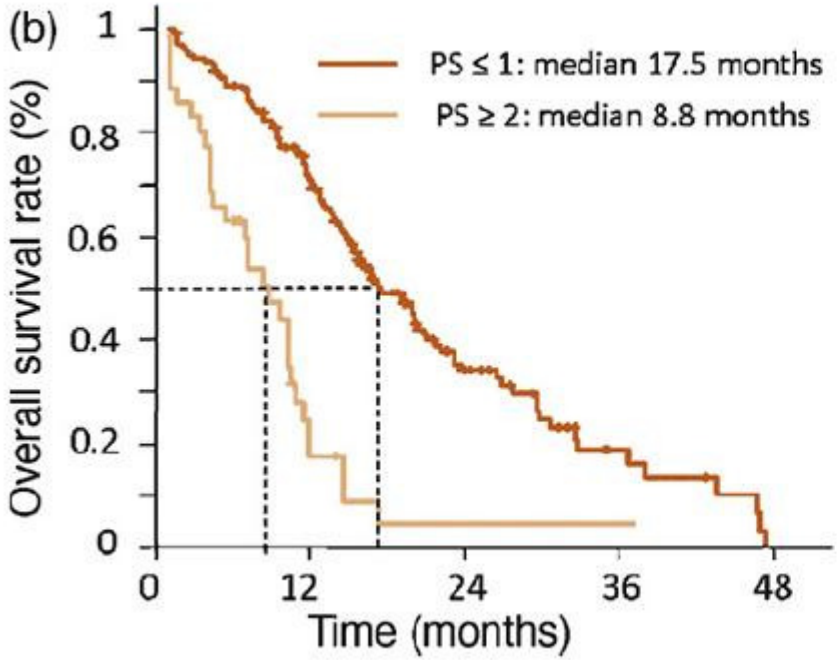


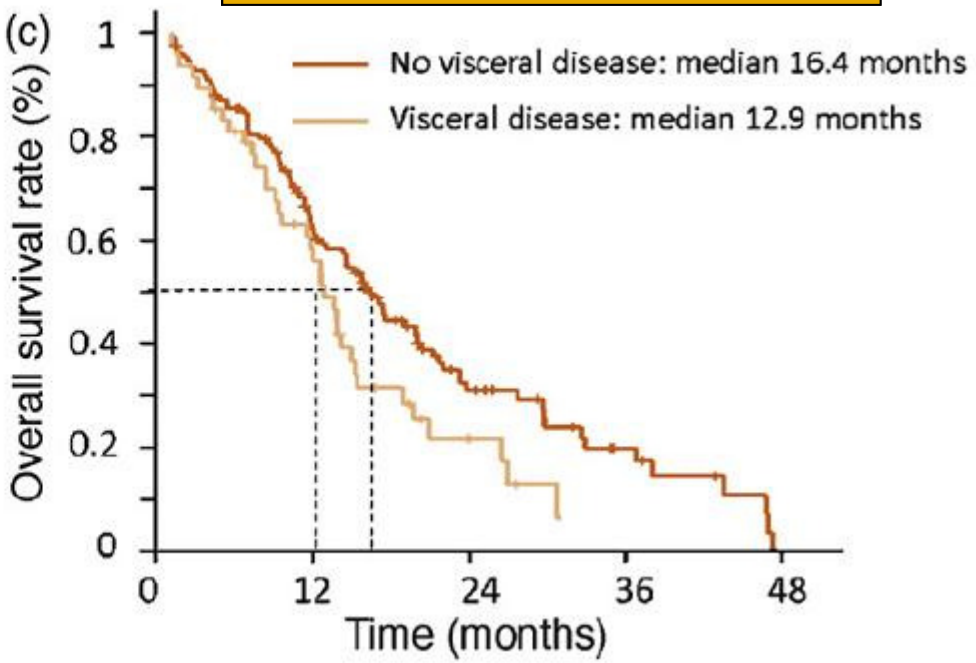
Italiano, A. et al Eur. Urol. (2008), doi:10.1016/j.eururo.2008.07.078

Der ältere Patient

Alter kein unabhängiger Risikofaktor!

unabhängige Risikofaktoren: ECOG PS, Schmerzen, viszerale Metastasen





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Italiano, A. et al Eur. Urol. (2008), doi:10.1016/j.eururo.2008.07.078

Der ältere Patient

Response unabhängig vom Alter!

keine erhöhte Tox bei älteren Patienten

The influence of age on the efficacy and tolerability of weekly docetaxel (36 mg/m^2) for six cycles was further analysed in a pooled analysis of two phase II studies in men with metastatic HRPC [30]. Men aged ≥70 years had lower baseline haemoglobin and higher baseline PSA levels than men aged <70 years, but the efficacy was similar in both groups. There were PSA responses in 47% of older men vs 40% of younger men ($P = 0.75$). Moreover, there was no significant difference in time to progression ($P = 0.28$) and overall survival ($P = 0.52$). Both groups also showed a similar incidence of severe (grade 3–4) haematological and non-haematological toxicity.

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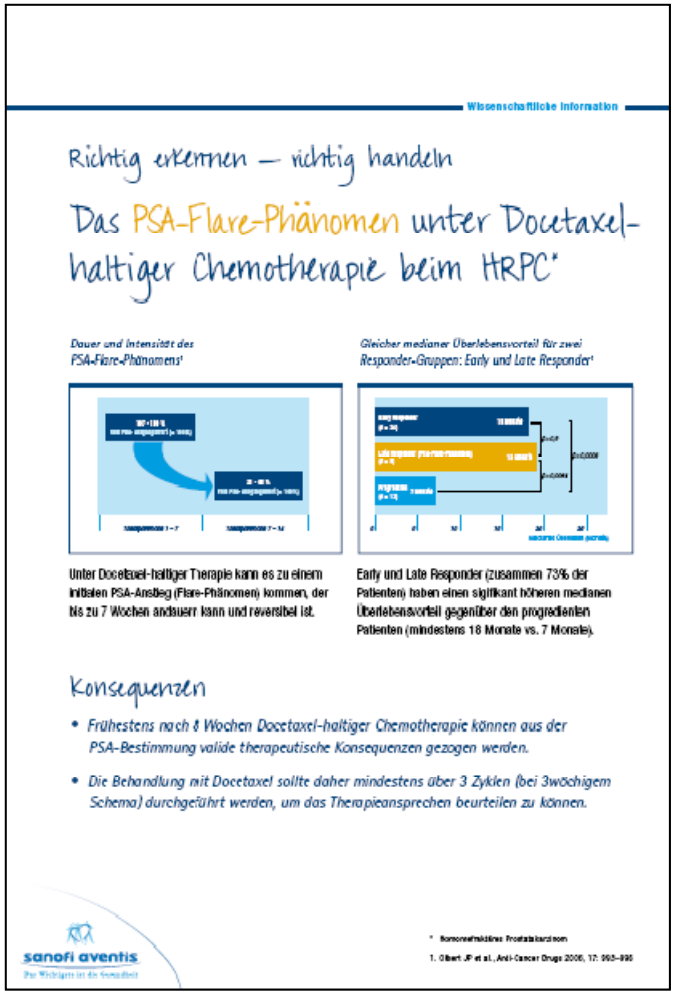
Das PSA Flare Phänomen

Das PSA Flare Phänomen



Wissenschaftliche Information

Richtig erkennen – richtig handeln

Das PSA-Flare-Phänomen unter Docetaxel-haltiger Chemotherapie beim HRPC*

Dauer und Intensität des PSA-Flare-Phänomens[1]

Unter Docetaxel-haltiger Therapie kann es zu einem initialen PSA-Anstieg (Flare-Phänomen) kommen, der bis zu 7 Wochen andauern kann und reversibel ist.

Gleicher medianer Überlebensvorteil für zwei Responder-Gruppen: Early und Late Responder[1]

Early und Late Responder (zusammen 73% der Patienten) haben einen signifikant höheren medianen Überlebensvorteil gegenüber den progredienten Patienten (mindestens 18 Monate vs. 7 Monate).

Konsequenzen

- *Frühestens nach 8 Wochen Docetaxel-haltiger Chemotherapie können aus der PSA-Bestimmung valide therapeutische Konsequenzen gezogen werden.*
- *Die Behandlung mit Docetaxel sollte daher mindestens über 3 Zyklen (bei 3wöchigem Schema) durchgeführt werden, um das Therapieansprechen beurteilen zu können.*

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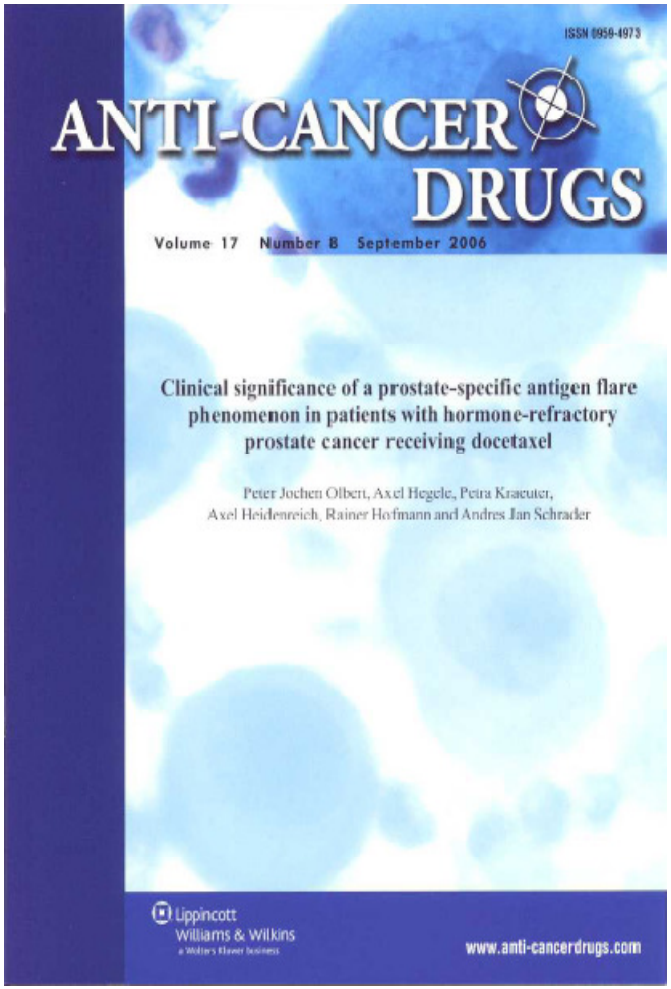
* Kastrationsrefraktäres Prostatakarzinom

1. Olbert JP et al., Anti-Cancer Drugs 2006; 17: 993–996



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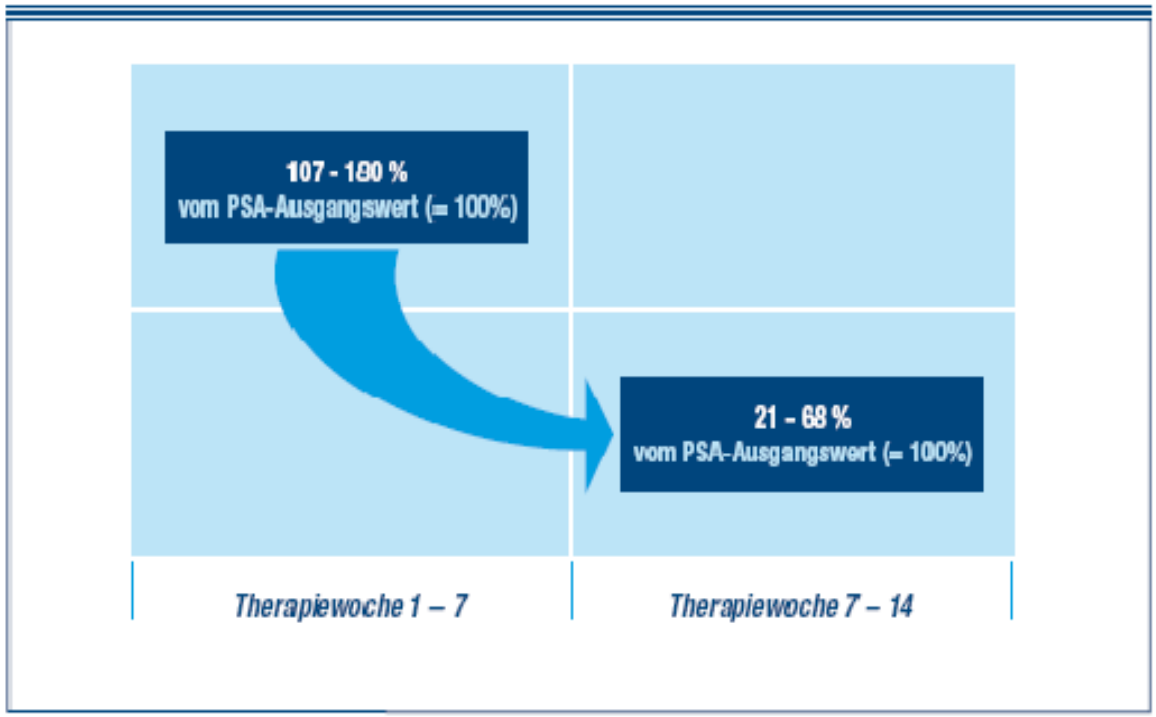
Olbert, P. et al. Anti-Cancer Drugs 2006; 17: 993-996

Das PSA Flare Phänomen



Unter Docetaxel-haltiger Therapie kann es zu einem initialen PSA-Anstieg (Flare-Phänomen) kommen, der bis zu 7 Wochen andauern kann und reversibel ist.

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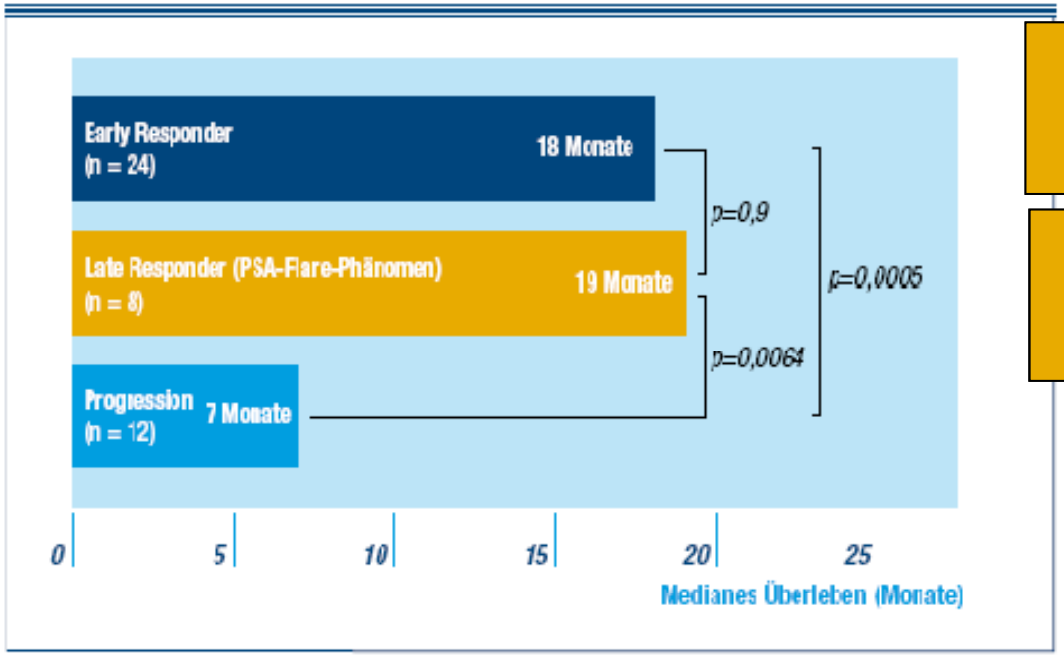
Olbert, P. et al. Anti-Cancer Drugs 2006; 17: 993-996

Das PSA Flare Phänomen

Docetaxel plus Mitoxantron (n = 4 Patienten)	Docetaxel plus Estramustin (n = 20 Patienten)	Docetaxel allein (n = 20 Patienten)
Mitoxantron 12 mg/m² plus Docetaxel 60 mg/m² an Tag 1, 3wöchig	Docetaxel 25 oder 35 mg/m² an Tag 1, 1wöchig, und Estramustin 3 x 280 mg oral an Tag 0 bis 3	Docetaxel 35 mg/m² an Tag 1, 1wöchig; 1wöchige Therapieunterbrechung nach 3 Zyklen

Olbert, P. et al. Anti-Cancer Drugs 2006; 17: 993-996

Das PSA Flare Phänomen



Vermeidung zu früher Behandlungsabbrüche

Mindestens 3 Zyklen!

Early und Late Responder (zusammen 73% der Patienten) haben einen sigifikant höheren medianen Überlebensvorteil gegenüber den progredienten Patienten (mindestens 18 Monate vs. 7 Monate).

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Olbert, P. et al. Anti-Cancer Drugs 2006; 17: 993-996

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Vielen Dank für Ihre Aufmerksamkeit!