CHARITÉ
UNIVERSITÄTSMEDIZIN BERLIN

Prostatakarzinom

Prof. Dr. Georg Maschmeyer
georg.maschmeyer@charite.de

Prostatakarzinom – Leitlinien 2023

onkopedia

onkopedia leitlinien

Prostatakarzinom

2019, nicht mehr gültig

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

2020

SPECIAL ARTICLE

Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

C. Parker[1], E. Castro[2], K. Fizazi[3], A. Heidenreich[4], P. Ost[5], G. Procopio[6], B. Tombal[7] & S. Gillessen[8,9,10], on behalf of the ESMO Guidelines Committee*

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

2023

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Updated treatment recommendations for prostate cancer from the ESMO Clinical Practice Guideline considering treatment intensification and use of novel systemic agents

K. Fizazi[1] & S. Gillessen[2], on behalf of the ESMO Guidelines Committee*

NCCN National Comprehensive Cancer Network®

S3-Leitlinie Prostatakarzinom

365 Seiten

Version 6.2 – Oktober 2021
AWMF-Registernummer: 043/022OL

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

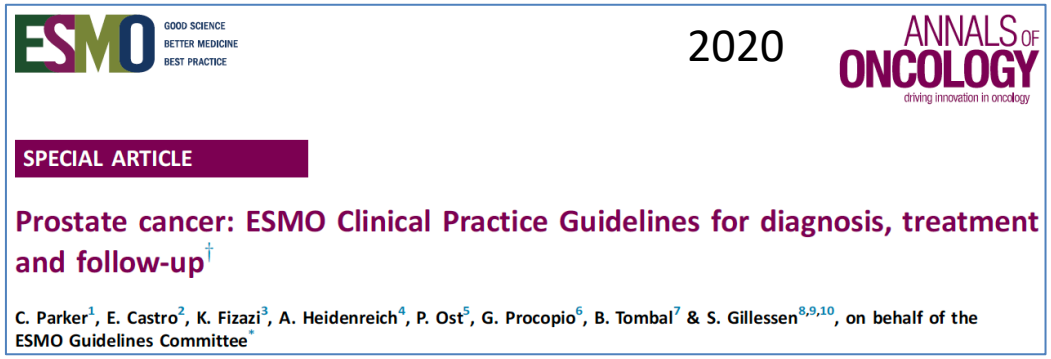
Prostate Cancer

Version 4.2023 — September 7, 2023

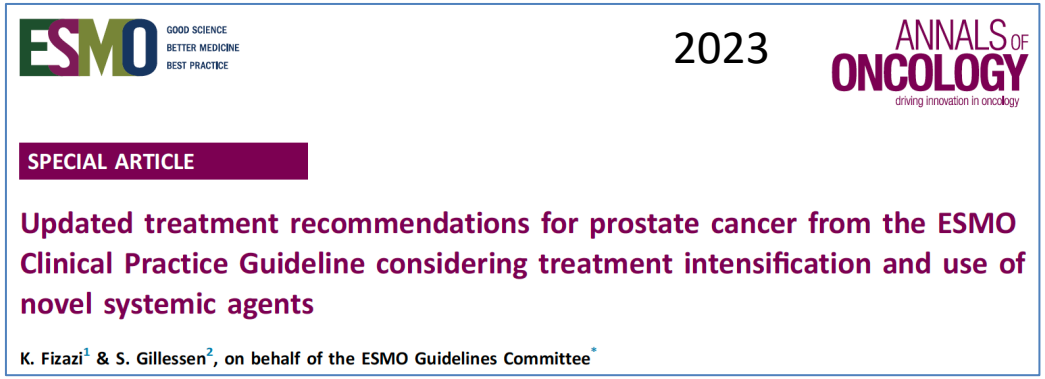
NCCN.org

213 Seiten

Prostatakarzinom – ESMO-Leitlinien 2020/23



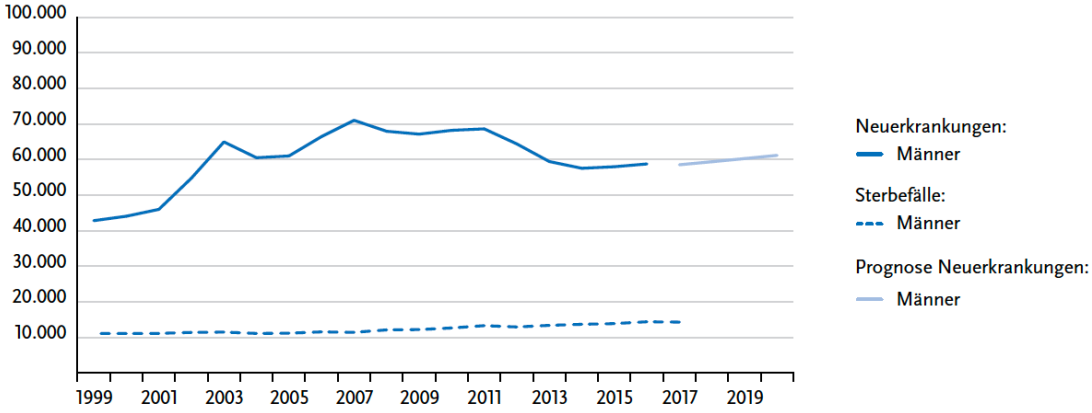
Ann Oncol 2020;31:1119-1134



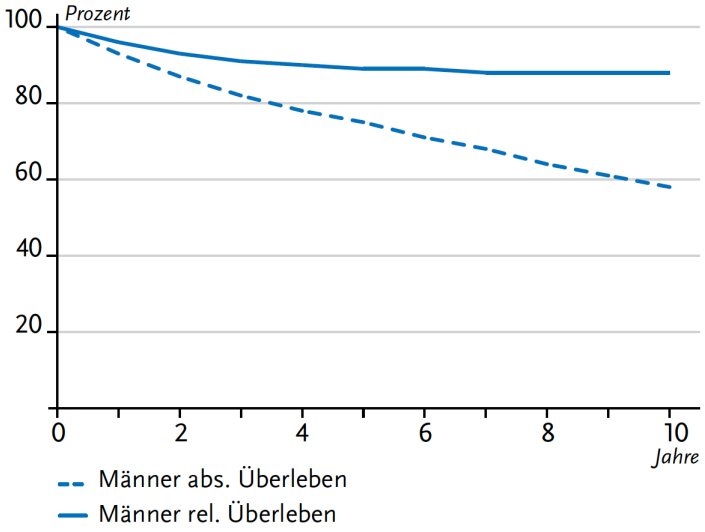
Ann Oncol 2023;34:557-563

Prostatakarzinom – Epidemiologie (2019)

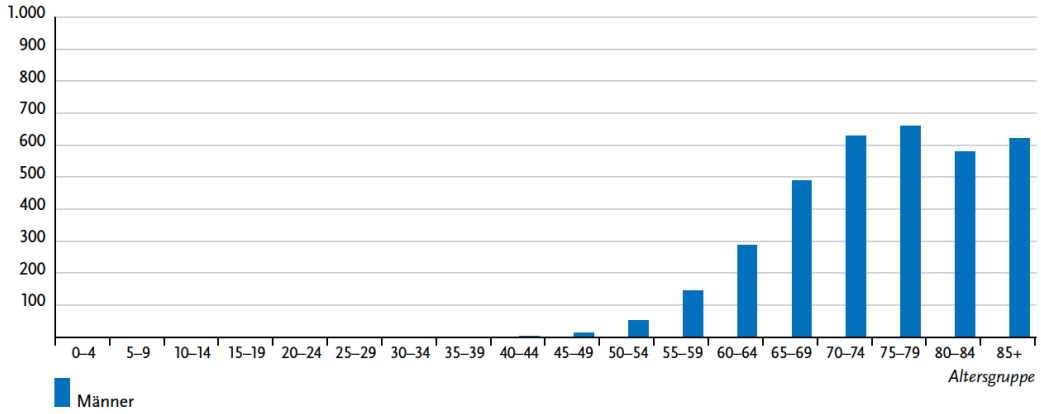
Absolute Zahl der Neuerkrankungs- und Sterbefälle, ICD-10 C61, Deutschland 1999–2016/2017, Prognose (Inzidenz) bis 2020



Absolute und relative Überlebensraten bis 10 Jahre nach Erstdiagnose, ICD-10 C61, Deutschland 2015–2016

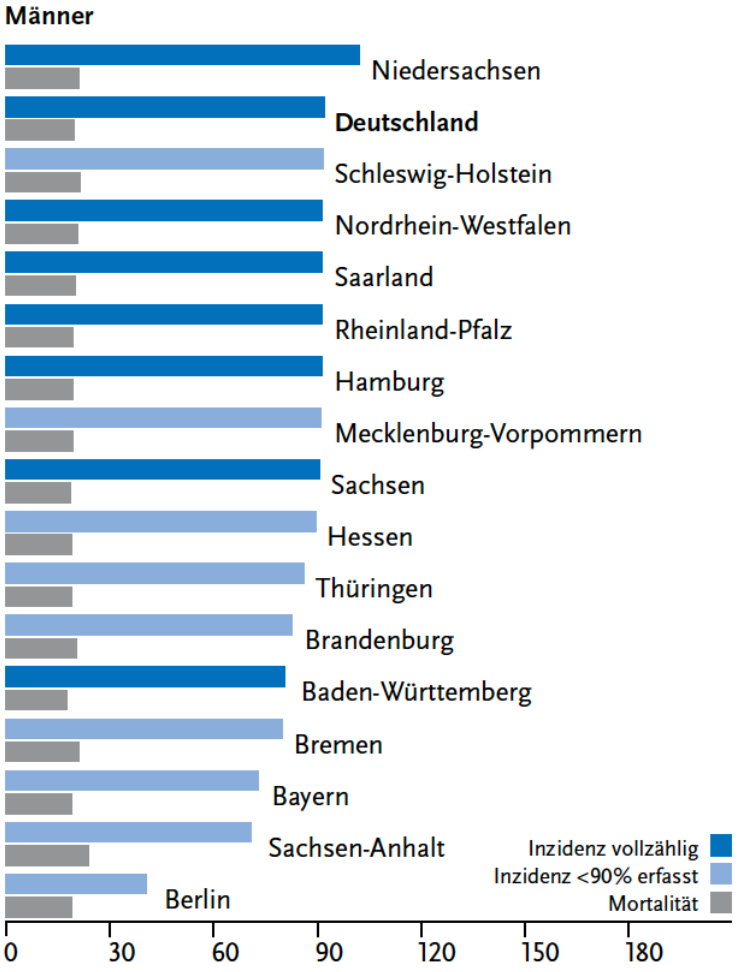


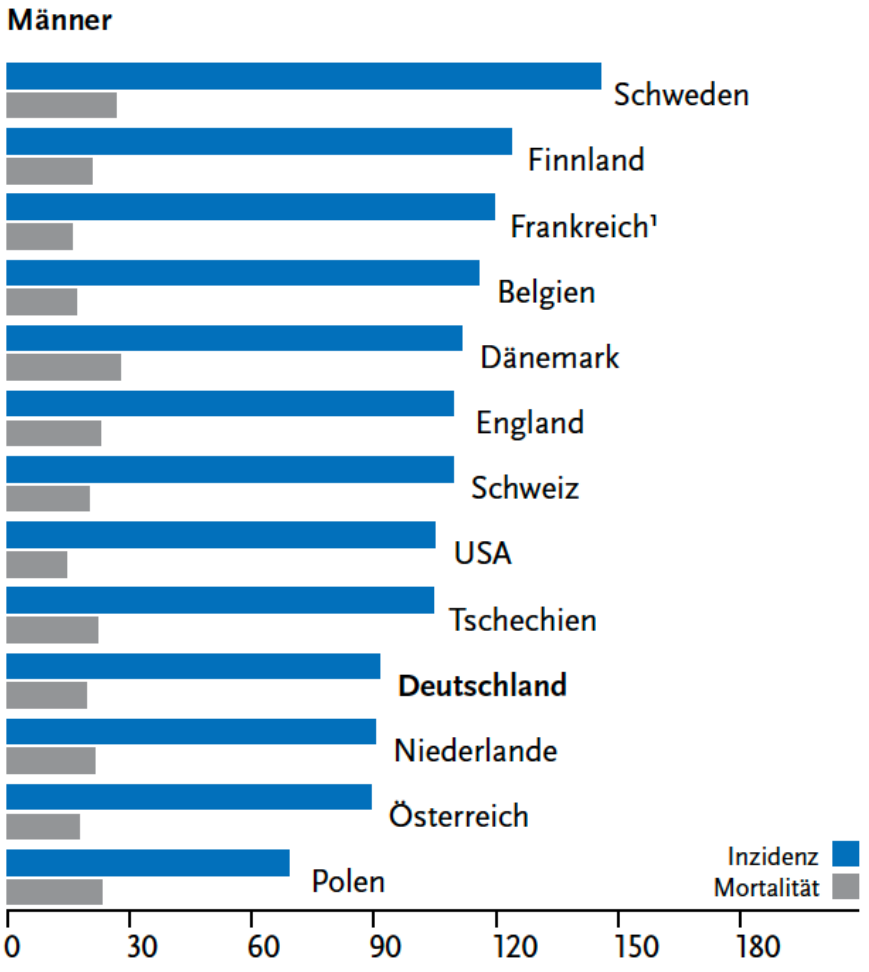
Altersspezifische Erkrankungsraten, ICD-10 C61, Deutschland 2015–2016
je 100.000



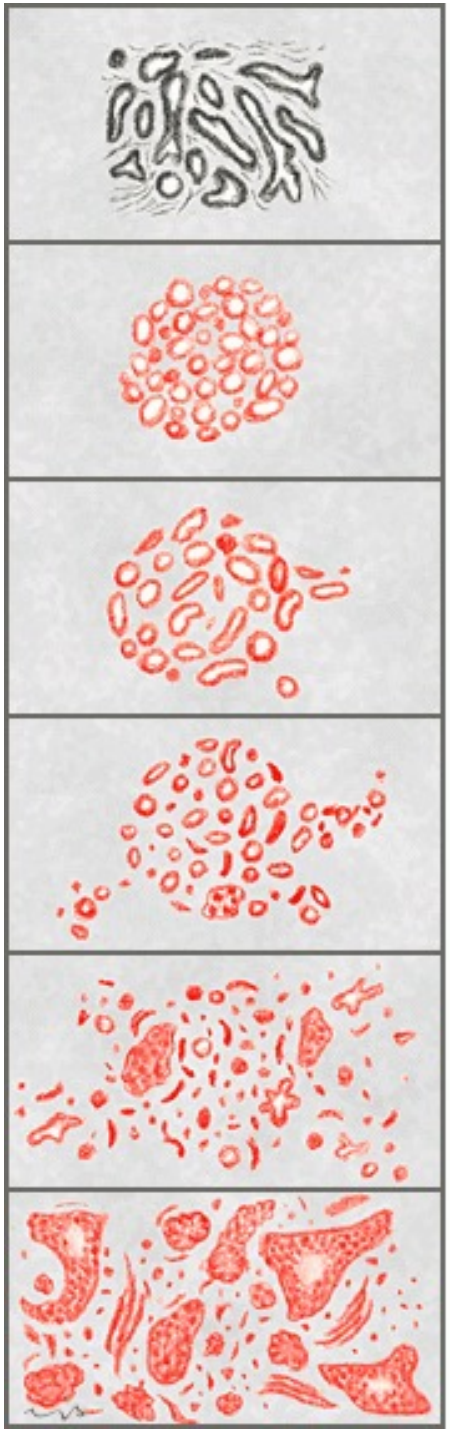
https://www.krebsdaten.de/Krebs/DE/Content/Publikationen/Krebs_in_Deutschland/kid_2019/kid_2019_c61_prostata.pdf?__blob=publicationFile

Prostatakarzinom – Epidemiologie (2019)





https://www.krebsdaten.de/Krebs/DE/Content/Publikationen/Krebs_in_Deutschland/kid_2019/kid_2019_c61_prostata.pdf?__blob=publicationFile



Normales Prostatagewebe:
Drüsen gewunden und verzweigt, dazwischen Muskulatur und Bindegewebe

Gleason Grad 1:
Scharf begrenzter Knoten, Drüsen gleichförmig, dicht gepackt und mittelgroß

Gleason Grad 2:
Nicht ganz scharf begrenzter Knoten, Drüsen lockerer und ungleichmäßiger

Gleason Grad 3:
Unscharfer Knoten, Drüsen klein und ungleichmäßig, evtl. kleine solide Bezirke

Gleason Grad 4:
Tumorbereich unscharf, Drüsen meist ohne Innenraum, verschmolzene Drüsen, solide Bezirke

Gleason Grad 5:
Tumorbereich unscharf, keine klaren Drüsen, solide Bezirke, weitere Veränderungen

Prostatakarzinom: Gleason Grading

- Grade 1 und 2 werden nicht mehr vergeben

www. prostata.de

Prostatakarzinom: Grading nach ISUP

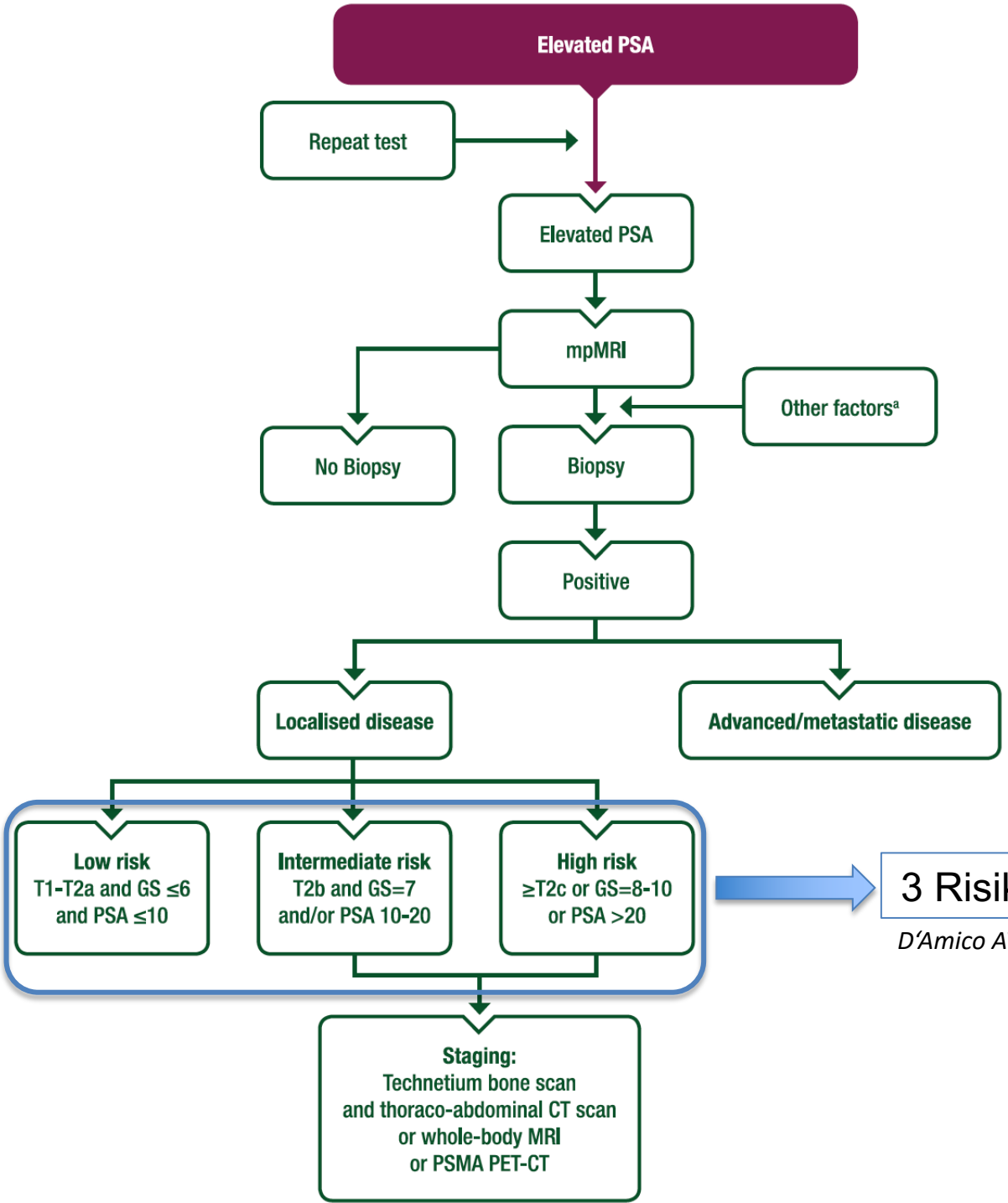
- Berechnung aus 2 Biopsien
- Addition des häufigsten + des schlechtesten Grades
- Grade 1 und 2 werden nicht mehr vergeben

Grade group	Gleason score and pattern
1	Grade 6 (3+3)
2	Grade 7 (3+4)
3	Grade 7 (4+3)
4	Grade 8 (4+4, 3+5, or 5+3)
5	Grade 9 or 10 (4+5, 5+4, or 5+5)

ISUP: International Society of Urological Pathology.

ESMO-Leitlinie 2020:

Diagnostik und Staging



3 Risikogruppen

D'Amico AV et al, JAMA 1998;280:969-974

Parker C et al (ESMO), Ann Oncol 2020;31:1119-1134

Risk stratification schema for localized prostate cancer, according to the National Comprehensive Cancer Network (NCCN)

Risk group	Clinical/pathologic features
Very low	▪ T1c AND ▪ Grade group 1 AND ▪ PSA <10 ng/mL AND ▪ Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core AND ▪ PSA density <0.15 ng/mL/g
Low	▪ T1 to T2a AND ▪ Grade group 1 AND ▪ PSA <10 ng/mL AND ▪ Does not qualify for very low risk
Favorable intermediate	▪ No high or very high risk features ▪ No more than one intermediate risk factor: • T2b to T2c OR • Grade group 2 or 3 • PSA 10 to 20 ng/mL AND ▪ Grade group 1 or 2 AND ▪ Percentage of positive biopsy cores <50%
Unfavorable intermediate	▪ No high or very high risk features ▪ Two or three of the intermediate risk factors: • T2b to T2c • Grade group 2 or 3 • PSA 10 to 20 ng/mL AND/OR ▪ Grade group 3 AND/OR ▪ ≥50% of positive biopsy cores
High	▪ No very high risk features AND ▪ T3a OR ▪ Grade group 4 or 5 OR ▪ PSA >20 ng/mL
Very high	▪ T3b to T4 OR ▪ Primary Gleason pattern 5 OR ▪ Two or three high-risk features OR ▪ >4 cores with Grade group 4 or 5

PSA: prostate-specific antigen.

Prostatakarzinom: Risikostratifikation nach NCCN

American Cancer Society:

Risikokategorien für lokal begrenzte Erkrankung

Very-low-risk group

cT1c, G1 (Gleason score ≤ 6), PSA level < 10

Low-risk group

cT1 to cT2a, G1 (Gleason score ≤ 6), PSA levels < 10

Intermediate-risk group (favorable or unfavorable)

cT2b or cT2c and/or G2 or 3 (Gleason score 7) and/or a PSA level 10-20 ng/ml

High-risk group

cT3a or G4 or 5 (Gleason score 8-10) or PSA level > 20

Very-high-risk group

cT3b or cT4

- Gleason score 9 or 10 or G5
- 2 or 3 of the features found in the high-risk group
- > 4 biopsy pieces are G4 or 5 (Gleason score 8-10)

https://www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/risk-groups.html

Prostate cancer TNM staging AJCC UICC 8th edition

Primary tumor (T)	
Clinical T (cT)	
T category	**T criteria**
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Clinically inapparent tumor that is not palpable
T1a	Tumor incidental histologic finding in 5% or less of tissue resected
T1b	Tumor incidental histologic finding in more than 5% of tissue resected
T1c	Tumor identified by needle biopsy found in one or both sides, but not palpable
T2	Tumor is palpable and confined within prostate
T2a	Tumor involves one-half of one side or less
T2b	Tumor involves more than one-half of one side but not both sides
T2c	Tumor involves both sides
T3	Extraprostatic tumor that is not fixed or does not invade adjacent structures
T3a	Extraprostatic extension (unilateral or bilateral)
T3b	Tumor invades seminal vesicle(s)
T4	Tumor is fixed or invades adjacent structures other than seminal vesicles such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall
Pathological T (pT)	
T category	**T criteria**
T2	Organ confined
T3	Extraprostatic extension
T3a	Extraprostatic extension (unilateral or bilateral) or microscopic invasion of bladder neck
T3b	Tumor invades seminal vesicle(s)
T4	Tumor is fixed or invades adjacent structures other than seminal vesicles such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall
NOTE: There is no pathological T1 classification. *NOTE:* Positive surgical margin should be indicated by an R1 descriptor, indicating residual microscopic disease.	
Regional lymph nodes (N)	
N category	**N criteria**
NX	Regional nodes were not assessed
N0	No positive regional nodes
N1	Metastases in regional node(s)
Distant metastasis (M)	
M category	**M criteria**
M0	No distant metastasis
M1	Distant metastasis
M1a	Nonregional lymph node(s)
M1b	Bone(s)
M1c	Other site(s) with or without bone disease
NOTE: When more than one site of metastasis is present, the most advanced category is used. M1c is most advanced.	
Prostate-specific antigen (PSA)	
PSA values are used to assign this category.	
PSA values	
<10	
≥10 <20	
<20	
≥20	
Any value	

Histologic grade group (G)		
Recently, the Gleason system has been compressed into so-called Grade Groups.		
Grade Group	**Gleason score**	**Gleason pattern**
1	≤6	≤3+3
2	7	3+4
3	7	4+3
4	8	4+4, 3+5, or 5+3
5	9 or 10	4+5, 5+4, or 5+5

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

Prostatakarzinom: TNM (AJCC/UICC 8th ed)

Localised disease	Low risk	Active surveillance Brachytherapy RP Radical RT
	Intermediate risk	RP Radical RT ± neoadjuvant ADT Brachytherapy Active surveillance
	High risk	Long-term ADT + radical RT ± neoadjuvant docetaxel RP + pelvic lymphadenectomy
Locally advanced disease		Neoadjuvant ADT + radical RT + adjuvant ADT ± neoadjuvant docetaxel RP + pelvic lymphadenectomy
M0 CRPC	High risk	ADT + apalutamide ADT + darolutamide ADT + enzalutamide
Metastatic disease	Hormone-naive	ADT + abiraterone ADT + docetaxel ADT + enzalutamide ADT + apalutamide RT for low volume ADT alone for frail patients who cannot tolerate the above treatments Bone health agent
	Castration-resistant (first line)	Abiraterone Docetaxel Enzalutamide ^{223}Ra for patients unfit for above treatments (and bone-only metastases)
	Second line or post-docetaxel	Abiraterone Cabazitaxel Enzalutamide ^{223}Ra

^{223}Ra, radium-223; ADT, androgen deprivation therapy; M0 CRPC, non-metastatic castration-resistant prostate cancer; RP, radical prostatectomy; RT, radiotherapy.

ESMO-Leitlinie 2020:

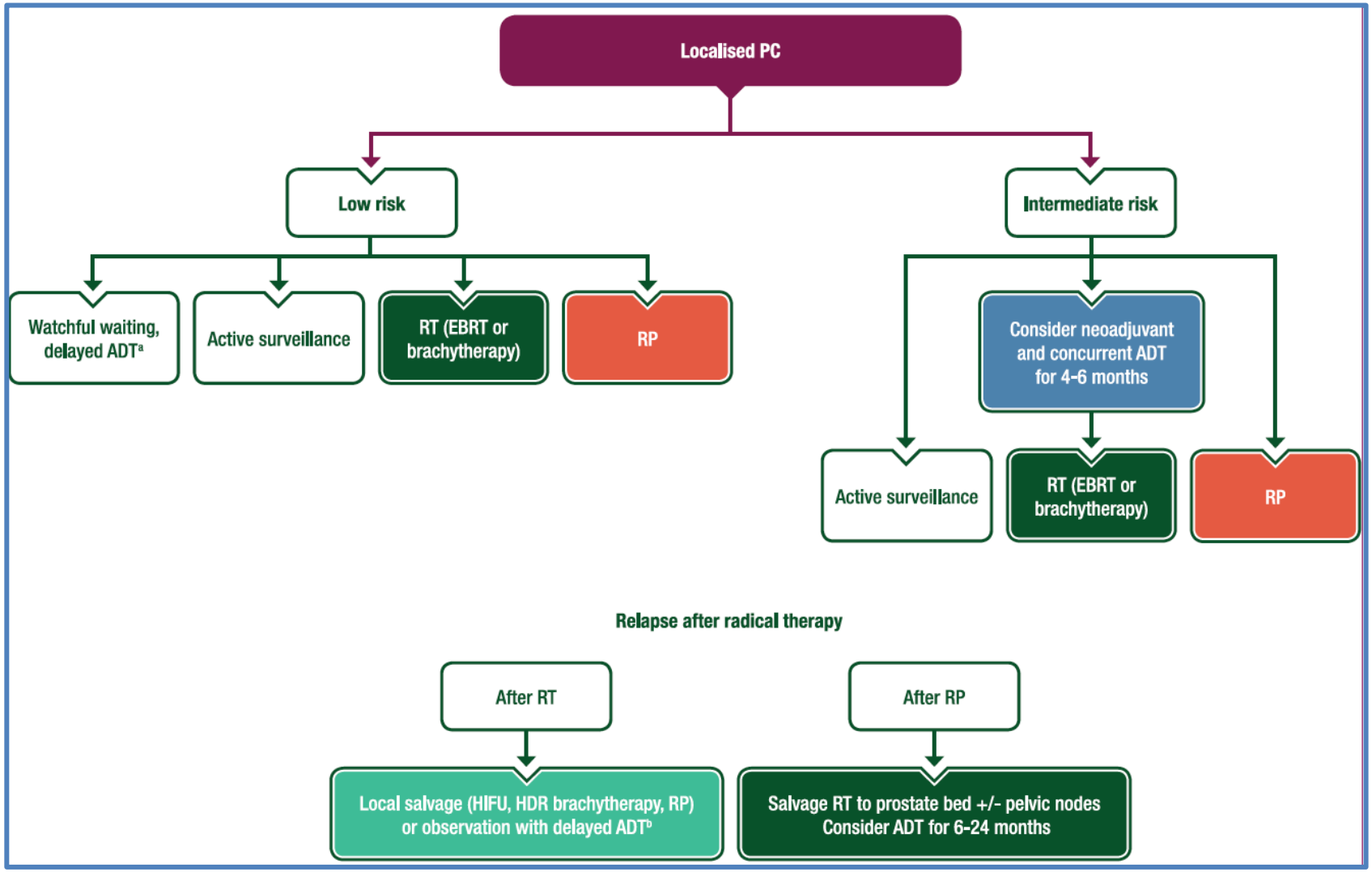
Stadiengerechte Therapie

ADT wird immer weitergeführt

Parker C et al (ESMO), Ann Oncol 2020;31:1119-1134

ESMO-Leitlinie 2020:

Therapie bei lokal begrenztem Prostata-Ca.



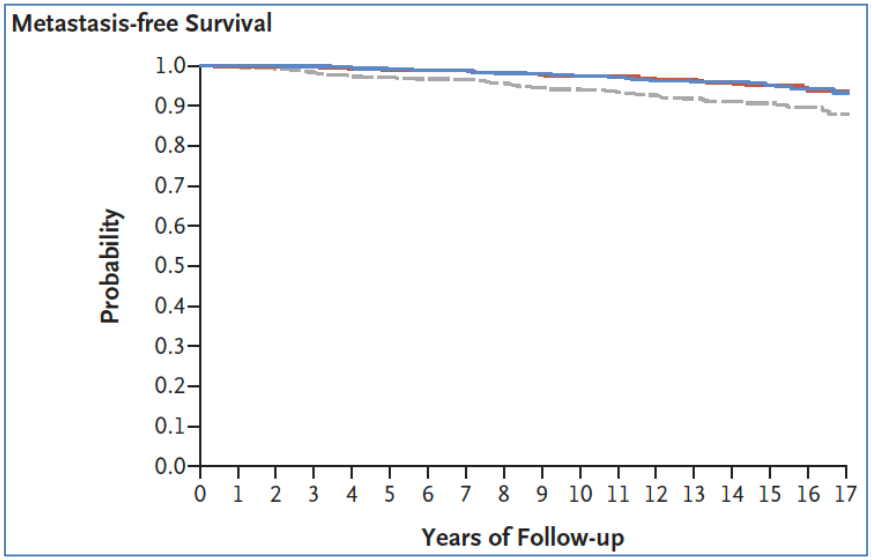
Parker C et al (ESMO), Ann Oncol 2020;31:1119-1134

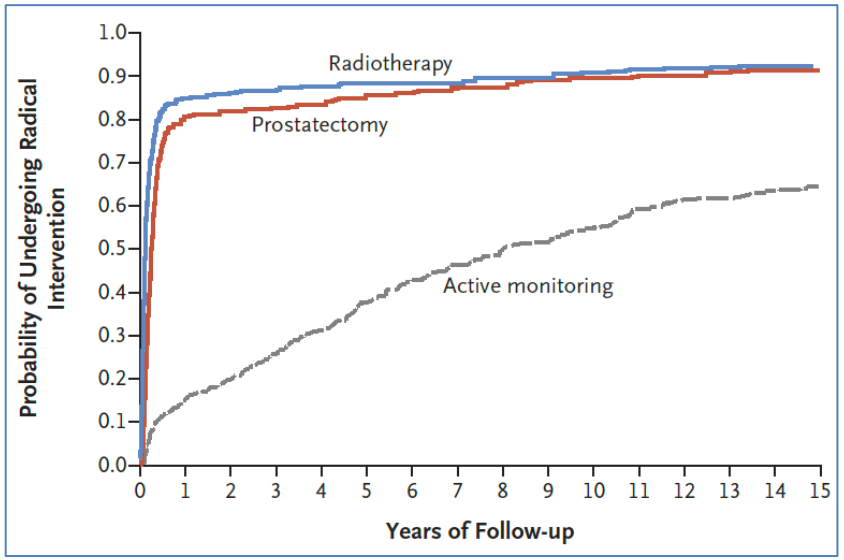
Fifteen-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer

F.C. Hamdy, J.L. Donovan, J.A. Lane, C. Metcalfe, M. Davis, E.L. Turner, R.M. Martin, G.J. Young, E.I. Walsh, R.J. Bryant, P. Bollina, A. Doble, A. Doherty, D. Gillatt, V. Gnanapragasam, O. Hughes, R. Kockelbergh, H. Kynaston, A. Paul, E. Paez, P. Powell, D.J. Rosario, E. Rowe, M. Mason, J.W.F. Catto, T.J. Peters, J. Oxley, N.J. Williams, J. Staffurth, and D.E. Neal, for the ProtecT Study Group*

Trial Group	Survival (95% CI)	
	At 10 Yr	At 15 Yr
	percentage of patients	
Active monitoring	98.7 (97.2–99.4)	96.6 (94.4–98.0)
Prostatectomy	99.0 (97.7–99.6)	97.2 (94.8–98.5)
Radiotherapy	99.4 (98.2–99.8)	97.7 (95.5–98.8)

- n = 1643
- Kein OS-Unterschied
- Frühere Metastasierung bei w&w
- Weitaus spätere Intervention bei w&w

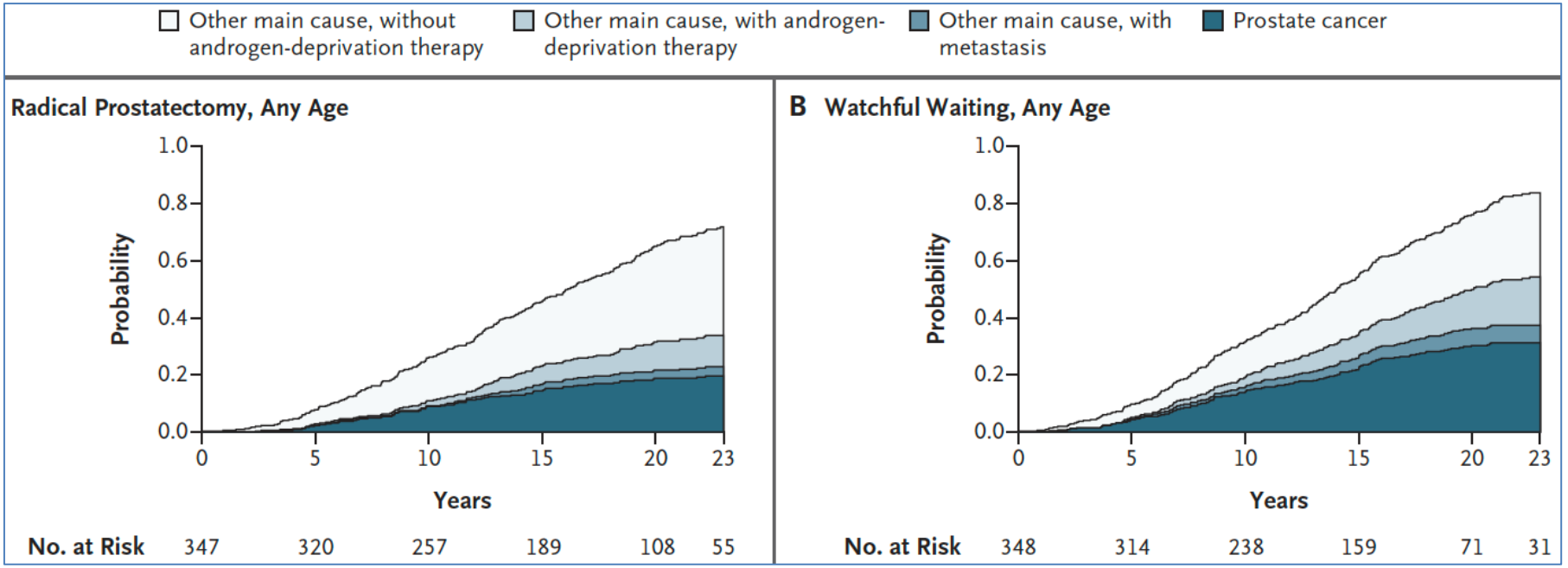




N Engl J Med 2023;388:1547-1558

Radical Prostatectomy or Watchful Waiting in Prostate Cancer — 29-Year Follow-up

Anna Bill-Axelson, M.D., Ph.D., Lars Holmberg, M.D., Ph.D., Hans Garmo, Ph.D., Kimmo Taari, M.D., Ph.D., Christer Busch, M.D., Ph.D., Stig Nordling, M.D., Ph.D., Michael Häggman, M.D., Ph.D., Swen-Olof Andersson, M.D., Ph.D., Ove Andrén, M.D., Ph.D., Gunnar Steineck, M.D., Ph.D., Hans-Olov Adami, M.D., Ph.D., and Jan-Erik Johansson, M.D., Ph.D.

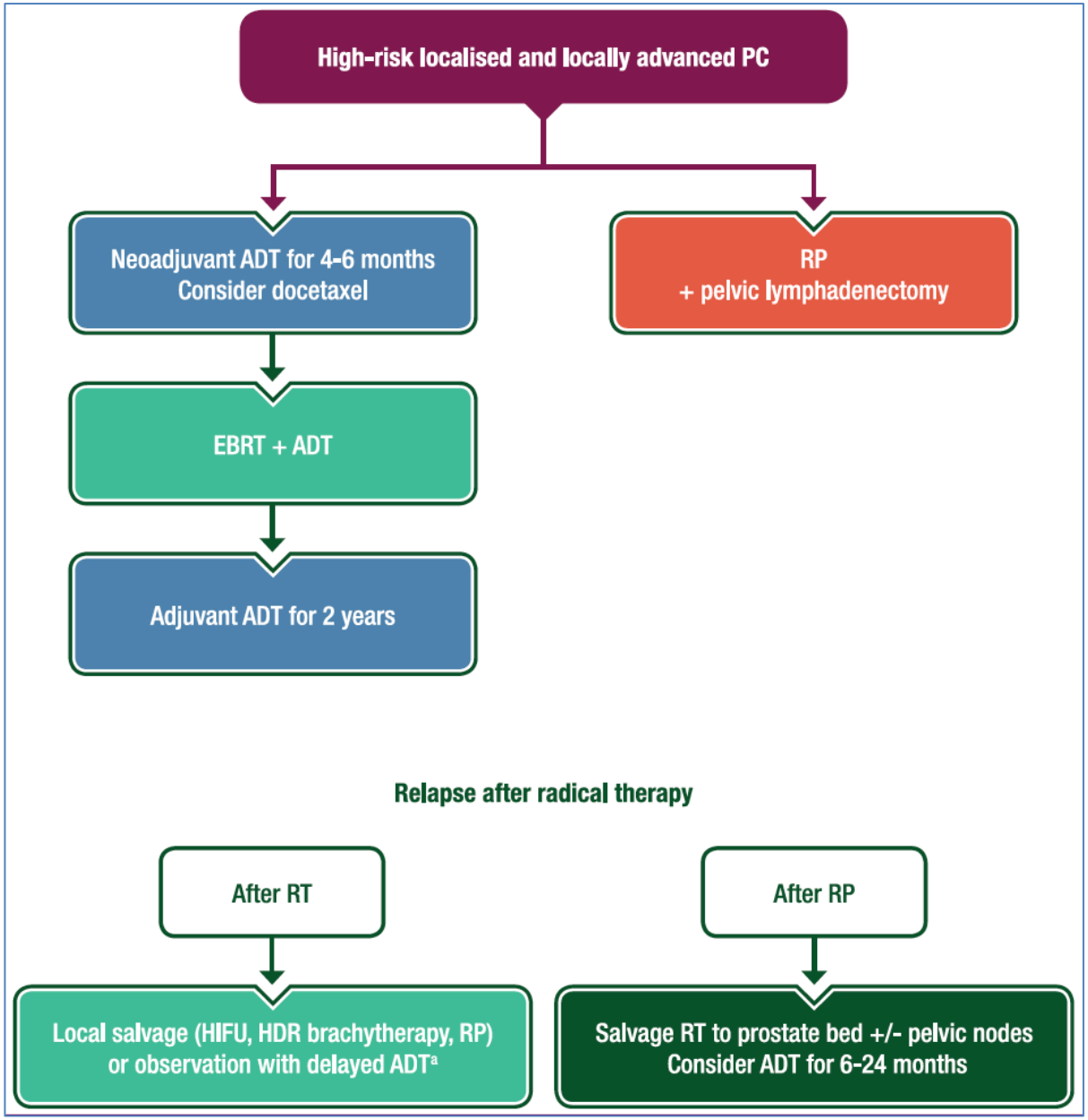


- Kumulative Sterblichkeit an Prostata-Ca nach 15 Jahren 14.6% *vs* 20.7% - RR 0.62 (95% CI 0.44-0.87; p = 0.01)

N Engl J Med 2018;379:2319-2329

ESMO-Leitlinie 2020:

Lokal fortgeschrittenes und Hochrisiko-Prostatakarzinom



Parker C et al (ESMO), Ann Oncol 2020;31:1119-1134

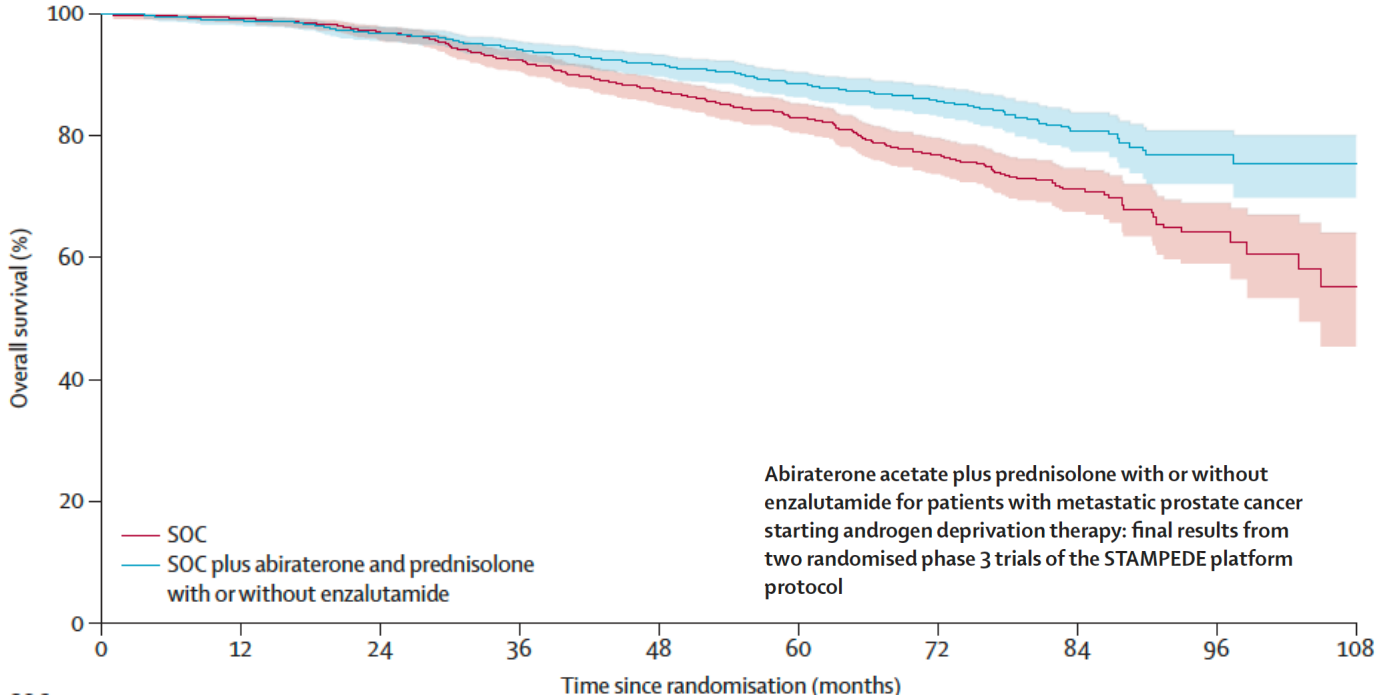
Prostatakarzinom – ESMO-Leitlinien 2023

Neuerungen

Prostatakarzinom – ESMO-Leitlinien 2023

Radiatio + systemische Therapie bei **lokal begrenzter** Hochrisikoerkrankung

- Abirateron/Prednison ± Enzalutamid *vs* SoC (Androgenblockade) bei nicht-metastasierter Erkrankung und **Hochrisikofaktoren**:
- N+ oder ≥ 2 von T3 oder T4, Gleason Score 8-10, and PSA ≥ 40 ng/mL



Attard G et al (STAMPEDE), Lancet 2022;399:447-460

Prostatakarzinom – ESMO-Leitlinien 2023

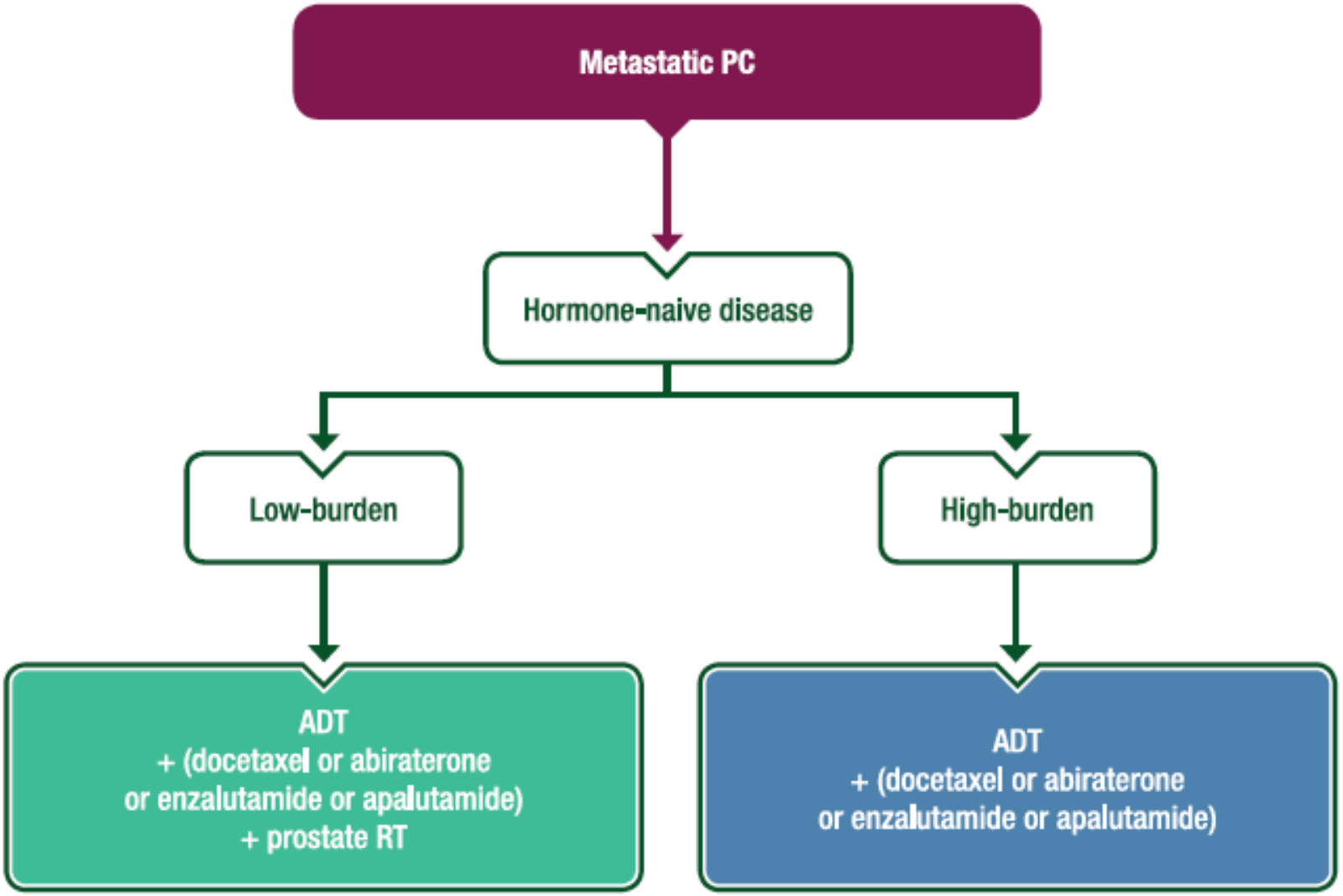
Radiatio + systemische Therapie bei **lokal begrenzter** Hochrisikoerkrankung

- „External beam radiotherapy (RT) plus ADT – abiraterone/prednisone - is recommended for men with very high-risk **M0** prostate cancer (defined by N1 disease or ≥ 2 risk factors among T3-T4, PSA > 40 ng/ml, Gleason score 8-10).“

Fizazi K et al (ESMO), Ann Oncol 2023;34:557-563

ESMO-Leitlinie 2020:

1L-Therapie bei metastasiertem Prostata-Ca.



Parker C et al (ESMO), Ann Oncol 2020;31:1119-1134

Definition von „metastatic burden“

Definition	Metastatic burden	Parameter
CHAARTED	Low	*No poor risk criteria*
CHAARTED	High	*≥ 4 bone metastases (≥ 1 beyond vertebral column and pelvis)* AND/OR *Visceral metastasis (M1c)*
LATITUDE	Low	*Maximal 1 risk criteria*
LATITUDE	High	*≥ 2 of the following criteria:* Gleason score ≥ 8 ≥ 3 bone metastases Visceral metastasis (M1c)

Müller AC et al (DEGRO und DKG-ARO), Strahlenther Onkol 2022;198:683-689

Prostatakarzinom – ESMO-Leitlinien 2023

Neuerungen

Prostatakarzinom – ESMO-Leitlinien 2023

Metastasierte **hormonsensitive** Erkrankung

- „**ADT-docetaxel-abiraterone/prednisone** is recommended as first-line treatment for fit men with de novo **metastatic** hormone-sensitive prostate cancer (mHSPC), especially in those with multiple bone metastases (>3) or visceral metastases.
- **ADT-docetaxel-darolutamide** is also recommended as first-line treatment of mHSPC, including patients with de novo mHSPC and those who have progressed to metastatic disease.“

Fizazi K et al (ESMO), Ann Oncol 2023;34:557-563

Prostatakarzinom – ESMO-Leitlinien 2023

Metastasierte **hormonsensitive** Erkrankung

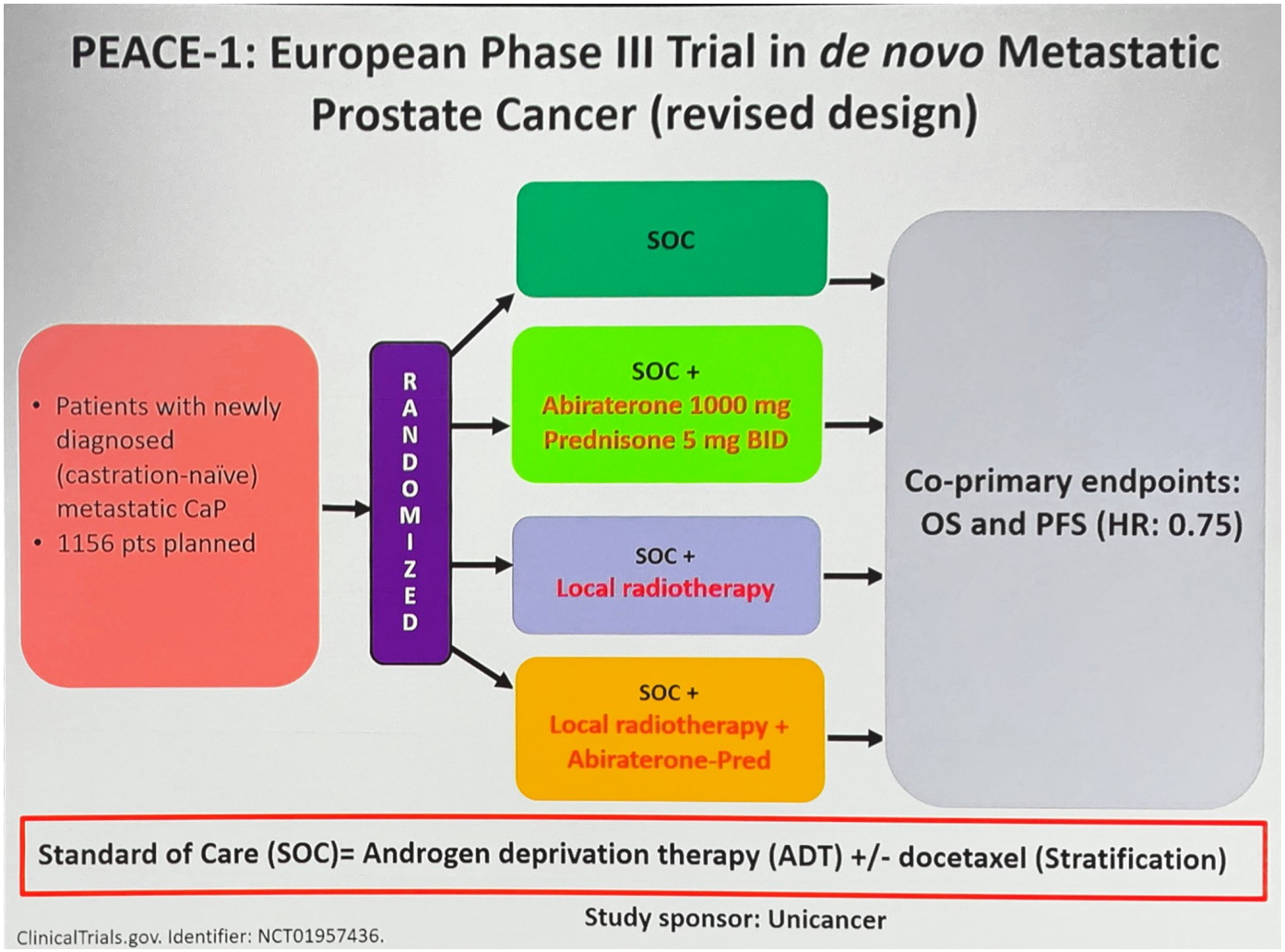
- „Other treatment options for men with mHSPC:
  - ADT-abiraterone+prednisone
  - ADT-apalutamide or
  - ADT-enzalutamide“

- „In men with mHSPC, ADT alone should be used only in vulnerable men who cannot tolerate treatment intensification.“

Fizazi K et al (ESMO), Ann Oncol 2023;34:557-563

ADT + Docetaxel + Abirateron First-Line

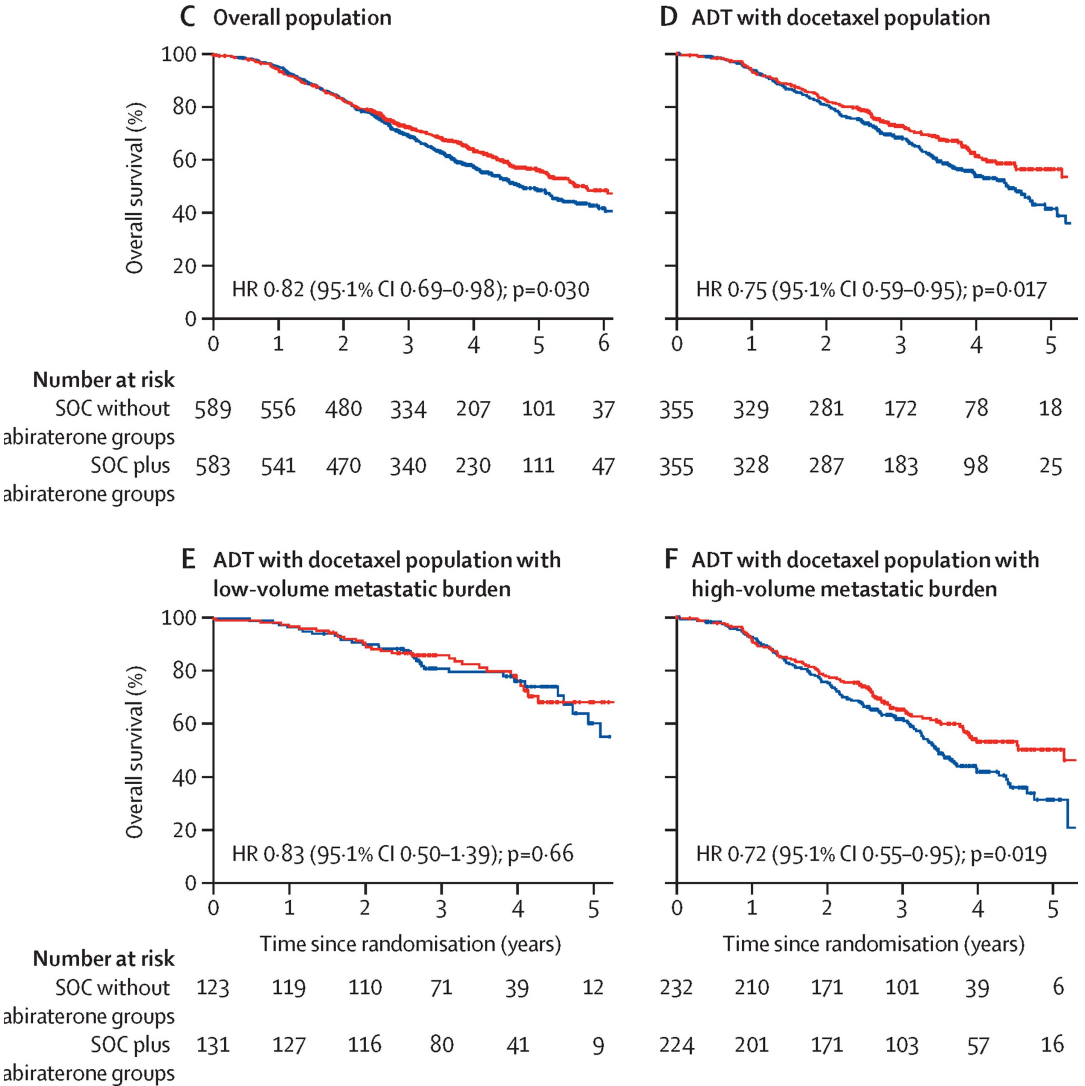
Metastasierte **hormonsensitive** Erkrankung



Fizazi K et al (PEACE-1), Lancet 2022;399:1695-1707

ADT + Docetaxel + Abirateron First-Line

Metastasierte **hormonsensitive** Erkrankung



"Combining androgen deprivation therapy, docetaxel, and abiraterone in de novo **metastatic** castration-sensitive prostate cancer **improved OS and radiographic PFS** with a modest increase in toxicity, mostly hypertension. This triplet therapy could become a standard of care for these patients."

Fizazi K et al (PEACE-1), Lancet 2022;399:1695-1707

Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer

Metastasierte **hormonsensitive** Erkrankung

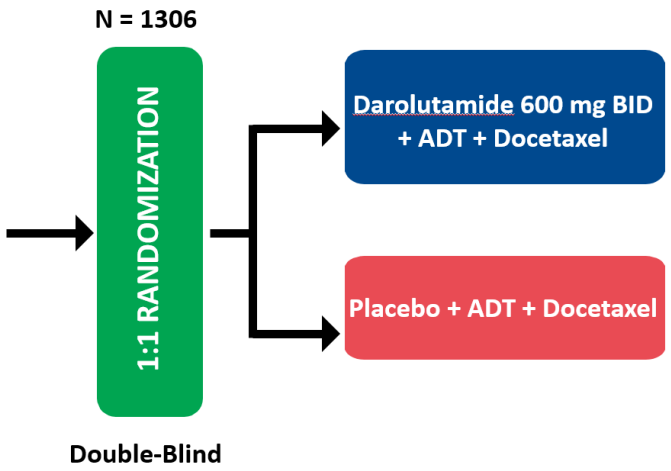
ARASENS Study Design, Phase 3 Randomized Controlled trial

Broad patient population

Key Eligibility Criteria
Castration sensitive
Metastatic disease
ECOG PS 0 or 1
Candidates for ADT and docetaxel

Exclusion Criteria
Prior treatment with enzalutamide, apalutamide, darolutamide, abiraterone acetate, ketoconazole, chemotherapy, or immunotherapy.

Stratifications
Extent of disease (M1a-M1c)
Alkaline phosphatase concentration



Primary endpoint
- Overall Survival

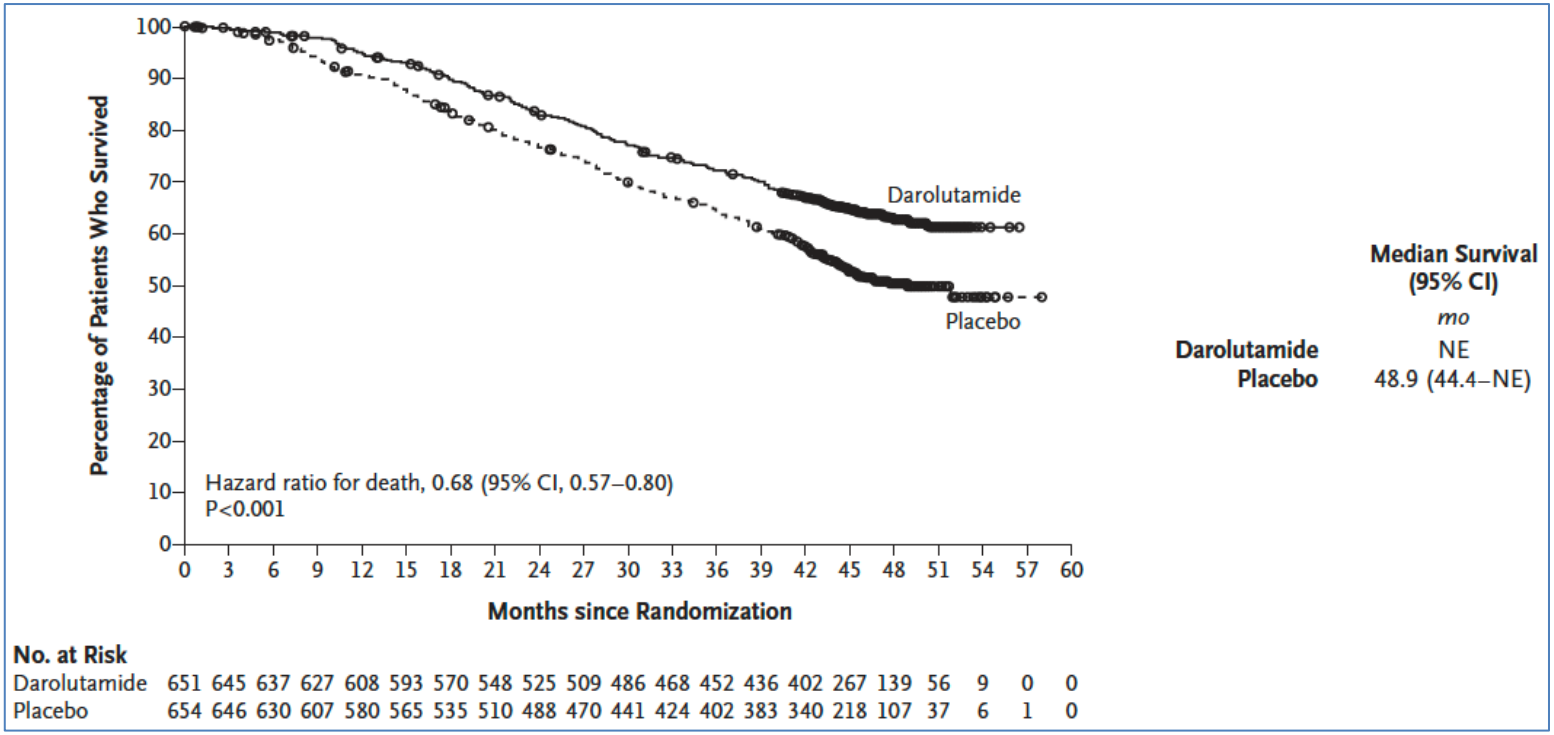
Secondary end points
- Time to castration-resistance
- Time to initiation of subsequent
- therapy
- Symptomatic skeletal event free survival (SSE-FS)
- Time to first symptomatic skeletal event (SSE)
- Time to initiation of opioid use ≥7 days
- Time to pain progression
- Time to worsening of physical symptoms of disease (NCCN-FACT FPSI-17)
- Safety and tolerability

Smith MR et al (ARASENS), N Engl J Med 2022;386:1132-1142

Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer

Metastasierte **hormonsensitive** Erkrankung

- International, Phase 3, metast. hormonsensitives PCa (n = 1306): **Darolutamid** (2x300 mg/d) vs Placebo, jeweils in **Kombination mit Androgendeprivation und Docetaxel**



Smith MR et al (ARASENS), N Engl J Med 2022;386:1132-1142

Prostatakarzinom – ESMO-Leitlinien 2023

Metastasierte **hormonrefraktäre** Erkrankung

- Docetaxel is recommended for men with mCRPC
- In patients with mCRPC in the post-docetaxel setting, abiraterone, enzalutamide and cabazitaxel are recommended options

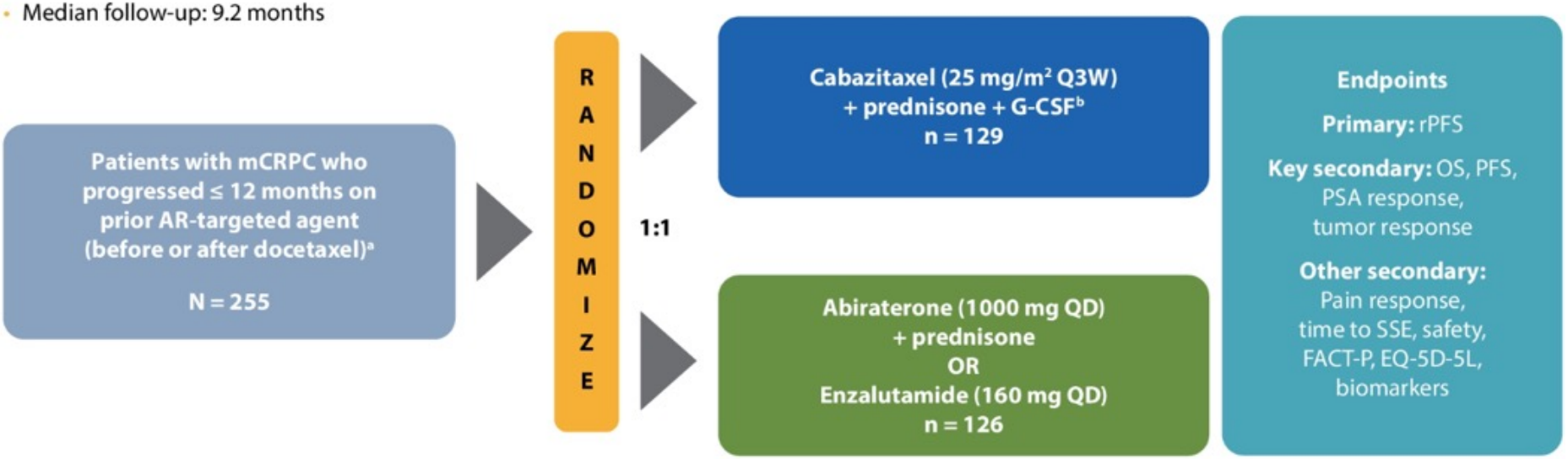
Fizazi K et al (ESMO), Ann Oncol 2023;34:557-563

Cabazitaxel versus Abiraterone or Enzalutamide in Metastatic Prostate Cancer

Metastasierte **hormonrefraktäre** Erkrankung

- CARD-Studie

- Multicenter, randomized, open-label study
- Enrollment: Nov 2015 – Nov 2018
- Median follow-up: 9.2 months



Stratification factors:

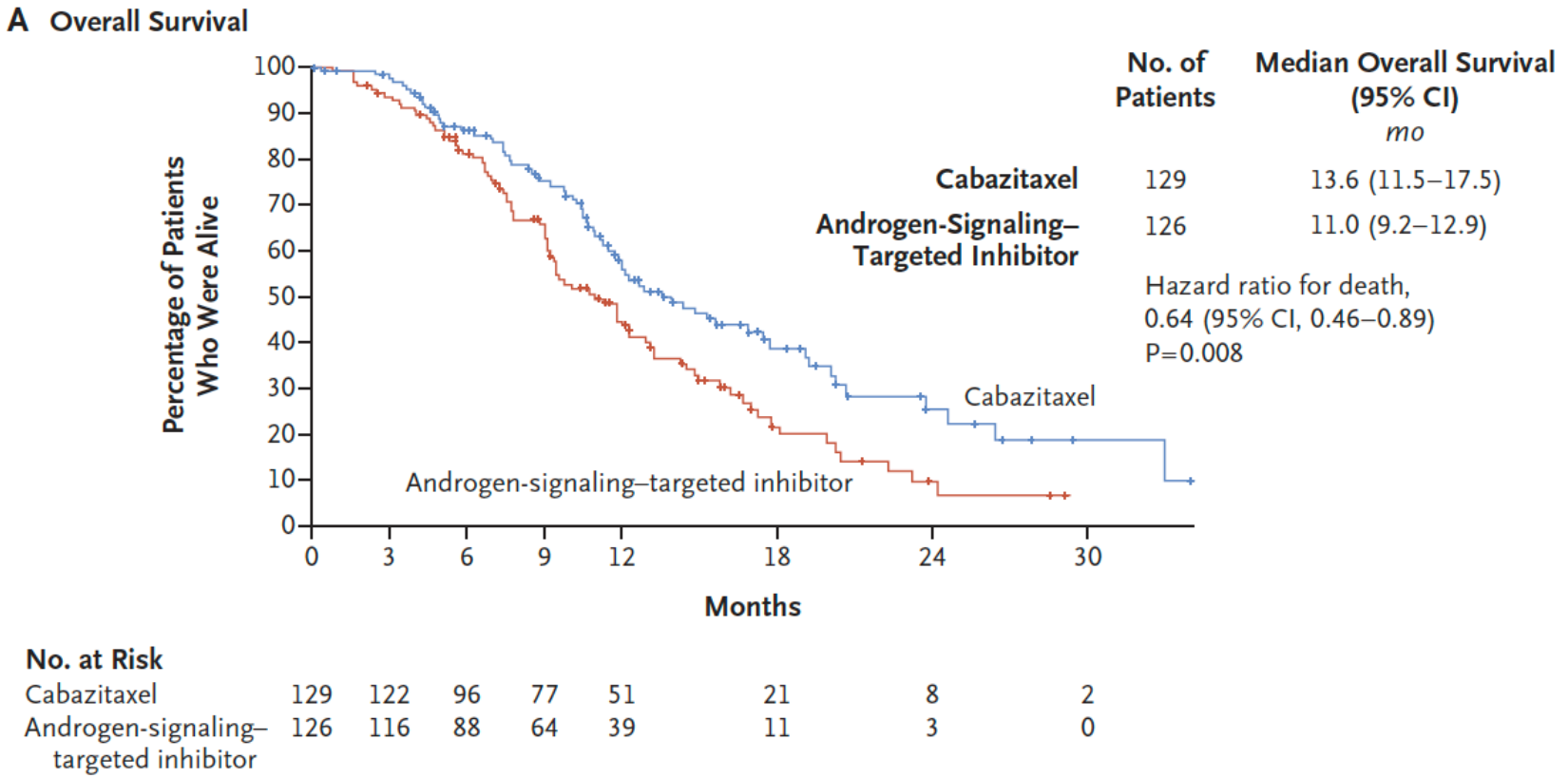
- ECOG PS (0/1 vs 2)
- time to disease progression (≤ 6 vs > 6–12 months)
- timing of previous alternative AR targeted agent (before vs after docetaxel)

de Wit R et al (CARD), N Engl J Med 2019;381:2506-2518

Cabazitaxel versus Abiraterone or Enzalutamide in Metastatic Prostate Cancer

Metastasierte **hormonrefraktäre** Erkrankung

- CARD-Studie



de Wit R et al (CARD), N Engl J Med 2019;381:2506-2518

Androgen receptor splice variant-7 expression emerges with castration resistance in prostate cancer

Adam Sharp,[1,2] Ilsa Coleman,[3] Wei Yuan,[1] Cynthia Sprenger,[4] David Dolling,[1] Daniel Nava Rodrigues,[1] Joshua W. Russo,[5] Ines Figueiredo,[1] Claudia Bertan,[1] George Seed,[1] Ruth Riisnaes,[1] Takuma Uo,[4] Antje Neeb,[1] Jonathan Welti,[1] Colm Morrissey,[4] Suzanne Carreira,[1] Jun Luo,[6] Peter S. Nelson,[3,4] Steven P. Balk,[5] Lawrence D. True,[4] Johann S. de Bono,[1,2] and Stephen R. Plymate[4,7]

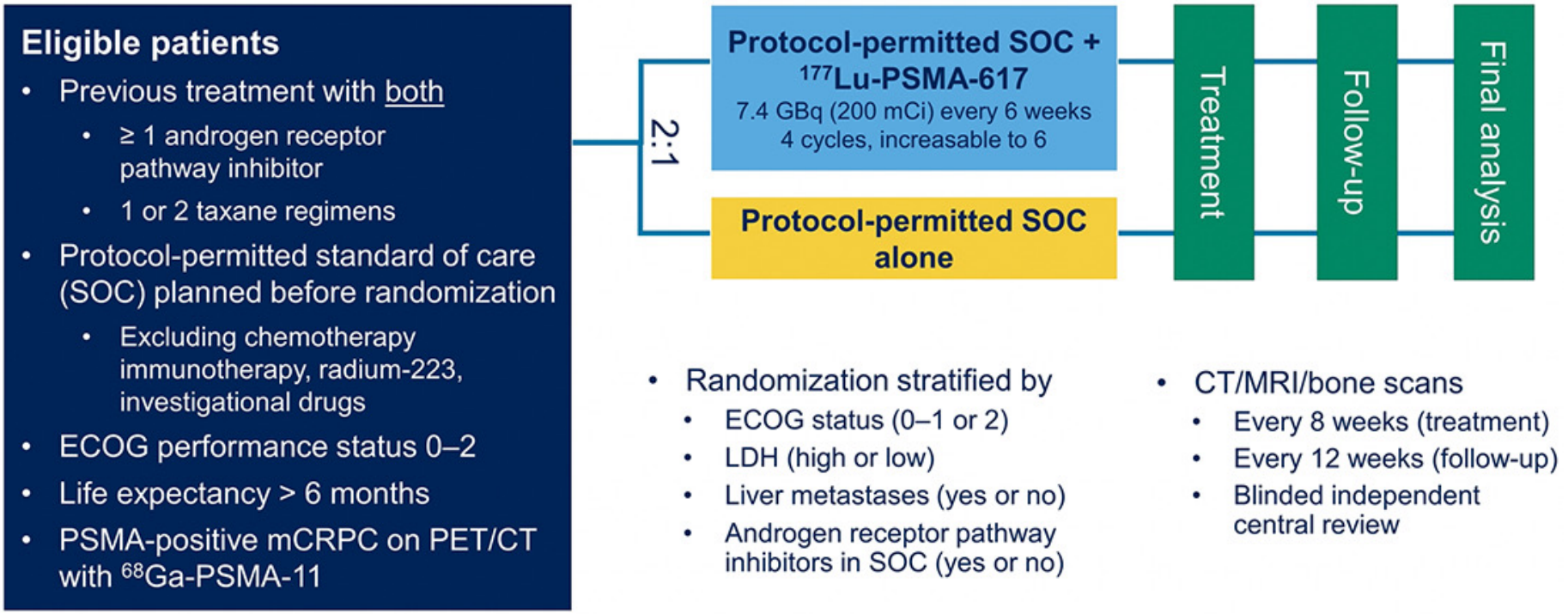
- Wechsel von Enzalutamid auf Abirateron oder umgekehrt bei Progreß?
- **AR-V7** < 1% im Primärtumor => 75% nach Androgendeprivation => weiterer Anstieg unter Abi/Enza
- **Vermittelt Resistenz gegen beide Medikamente**

Sharp A et al, J Clin Invest 2019;129:192-208

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

Metastasierte **hormonrefraktäre** Erkrankung

- VISION-Studie

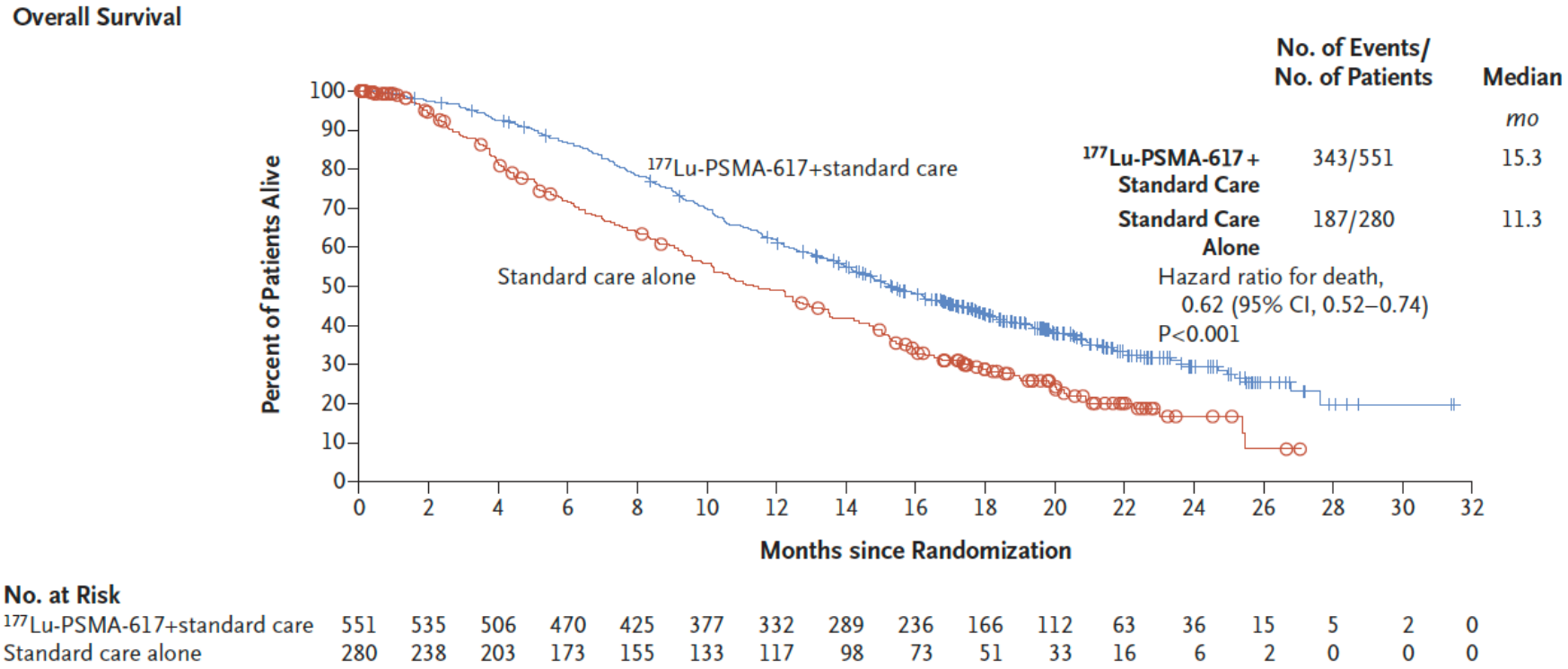


Sartor O et al (VISION), N Engl J Med 2021;385:1091-1103

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

Metastasierte **hormonrefraktäre** Erkrankung

- VISION-Studie



Sartor O et al (VISION), N Engl J Med 2021;385:1091-1103

Prostatakarzinom – ESMO-Leitlinien 2023

Metastasierte **hormonrefraktäre** Erkrankung

- In patients with mCRPC **who have received** a novel androgen receptor axis inhibitor (**abiraterone, apalutamide, darolutamide *or* enzalutamide**) and **docetaxel**, the following treatments should be used in patients who are considered fit enough to receive these treatments:
  - **177Lu-PSMA-617** in men with cancer expressing PSMA on PET-PSMA and without PSMA non-expressing lesions
  - **Cabazitaxel**

Fizazi K et al (ESMO), Ann Oncol 2023;34:557-563

Prostatakarzinom – ESMO-Leitlinien 2023

Metastasierte **hormonrefraktäre** Erkrankung
mit **BRCA1/2-Mutation**

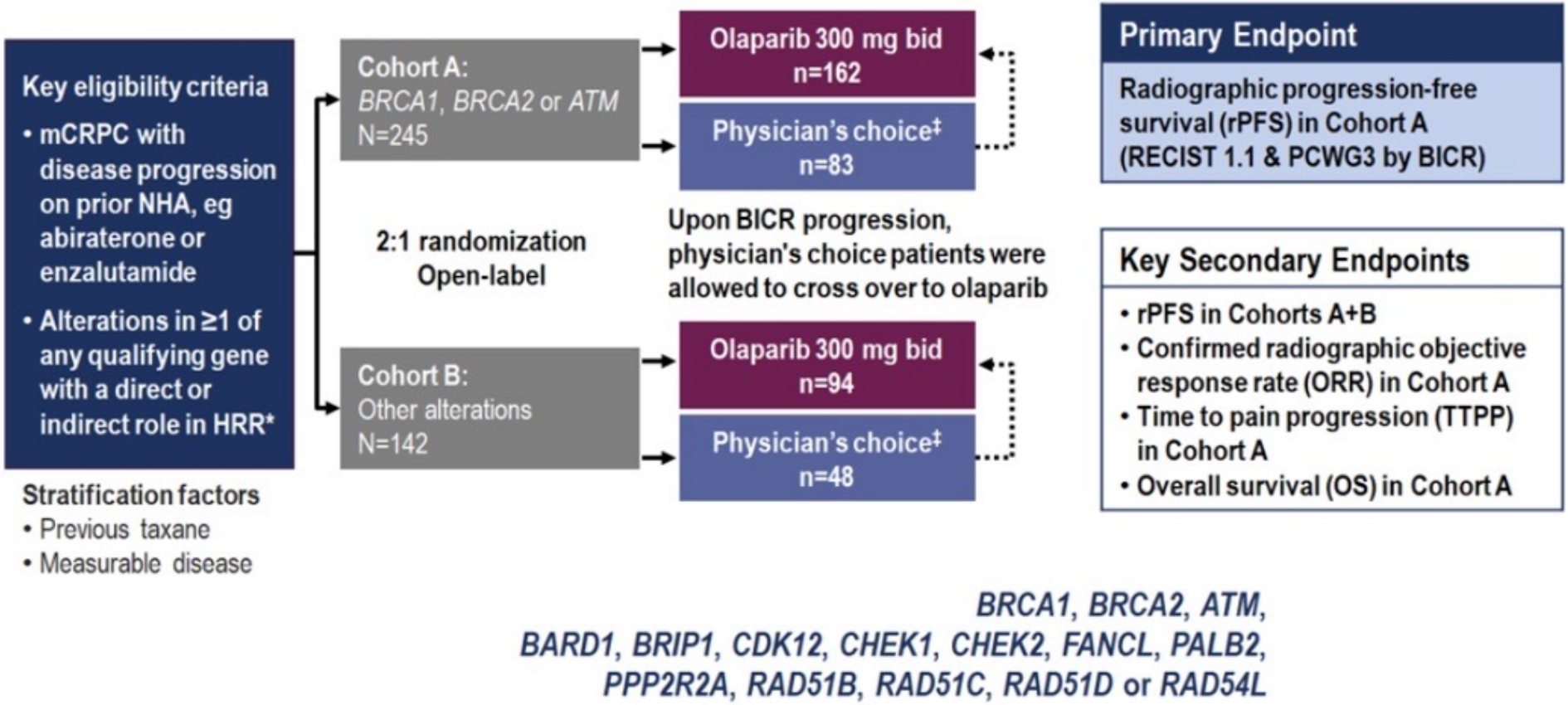
- „Olaparib should be considered **after** novel androgen receptor axis inhibitors (**with or without prior taxane** treatment) for patients with mCRPC and BRCA1/2 alterations.“

Fizazi K et al (ESMO), Ann Oncol 2023;34:557-563

Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

Metastasierte **hormonrefraktäre** Erkrankung mit **BRCA1/2-Mutation**

- PROfound Studie

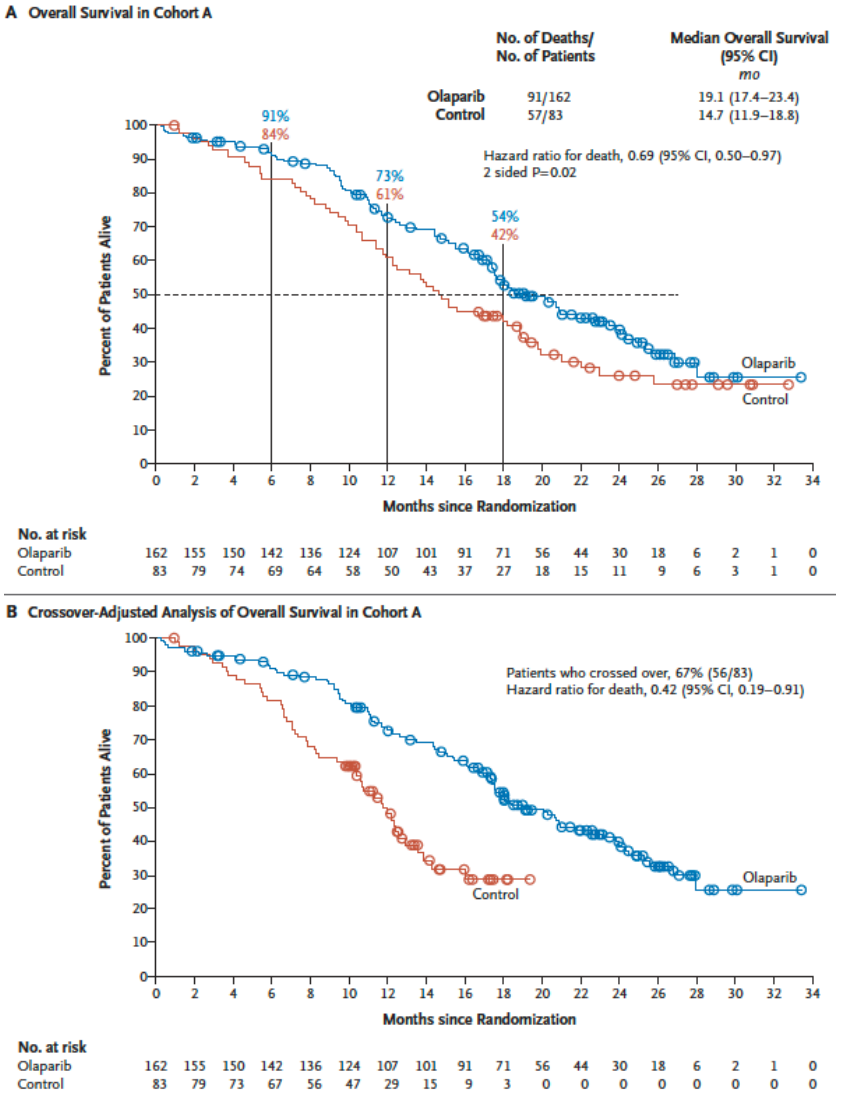


Husain M et al (PROfound), N Engl J Med 2020;383:2345-2357

Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

Metastasierte **hormonrefraktäre** Erkrankung mit **BRCA1/2-Mutation**

- PROfound Studie



Husain M et al (PROfound), N Engl J Med 2020;383:2345-2357

Hormonrefraktäres Prostatakarzinom: NCCN 2023

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2023
Prostate Cancer

NCCN Guidelines Index
Table of Contents
Discussion

SYSTEMIC THERAPY FOR M1 CRPC: ADENOCARCINOMA[iii,kkk,lll]

No prior docetaxel/no prior novel hormone therapy[mmm]

- Preferred regimens
  - Abiraterone[u,nnn,ooo] (category 1)
  - Docetaxel[fff,ppp] (category 1)
  - Enzalutamide[u] (category 1)
- Useful in certain circumstances
  - Niraparib/abiraterone[u,fff,zzz] for BRCA mutation (category 1)
  - Olaparib/abiraterone[u,fff,nnn,qqq] for BRCA mutation (category 1)
  - Radium-223[rrr] for symptomatic bone metastases (category 1)
  - Sipuleucel-T[fff,sss] (category 1)
  - Talazoparib/enzalutamide for HRRm[u,fff,yyy] (category 1)
- Other recommended regimens
  - Other secondary hormone therapy[u]

Prior novel hormone therapy/no prior docetaxel[mmm,ttt]

- Preferred regimens
  - Docetaxel (category 1)[fff]
- Useful in certain circumstances
  - Cabazitaxel/carboplatin[fff,jjj]
  - Niraparib/abiraterone[u,fff,zzz] for BRCA mutation (category 2B)
  - Olaparib for HRRm[uuu] (category 1)
  - Radium-223[rrr] for symptomatic bone metastases (category 1)
  - Rucaparib for BRCA mutation[vvv]
  - Sipuleucel-T[fff,sss]
  - Talazoparib/enzalutamide for HRRm[u,fff,yyy] (category 2B)
- Other recommended regimens
  - Abiraterone[u,nnn]
  - Abiraterone[u] + dexamethasone[nnn,www]
  - Enzalutamide[u]
  - Other secondary hormone therapy[u]

Prior docetaxel/no prior novel hormone therapy[mmm]

- Preferred regimens
  - Abiraterone[u,nnn] (category 1)
  - Cabazitaxel[fff]
  - Enzalutamide[u] (category 1)
- Useful in certain circumstances
  - Cabazitaxel/carboplatin[fff,jjj]
  - Mitoxantrone for palliation in symptomatic patients who cannot tolerate other therapies[fff]
  - Niraparib/abiraterone[u,fff,zzz] for BRCA mutation
  - Olaparib/abiraterone[u,fff,nnn,qqq] for BRCA mutation
  - Radium-223[rrr] for symptomatic bone metastases (category 1)
  - Sipuleucel-T[fff,sss]
  - Talazoparib/enzalutamide for HRRm[u,fff,yyy]
- Other recommended regimens
  - Other secondary hormone therapy[u]

Prior docetaxel and prior novel hormone therapy[mmm,ttt]

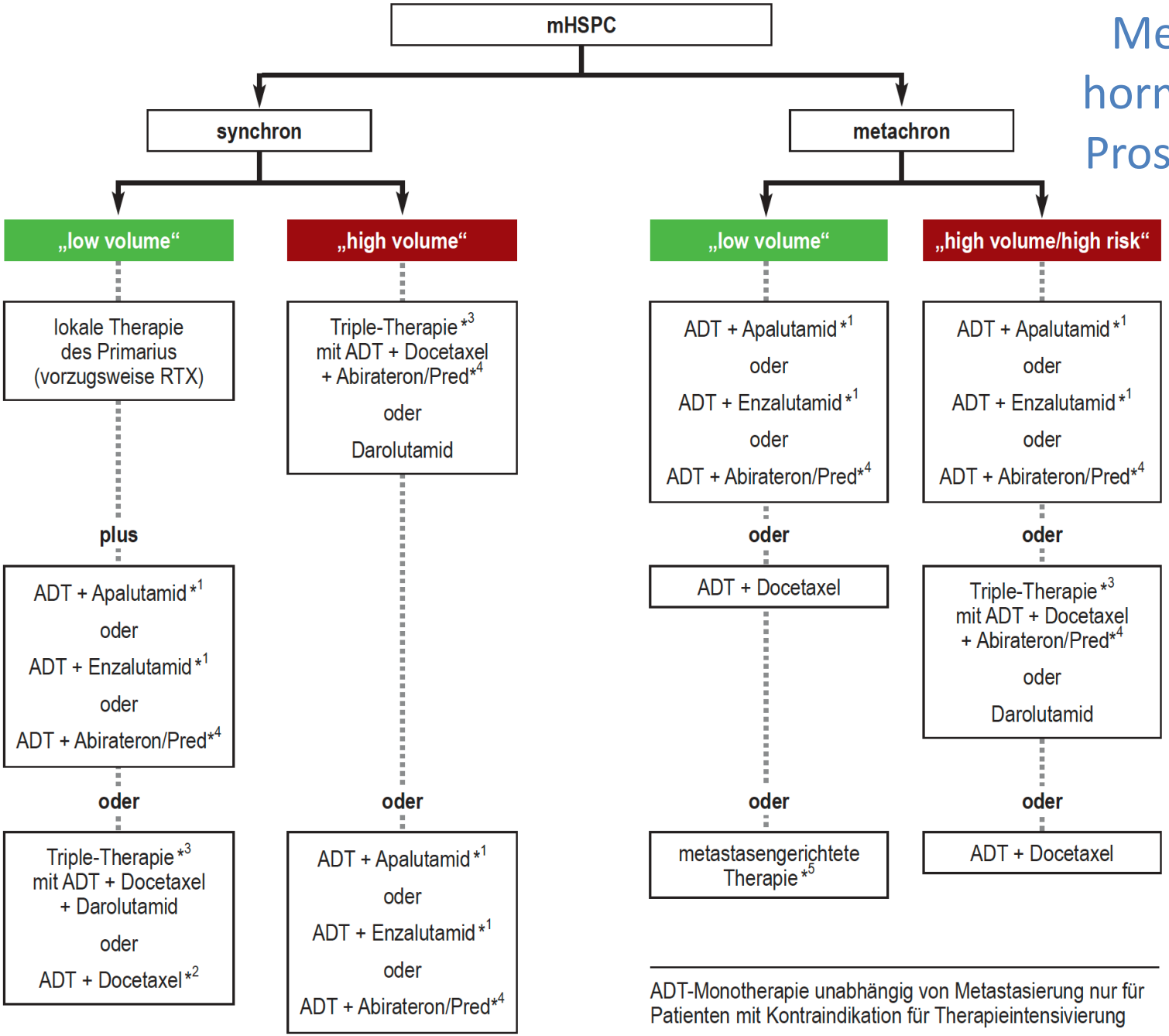
- Useful in certain circumstances
  - Lutetium Lu 177 vipivotide tetraxetan (Lu-177–PSMA-617) for PSMA-positive metastases[xxx] (category 1)

(The following systemic therapies are category 2B if visceral metastases are present)

- Preferred regimens
  - Cabazitaxel[fff,ooo] (category 1)
  - Docetaxel rechallenge[fff]
- Useful in certain circumstances
  - Cabazitaxel/carboplatin[fff,jjj]
  - Mitoxantrone for palliation in symptomatic patients who cannot tolerate other therapies[fff]
  - Olaparib for HRRm[ooo,uuu] (category 1)
  - Pembrolizumab for MSI-H, dMMR, or TMB ≥10 mut/Mb[fff]
  - Radium-223[rrr] for symptomatic bone metastases[ooo] (category 1)
  - Rucaparib for BRCA mutation[vvv]
- Other recommended regimens
  - Abiraterone[u,nnn]
  - Enzalutamide[u]
  - Other secondary hormone therapy[u]

www.nccn.org

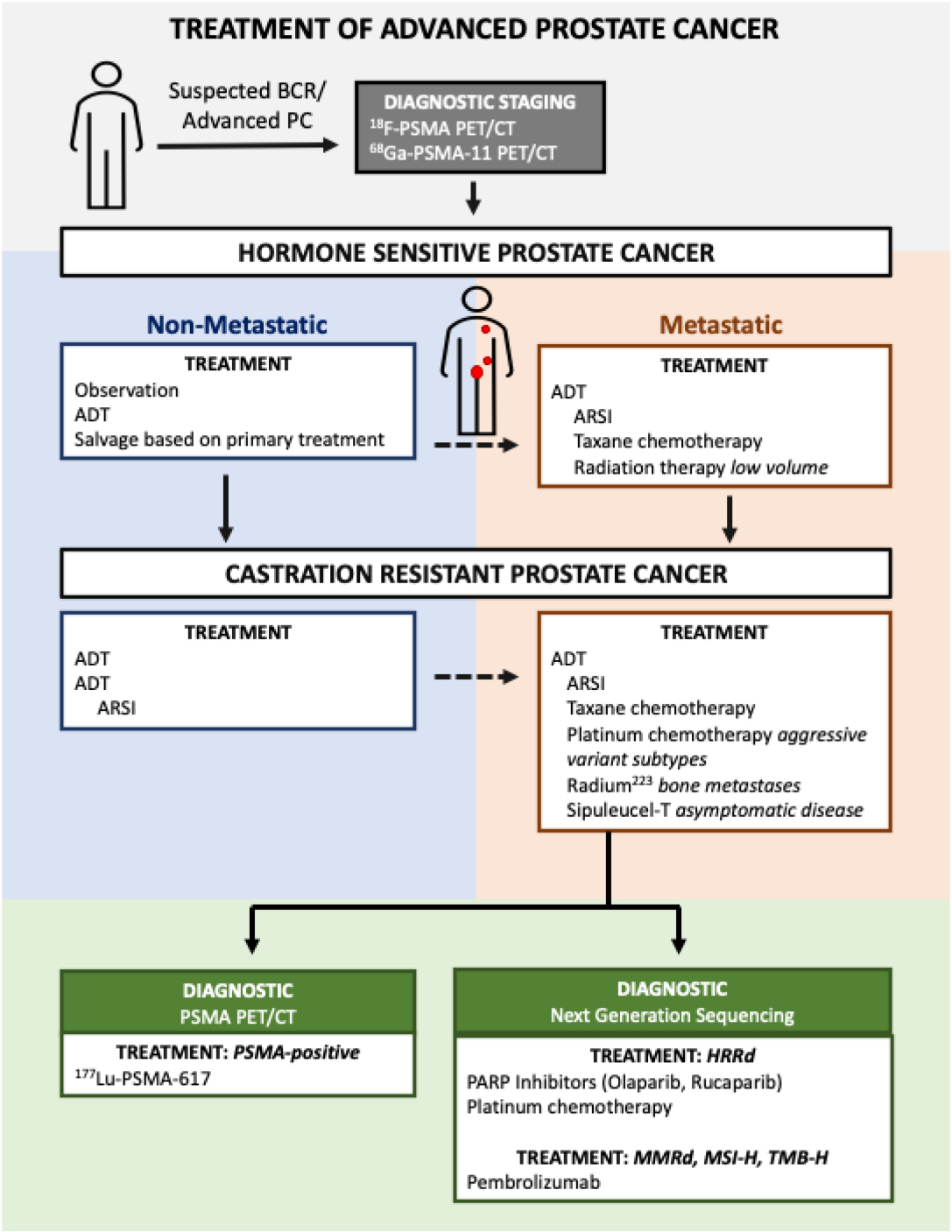
Metastasiertes hormonsensitives Prostatakarzinom



ADT-Monotherapie unabhängig von Metastasierung nur für Patienten mit Kontraindikation für Therapieintensivierung

Merseburger AS et al, Dt Ärztebl 2022;119:622-632

Prostatakarzinom: Therapiealgorithmus 2023



Gillette CM et al, Cancers 2023;15:2552

Prostatakarzinom: Zulassungsstatus 2023

- Abirateron/Prednison ✓
- Apalutamid ✓
- Bicalutamid ✓
- Darolutamid ✓
- Enzalutamid ✓
- Olaparib ✓
- Cabazitaxel ✓
- Docetaxel ✓
- Mitoxantron/Pred ✓
- Estramustin **nicht mehr gelistet**
- GnRH-Agonisten (Buserelin ✓, Goserelin ✓, Leuprorelin ✓, Triptorelin ✓)
- GnRH-Antagonisten (Abarelix **nicht mehr gelistet**, Degarelix ✓, Relugolix ✓)
- Cabozantinib **-**
- 177Lu-PSMA-617 ✓
- Radium-223-dichlorid ✓

Prostatakarzinom: Nachsorge nach kurativ intendierter Lokaltherapie (AWMF 2021)

Empfehlungsgrad **A**	a. Asymptomatische Patienten nach lokaler kurativ intendierter Therapie sollen innerhalb von zwölf Wochen nach Ende der Therapie eine Nachsorgeuntersuchung erhalten.
Empfehlungsgrad **B**	b. Bei asymptomatischen Patienten sollten die Untersuchungen innerhalb der ersten zwei Jahre vierteljährlich, im 3. und 4. Jahr halbjährlich und vom 5. Jahr an in jährlichen Intervallen wiederholt werden.
Empfehlungsgrad **A**	Bei asymptomatischen Patienten nach kurativ intendierter Therapie soll die Bestimmung des Serum-PSA-Werts zur Nachsorge eingesetzt werden.
Level of Evidence **4**	Bei Patienten ohne biochemisches Rezidiv ist die DRU in der Nachsorge des Prostatakarzinoms nicht routinemäßig indiziert.
Empfehlungsgrad **A**	Bildgebende Verfahren sollen nur dann eingesetzt werden, wenn therapeutische Maßnahmen möglich sind und/oder Symptome bestehen.

https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Prostatatkarzinom/Version_6/LL_Prostatakarzinom_Langversion_6.2.pdf

Prostatakarzinom: Nachsorgeempfehlung der Deutschen Krebsgesellschaft

- Bei Patienten ohne Metastasen sind Untersuchungen im Abstand von 3-6 Monaten ausreichend.
- Bei Patienten mit Metastasen, deren PSA unter 4 ng/ml liegt, deren Allgemeinzustand gut ist und die keine oder nur milde Symptome (z. B. Schmerzen) haben, genügen Kontrolluntersuchungen alle 6 Monate.
- Bei Patienten im kastrationsresistenten Stadium werden die Kontrollintervalle individuell festgelegt.

https://www.krebsgesellschaft.de/onko-internetportal/basis-informationen-krebs/krebsarten/prostatakrebs/therapie/behandlung-im-fortgeschrittenen-stadium.html

Prostatakarzinom: Studienübersicht (1)

Randomisierte Phase-III-Studien zur Hormonchemotherapie beim metastasierten hormonsensitiven Prostatakarzinom

N	medianes Follow Up (Monate)	Kontrollarm	experimenteller Arm	Anteil der Patienten*[1]	Gesamtüberleben: Schätzung in Monaten	Gesamtüberleben: Hazard Ratio [95-%-KI] p-Wert
CHAARTED (13)						
790	53,7	ADT	ADT + Doce	65 %	57,6 versus 47,2	HR 0,72 [0,59; 0,89] p = 0,0018
STAMPEDE* (14)						
1 002	78,2	ADT	ADT + Doce	43 %	60,0 versus 45,0	HR 0,81*[2] [0,69; 0,95] p = 0,009
LATITUDE (7)						
1 199	51,8	ADT	ADT + Abi + Pred	100 %	53,3 versus 36,5	HR 0,66 [0,56; 0,78] p < 0,0001
STAMPEDE*[2] (19)						
901	73	ADT	ADT + Abi + Pred	52 %	79,2 versus 46,6	HR 0,60* [0,50; 0,71] p < 0,001
ENZAMET (20)						
1 125	68	ADT + Bicalutamid (+ Doce parallel 45 %)	ADT + Enza (+ Docetaxel parallel 45 %)	52 %	N.E. versus 73,2	HR 0,70 [0,58; 0,84] p < 0,0001
ARCHES (21)						
1 150	44,6	ADT (+ Vortherapie Doce 18 %)	ADT + Enza (+ Vortherapie Doce 18 %)	63 %	N.E. versus N.E.	HR 0,66 [0,53; 0,81] p < 0,001
TITAN (22)						
1 052	44	ADT (+ Vortherapie Doce 11 %)	ADT + Apa (+ Vortherapie Doce 18 %)	63 %	N.E. versus 52,2	HR 0,65 [0,53; 0,79] p < 0,0001

Merseburger AS et al, Dt Ärztebl 2022;119:622-632

Prostatakarzinom: Studienübersicht (2)

Eckdaten zu den Triple-Therapie-Studien PEACE-1 und ARASENS

	PEACE-1		ARASENS	
	ADT/Doce/Abi	ADT/Doce	ADT/Doce/Daro	ADT/Doce
Patientencharakteristika				
de-novo-metastasierte Patienten (%)	100	100	85,7	86,5
Gleason ≥ 8 (%)	77	79	77,6	78,9
hohe Tumorlast (%)	63	65	k.A.	
viszerale Metastasierung (%)	12	13	17,1	18,0
Ergebnisse				
Gesamtüberleben (Jahre; KI)	N.E. (4,5 – N.E.)	4,4 (3,8 – 4,9)	N.E.	4,1 (3,7 – N.E.)
– hohe Tumorlast	5,1 (3,8 – N.E.)	3,5 (3,2 – 4,0)	k.A.	
– niedrige Tumorlast	N.E. (N.E. – N.E.)	N.E. (4,7 – N.E.)	k.A.	

Merseburger AS et al, Dt Ärztebl 2022;119:622-632