Med Uni Graz *Pioneering Minds*

Radiotherapie im Kontext der antihormonellen Therapie

Von PARP-Inhibitoren (und weiteren Pfeilen) im Köcher der/s internistischen Onkolog*in!

Leo Edlinger

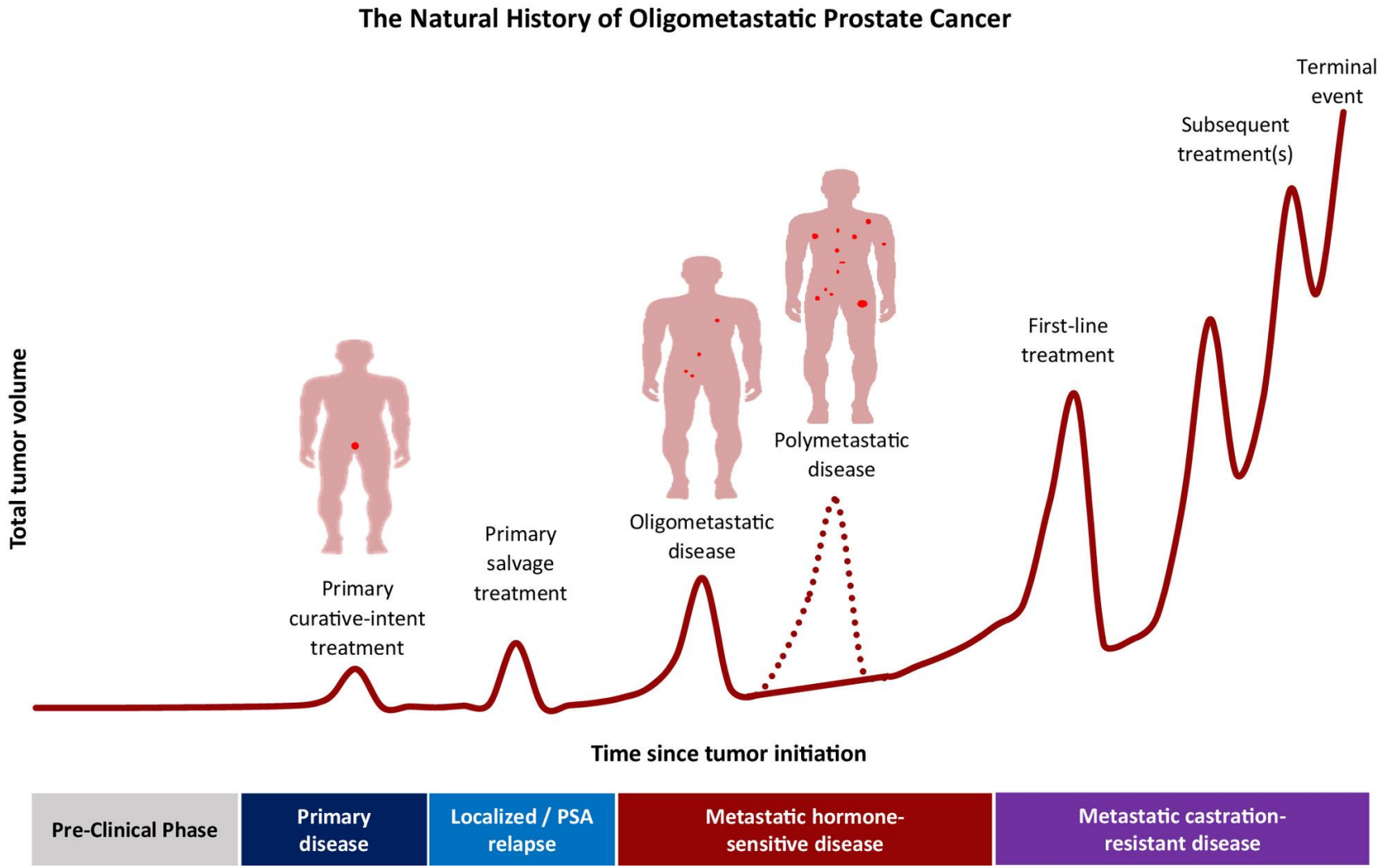
Onkologie, Meduni Graz

Potentielle Interessenskonflikte

Reisekosten / Kongressteilnahme: AstraZeneca, Johnson & Johnson, Roche, PharmaMar, Daiichi Sankyo, Servier, Pierre Fabre, MSD, Bayer

Honoraria: Bayer

Oligometastasiertes Prostatakarzinom



Rao A. et al. Am Soc Clin Oncol Educ Book. 2019

Oligometastasiertes Prostatakarzinom

7.60	Evidenzbasiertes Statement	neu 2021
Evidenzlevel 1 -	Unter einem oligometastasierten Prostatakarzinom wird ein Tumor mit maximal 4 in konventioneller Bildgebung (Skelettszintigraphie und CT oder MRT) nachweisbaren Knochenmetastasen ohne extraossäre viszerale Metastasen verstanden.	

Study	Type	Sample Size, No.	Cutoff for Oligometastases, No.	Location of Metastases	Imaging Modality
Singh et al[5]	R; NA	369	≤ 5	Any	^{99m}Tc bone scan
Berkovic et al[14]	P; SA	24	≤ 3	Bone or LN	^{99m}Tc bone scan, ^{18}F-FDG PET/CT, ^{11}C-choline PET/CT
Schick et al[15]	P; SA	50	≤ 4	NR	^{99m}Tc bone scan, ^{18}F-choline PET/CT, ^{11}C-acetate PET/CT
Decaestecker et al[16]	P; SA	50	≤ 3	Bone or LN	^{18}F-FDG PET/CT, ^{18}F-choline PET/CT
Jereczek-Fossa et al[17]	P; SA	69	≤ 1	LN	^{18}F-FDG PET/CT, ^{11}C-choline PET/CT, CT
Ost et al[18]	P; SA	119	≤ 3	Any	^{18}F-FDG PET/CT, ^{18}F-choline PET/CT
Ost et al[19]	P; RA	62	≤ 3	Any	^{18}F-choline PET/CT

Abbreviations: FDG, 18-fluorodeoxyglucose; LN, lymph node; NA, not applicable; NR, not reported; P, prospective; R, retrospective; RA, randomized; SA, single arm.

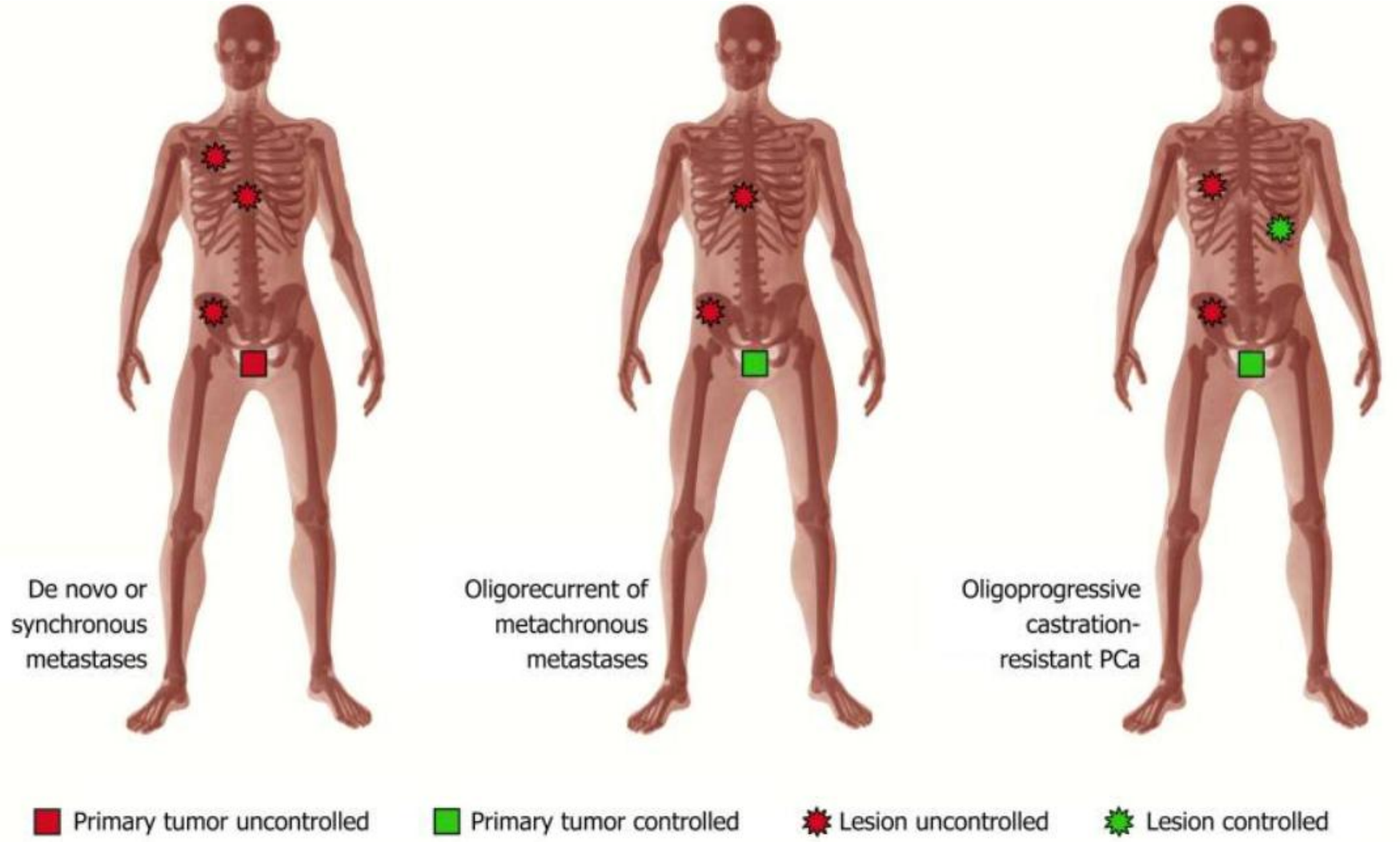
S3-Leitlinie Prostatakarzinom Langversion 8.1 2025
Rao A. et al. Am Soc Clin Oncol Educ Book. 2019

Oligometastasiertes Prostatakarzinom

Oligometastatic state	All metastatic prostate cancer with between one and 10 metastatic lesions. No uniform agreement on upper limit exists
De novo or synchronous oligometastasis	Initial presentation of an untreated primary prostate cancer with oligometastatic disease where the patient is hormone sensitive
Metachronous oligometastasis	Oligometastasis despite prior controlled primary prostate cancer treatment (eg, radical prostatectomy and radiotherapy)
Oligorecurrence	Recurrence of previously treated oligometastases within the vicinity of previous radical therapy such as the high-dose region of previous irradiation or resection. This may also apply to the prostate gland
Oligoprogressive	Progression of selected metastatic deposits, whilst other remain controlled by systemic therapy
Polymetastatic	Greater than four metastatic lesions from primary prostate cancer

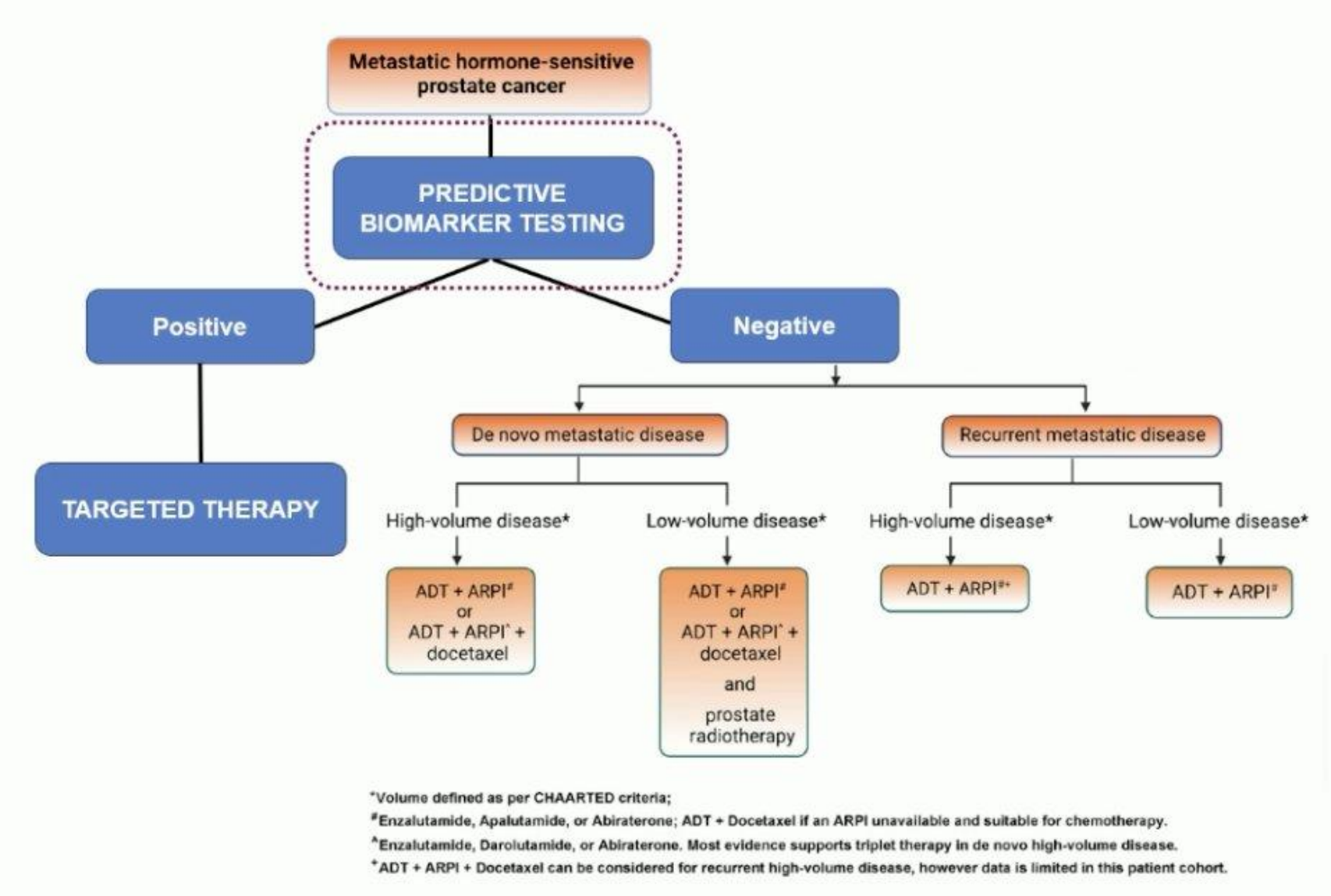
Connor MJ et al. Eur Urol Oncol. 2020

Oligometastasiertes Prostatakarzinom

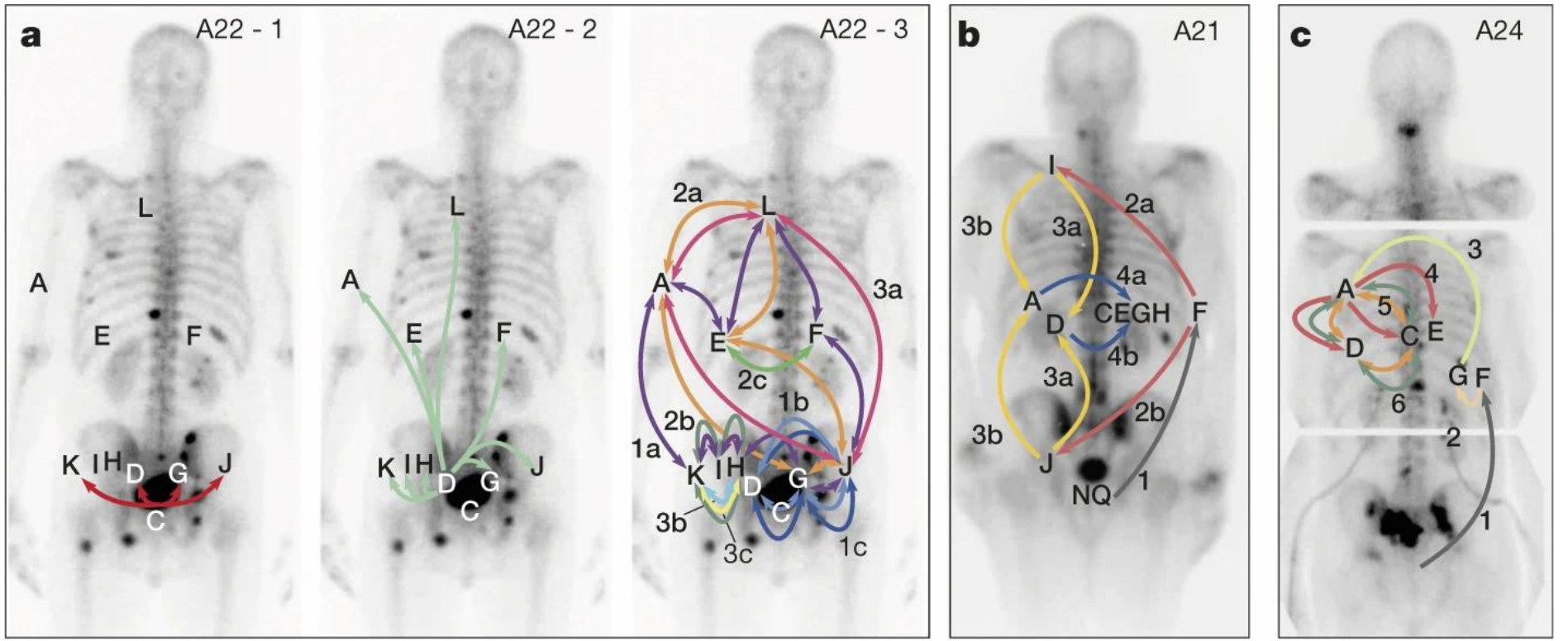


Palacios-Eito A. et al. World J Clin Oncol. 2019

Oligometastasiertes Prostatakarzinom



Oligometastasiertes Prostatakarzinom



A - L. humerus BM
D - Sem. vesicle
C - Prostate
E - L. adrenal

F - R. adrenal
G - Bladder
H - Pelvic LN
I - L. pelvic LN

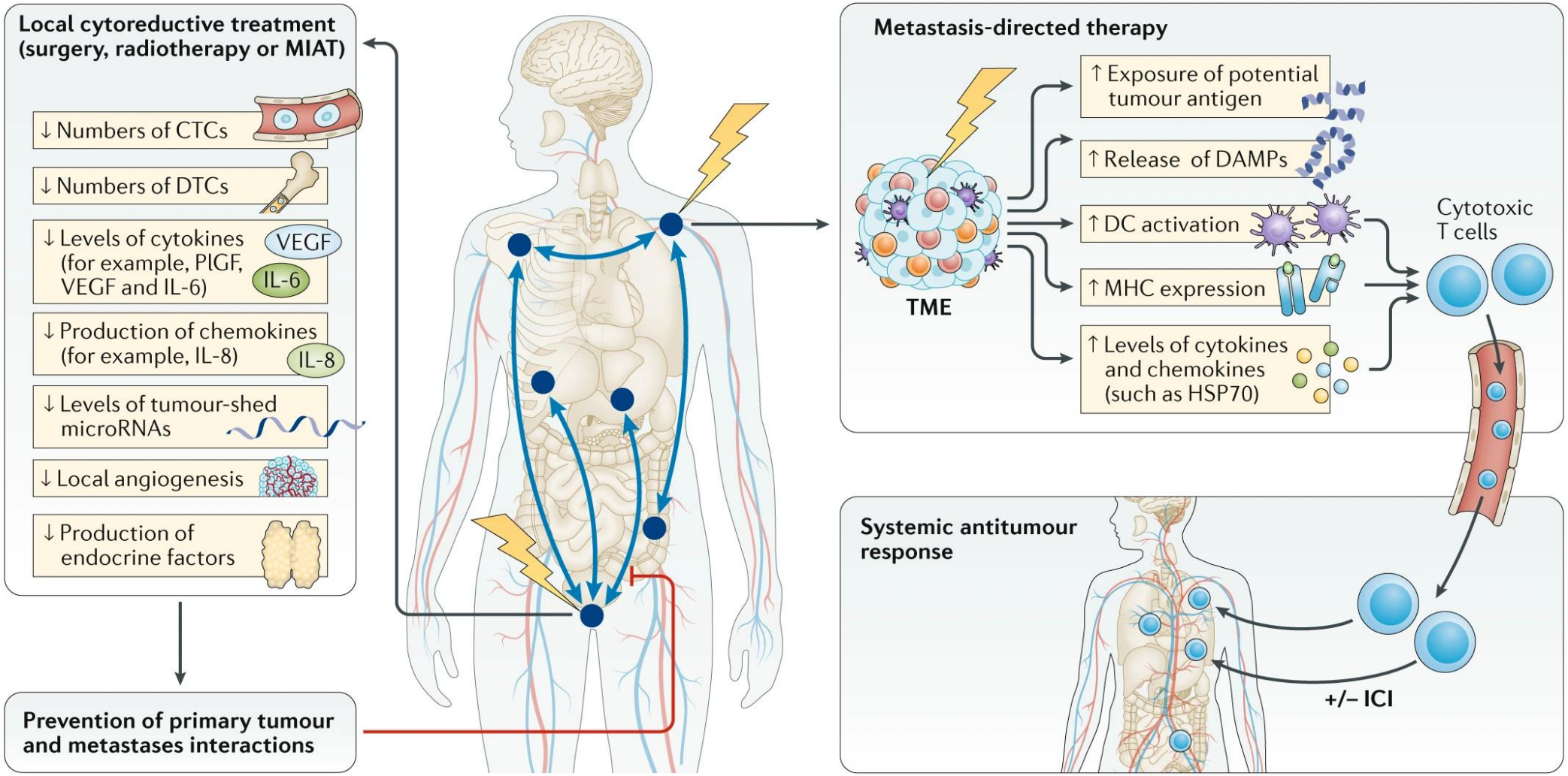
J - R. pelvic LN
K - L. pelvic LN
L - L. media. LN

A - L. rib
C - Liver
E - Liver
G - Liver
H - Liver
D - L. adrenal
F - R. rib nod.
I - L. clavicle
J - L. iliac crest
N - GL5 EPE
Q - GL3/5

A - R. axillary LN
C - R. diaphragm
D - R. rib
E - Xiphoid
F - L. lobe liver
G - Falciform ligam.

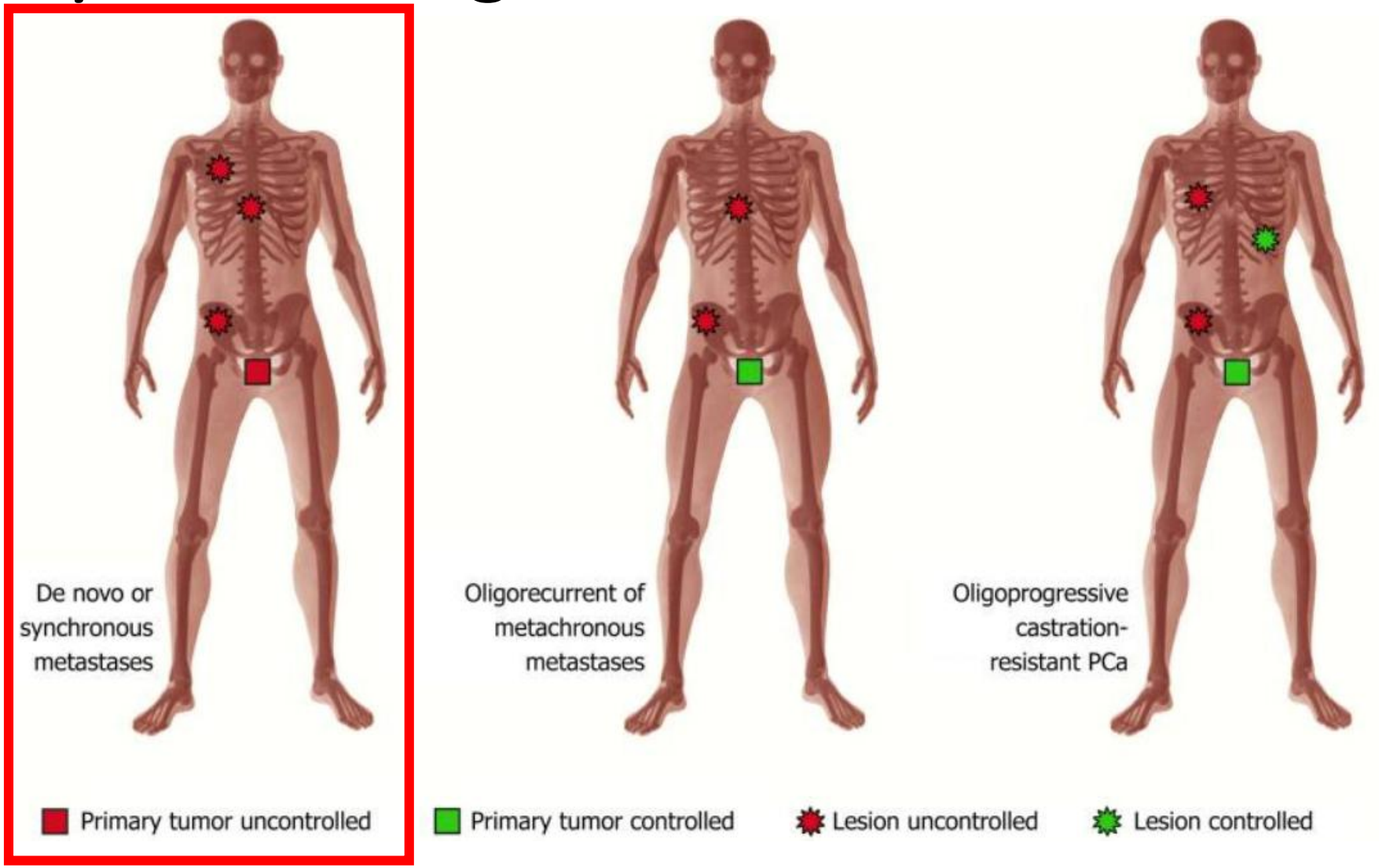
Gundem G. et al. Nature. 2015

Oligometastasiertes Prostatakarzinom



Connor, MJ et al. Nat Rev Clin Oncol 2020

Synchron oligometastasiertes HSPC



Palacios-Eito A. et al. World J Clin Oncol. 2019

Synchron oligometastasiertes HSPC

Clinical Outcomes of Combined Prostate- and Metastasis-Directed Radiation Therapy for the Treatment of De Novo Oligometastatic Prostate Cancer

Brandon S. Imber, MD,[a] Melissa Varghese, BA,[a] Debra A. Goldman, MS,[b] Zhigang Zhang, PhD,[b] Richard Gewanter, MD,[a] Ariel E. Marciscano, MD,[a] Borys Mychalczak, MD,[a] Daniel Gorovets, MD,[a] Marisa Kollmeier, MD,[a] Sean M. McBride, MD,[a] and Michael J. Zelefsky, MD[a,*]

47 patients with DNOPC with predominantly M1b disease received neoadjuvant, concurrent, and adjuvant ADT plus PDRT + ORT to 1 to 6 oligometastases. At 1- and 2-years post-RT, cumulative incidence of distant metastatic progression (DMP) was 21% and 32%, whereas overall survival was 90% and 87%, respectively. **After neoadjuvant ADT, 9 (19%) patients had undetectable PSA (<0.05 ng/mL), which increased to 32 (68%) after PDRT + ORT.** Overall 2-year incidence of BCR and development of castrate resistance were 23% and 36%, respectively.

Treatment: local RT, ADT and MDT to all M+ sites (up to 6), 68% with undetectable PSA

Imber BS et al. Advances Radiat Oncol 2020

Synchron oligometastasiertes HSPC

Multidisciplinary total eradication therapy (TET) in men with newly diagnosed oligometastatic prostate cancer

D. K. Reyes[1] · S. P. Rowe[1,2] · E. M. Schaeffer[3] · M. E. Allaf[1] · A. E. Ross[4] · C. P. Pavlovich[1] · C. Deville[5] · P. T. Tran[1,5,6] · K. J. Pienta[1,6]

Men with ≤ 5 sites of metastases were enrolled in a prospective registry study, underwent neoadjuvant chemohormonal therapy, followed by radical prostatectomy, adjuvant radiation (RT) to prostate bed/pelvis, stereotactic body radiation therapy (SBRT) to oligometastases, and adjuvant hormonal therapy (HT), and abiraterone was added to neoadjuvant HT. Therapies included prostatectomy 12/12 (100%), neoadjuvant [docetaxel 11/12 (92%), LHRH agonist 12/12 (100%), abiraterone + prednisone 6/12 (50%)], adjuvant radiation [RT 2/12 (17%), RT + SBRT 4/12 (33%), SBRT 6/12 (50%)], and LHRH agonist 12/12 (100%)]. Overall survival was 12/12 (100%). 1-, 2-, and **3-year undetectable PSA's** were 12/12 (100%), 10/12 (83%) and 8/12 **(67%), respectively.**

Treatment: 12 pts., local RT, chemo + ADT and SBRT to all M+ sites, 67% with undetectable PSA

Reyes DK et al. Med Oncol. 2020

Synchron oligometastasiertes HSPC

Prostate cancer with low burden skeletal disease at diagnosis: outcome of concomitant radiotherapy on primary tumor and metastases

[1]CHIARA LUCREZIA DEANTONI, MD, [1]ANDREI FODOR, MD, [1]CESARE COZZARINI, MD, [2]CLAUDIO FIORINO, PhD, [3,4]CHIARA BROMBIN, PhD, [3,4]CLELIA DI SERIO, PhD, [2]RICCARDO CALANDRINO, PhD and [1,4]NADIA DI MUZIO, MD

Objective: To evaluate toxicity and clinical outcome in synchronous bone only oligometastatic (≤2 lesions) prostate cancer patients, simultaneously irradiated to prostate/prostatic bed, lymph nodes and bone metastases.

Results: After a median follow-up of 46.5 (1.2–103.6) months, 5 patients died from disease progression, 10 experienced biochemical relapse, 19, still in ADT, presented undetectable prostate-specific antigen (PSA) at the last follow-up. Five patients who discontinued ADT after a median of 34 months (5.8–41) are free from biochemical relapse.

The 4 year Kaplan–Meier estimates of biochemical relapse-free survival, clinical relapse-free survival, freedom from distant metastases and overall survival were 53.3%, 65.7%, 73.4% and 82.4% respectively.

Treatment: 39 pts., local RT, ADT + SBRT to all M+ sites

Deantoni CL et al. Br J Radiol 2020

Synchron oligometastasiertes HSPC

Systemic and Tumor-directed Therapy for Oligometastatic Prostate Cancer: The SOLAR Phase 2 Trial in De Novo Oligometastatic Prostate Cancer

Nicholas G. Nickols[a,b,c,*], Sonny Tsai[a], Nathanael Kane[a,b], Samantha Tran[a], Leila Ghayouri[a], Silvia Diaz-Perez[a,b], May Thein[d], Nancy Anderson-Berman[d], Jeanie Eason[e], Amar U. Kishan[b,c], Michael L. Steinberg[b,c], Robert E. Reiter[c], Steve P. Lee[d], Greg E. Gin[d], Robert Kwon[d], Michael G. Chang[e], Hann-Hsiang Chao[e], Abhiskek A. Solanki[f], Rachael Sexton[g], Michael Lewis[a], William Lorentz[a,b], Michael K. Cheung[a,b], Diana L. Gage[a,b], Sai Duriseti[a,b], Luca Valle[a,b], Gholam Berenji[a], William J. Aronson[a,c], Isla P. Garraway[a,c], Matthew B. Rettig[a,c,h]

Prospective: 28 de-novo mHSPC patients (2018-2022)
- PSMA PET (89%); Fluciclovine (3.5%), NaF (7%)
- M1a: 29%; M1b: 71%
- N0: 36%; N1: 64%
- ISUP GG 4-5: 61%
- Number of mets: 1 - 42%; 2 - 21%; 3-5: 38%
- **Treatment**: ADT + Abi + Apa for 6 mo + RP with LND or RT with WPRT + MDT to all metastatic sites
- **Primary endpoint**: testosterone recovery and controlled PSA at 6 mo after recovery (PSA <0.2 ng/ml after RP ad <2 ng/ml after RT)

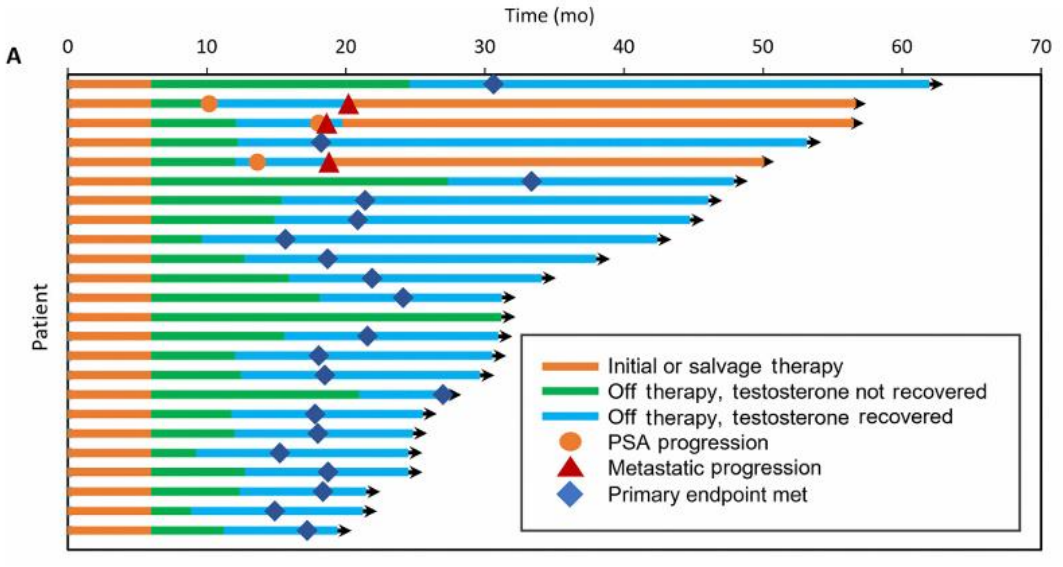
Parameter	Result
Median age at enrollment, yr (range)	69 (62–86)
Self-identified race/ethnicity, *n* (%)	
Hispanic	5 (18)
African American	9 (32)
Non-Hispanic White	14 (50)
Imaging used for initial staging, *n* (%)	
PSMA PET/CT	25 (89)
Fluciclovine PET/CT	1 (3.5)
NaF PET/CT[a]	2 (7)
Initial M stage, *n* (%)	
M1a	8 (29)
M1b	20 (71)
Initial N stage, *n* (%)	
N0	10 (36)
N1	18 (64)
Initial cT stage, *n* (%)	
cT1/2	11 (39)
cT3/4	17 (61)
IUSP grade group, *n* (%)	
Grade group 1–3	11 (39)
Grade group 4–5	17 (61)
Mean/median initial PSA, ng/ml (range)	17.29/9.89 (3.97–106)
Number of M1 metastases, *n* (%)	
1 metastasis	10 (42)
2 metastases	5 (21)
3–5 metastases	13 (38)
Mean/median number	2/2

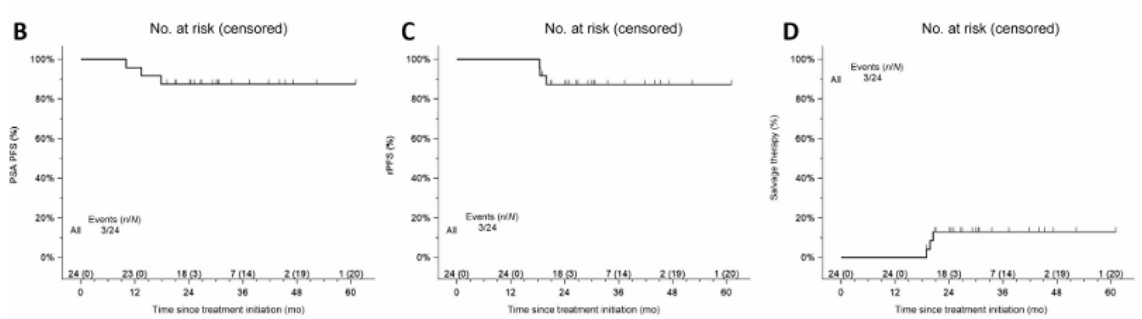
Deantoni CL et al. Br J Radiol 2020

Synchron oligometastasiertes HSPC

Treatment: ADT + Abi + Apa for 6 mo + RP with LND or RT with WPRT + MDT to all M+ sites

Primary endpoint: testosterone recovery and controlled PSA at 6 mo after recovery (PSA < 0.2 ng/ml after RP ad < 2 ng/ml after RT)





Lokoregionäre Bestrahlung + SBRT aller PET+ Metastasen + 6 Monate intensivierte systemische Therapie führt zu anhaltender Remission ohne anhaltende Kastration

Deantoni CL et al. Br J Radiol 2020

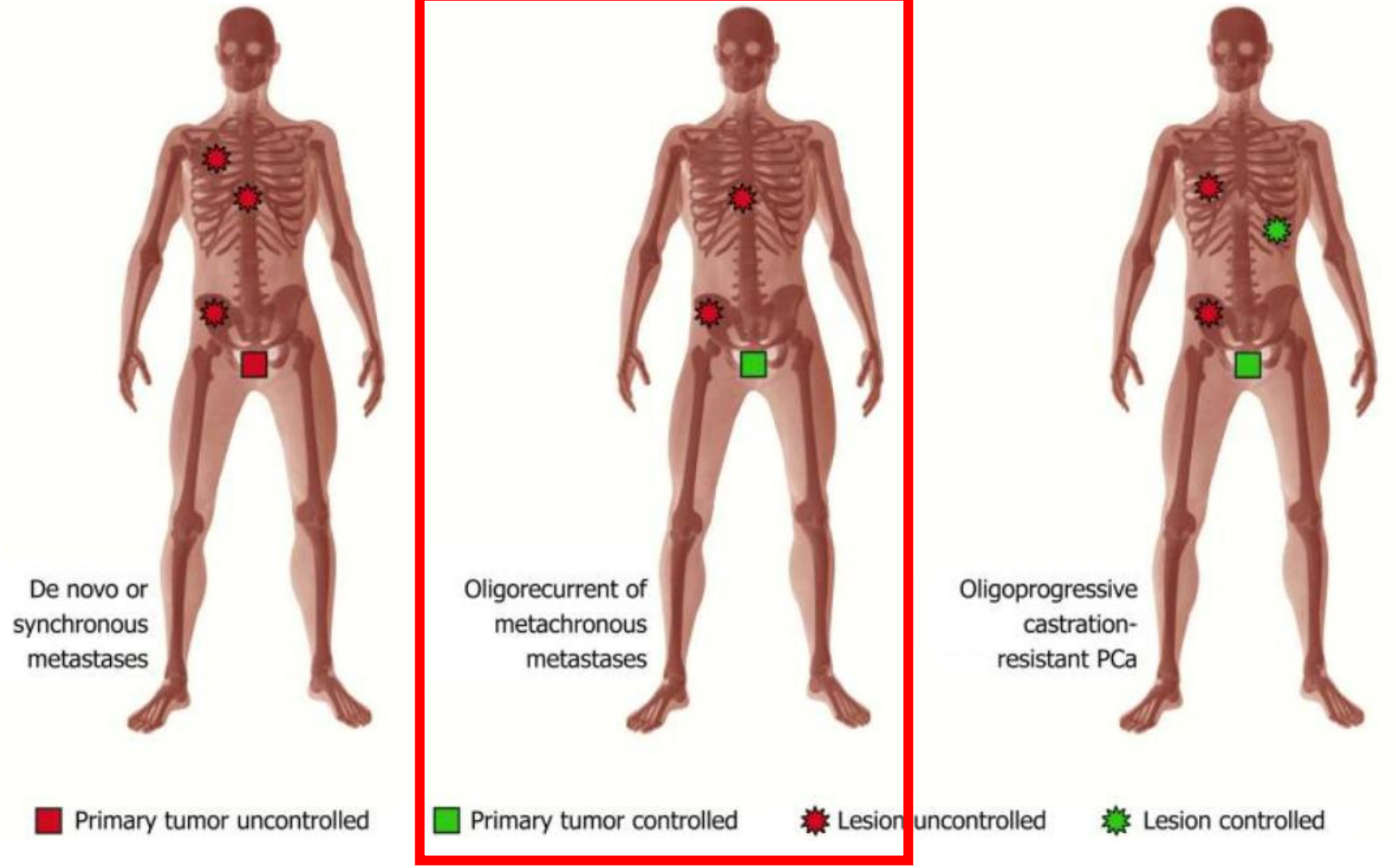
Synchron oligometastasiertes HSPC

Systemic therapy backbone	Timing of metastases	Number of metastases[a]	Intensification approach	Advanced Prostate Cancer Consensus Conference votes in favour[b]
All patients: ADT + ARPI (abiraterone, apalutamide, enzalutamide or darolutamide) or ADT alone for those with a very short life expectancy owing to age or comorbidities	Metachronous	≤3 bone metastases (±non-regional lymph node metastases)	Stereotactic ablative radiotherapy to metastases	68% (91% of respondents chose ADT + ARPI doublet as preferred systemic therapy)
		≥4 bone metastases (visceral metastases rare)	Docetaxel (for patients deemed fit for chemotherapy)	84% (34% recommend the ADT + ARPI + docetaxel triplet for the majority of patients with ≥4 metachronous bone metastases, and 50% recommend this approach for selected patients)
	Synchronous (de novo)	≤3 bone metastases (±non-regional lymph node metastases)	Prostate radiotherapy and stereotactic ablative radiotherapy	82%
		≥4 bone metastases or any liver metastasis	Docetaxel (for patients deemed fit for chemotherapy)	94% (54% recommend ADT + ARPI + docetaxel triplet for the majority of patients with ≥4 synchronous bone metastases, and 40% recommend this approach for selected patients)

ADT, androgen-deprivation therapy; ARPI, androgen receptor pathway inhibitors. [a]Detectable on conventional imaging with CT (including CT as part of prostate-specific membrane antigen PET–CT) and technetium-99m whole-body bone scintigraphy; future refinements to be made based on prostate-specific membrane antigen PET and molecular biomarkers. [b]Advanced Prostate Cancer Consensus Conference votes in favour combines votes for 'in the majority of patients' and 'in selected patients'[131].

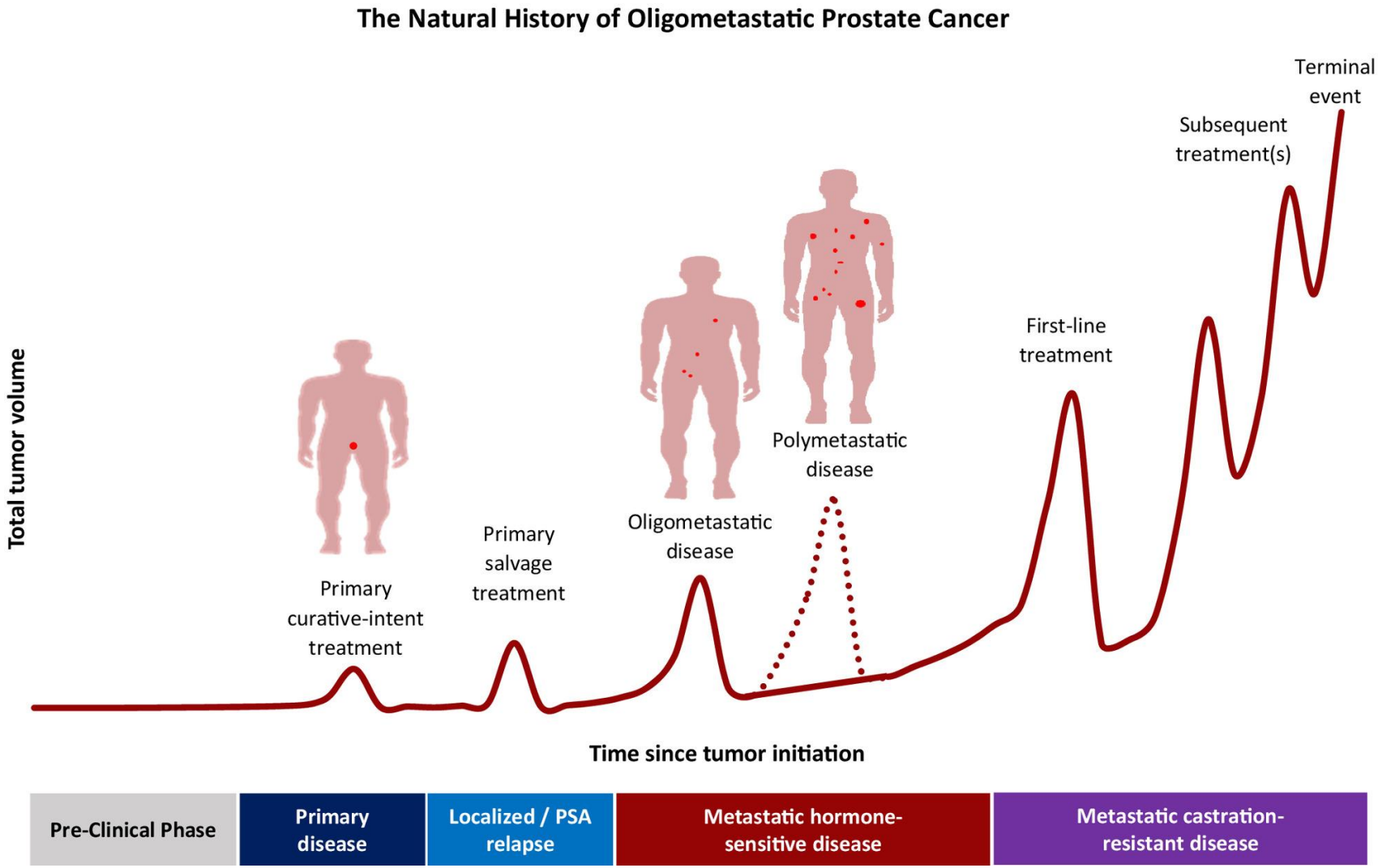
Cilento, M.A. et al. Nat Rev Clin Oncol 2026

Metachron oligometastasiertes HSPC



Palacios-Eito A. et al. World J Clin Oncol. 2019

Intensivierung durch MDT

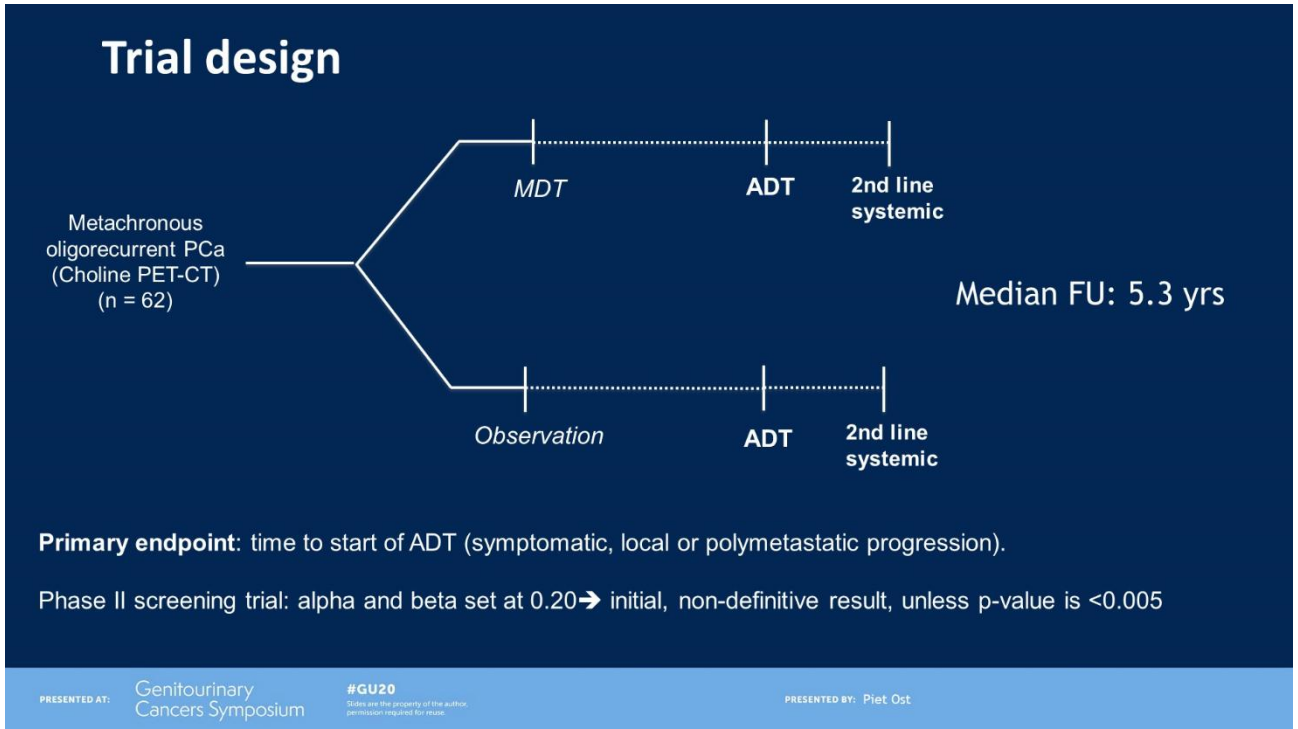


Rao A. et al. Am Soc Clin Oncol Educ Book. 2019

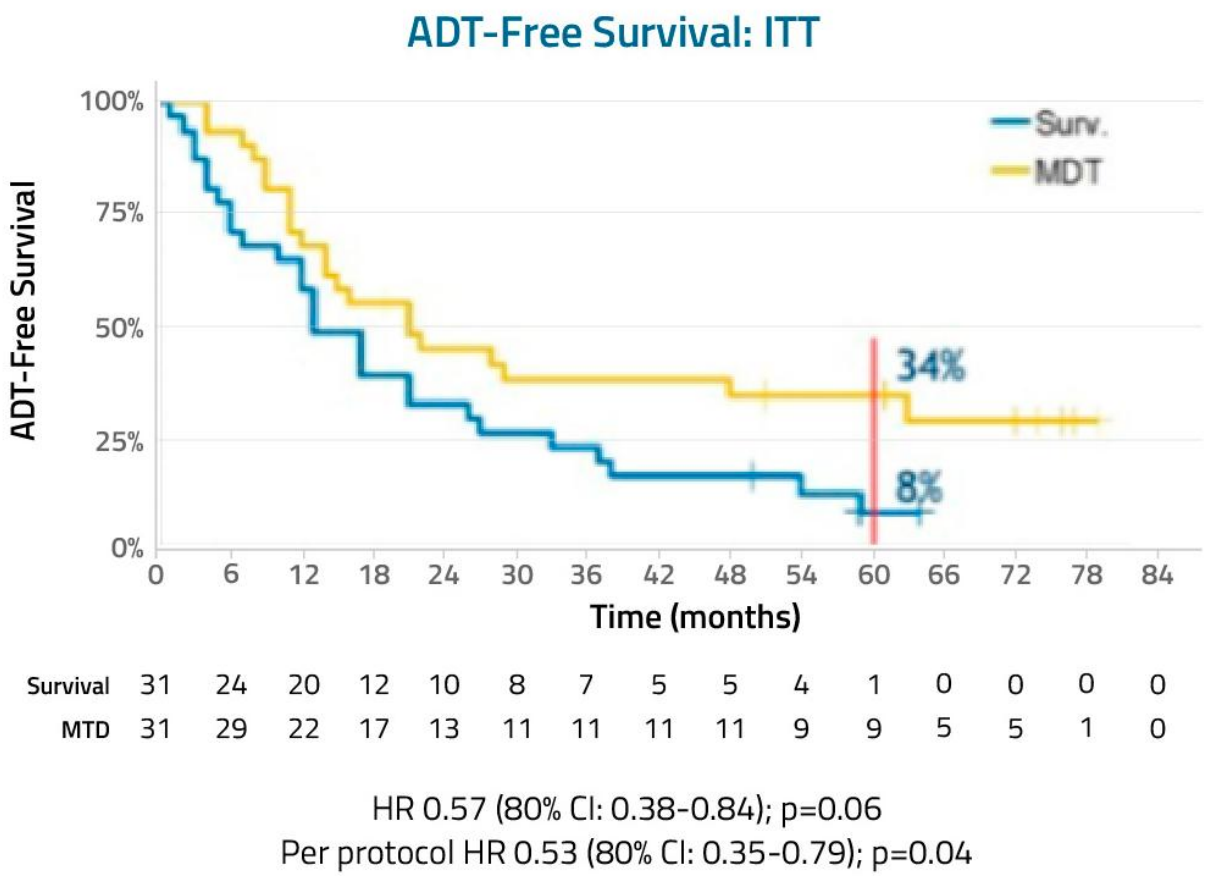
Metachron oligometastasiertes HSPC – STOMP

Surveillance or Metastasis-Directed Therapy for Oligometastatic Prostate Cancer Recurrence: A Prospective, Randomized, Multicenter Phase II Trial

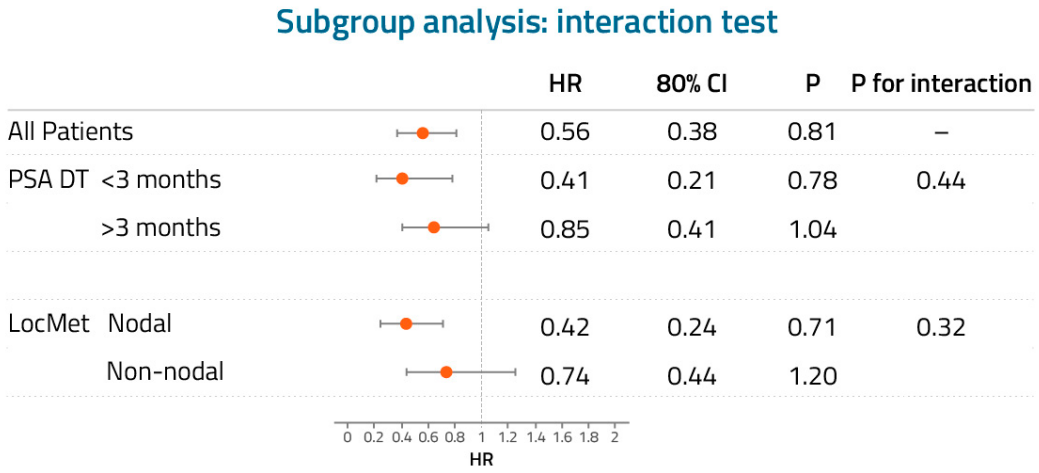
Authors: Piet Ost , Dries Reynders, Karel Decaestecker, Valérie Fonteyne, Nicolaas Lumen, Aurélie De Bruycker, Bieke Lambert, ... SHOW ALL ... , and Gert De Meerleer | AUTHORS INFO & AFFILIATIONS



Metachron oligometastasiertes HSPC – STOMP



HR 0.57 (80% CI: 0.38-0.84); p=0.06
Per protocol HR 0.53 (80% CI: 0.35-0.79); p=0.04



ADT-free survival
21 mo MDT *vs.* 12 mo Surveillance

MDT verzögert den Einsatz einer ADT und verbessert das PFS

Metachron oligometastasiertes HSPC – ORIOLE

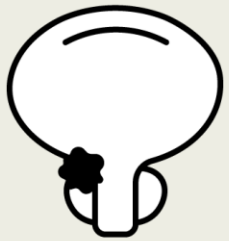
JAMA Oncology

RCT **Observation vs Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer**

Progression at 6 mo:
19% SBRT *vs.* 61% Observation

POPULATION

54 Men



Adult men with recurrent, hormone-sensitive prostate cancer and 1-3 metastases detectable by conventional imaging

Median age: 68 y

SETTINGS / LOCATIONS

3 Radiation treatment facilities in 2 US locations

INTERVENTION

54 Patients randomized

36 Stereotactic radiotherapy

Stereotactic ablative radiotherapy (SABR) to all metastases

18 Observation

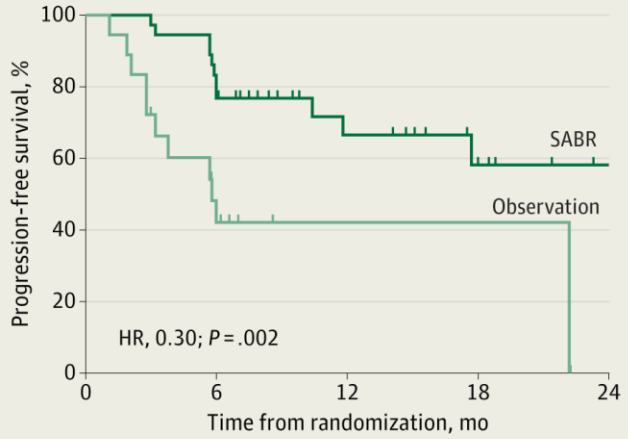
Observation only for 6 mo

PRIMARY OUTCOME

Progression of disease measured by any of the following: prostate-specific antigen testing, conventional imaging, symptomatic progression, androgen deprivation therapy initiation for any reason, death

FINDINGS

Progression of disease at 6 mo was less common with SABR compared with observation (19% vs 61%; *P* = .005)



Proportion of patients with progression at 6 mo

Stereotactic radiotherapy: **19%**

Observation: **61%**

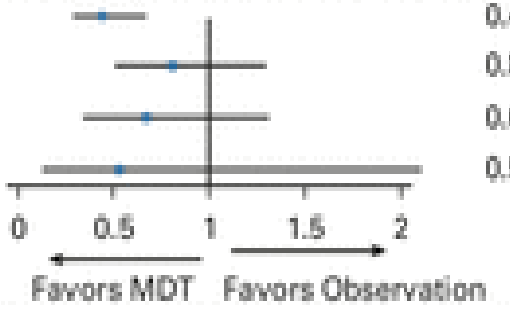
Phillips R et al. JAMA Oncol. 2020

Metachron oligometastasiertes HSPC

Long-Term Outcomes and Genetic Predictors of Response to Metastasis-Directed Therapy Versus Observation in Oligometastatic Prostate Cancer: Analysis of STOMP and ORIOLE Trials

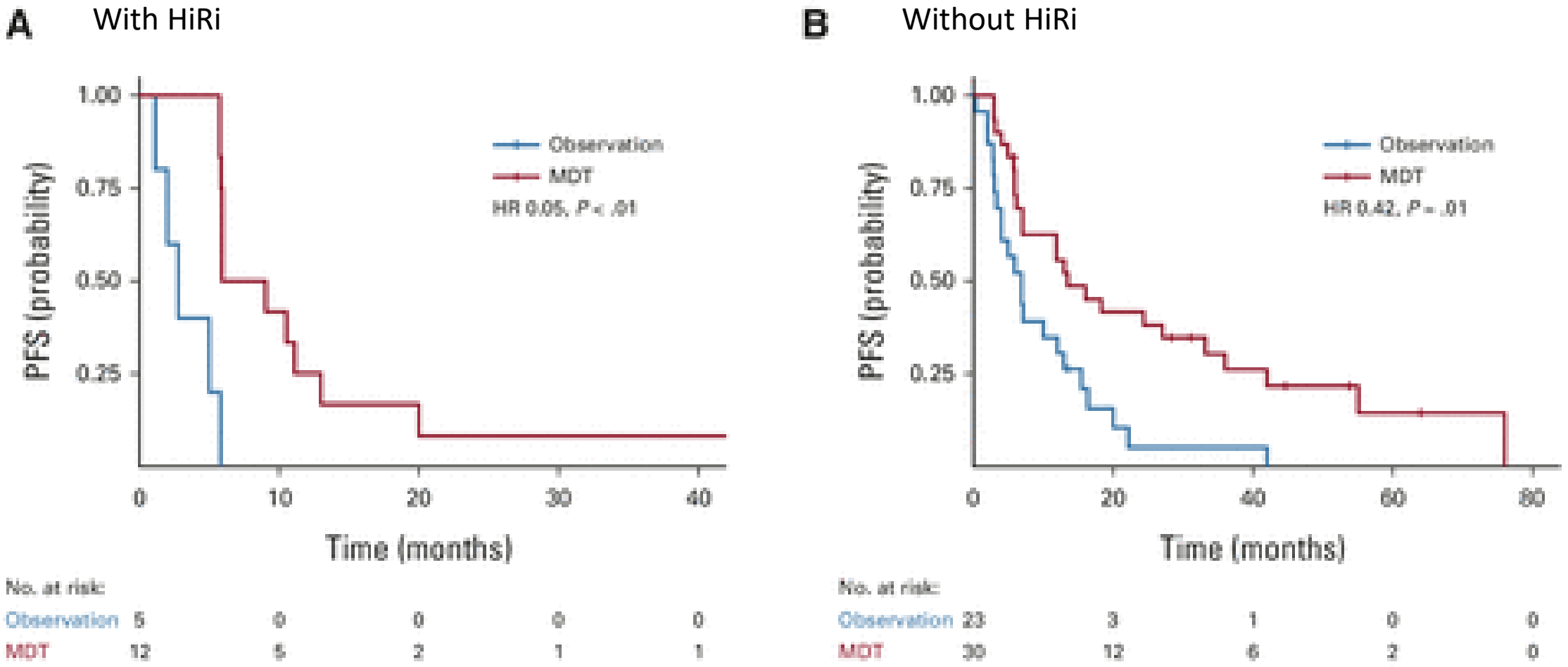
Authors: Matthew P. Deek, MD , Kim Van der Eecken, MD, PhD, Philip Sutera, MD , Rebecca A. Deek, MS, Valérie Fonteyne, MD, PhD, Adrianna A. Mendes, MD, Karel Decaestecker, MD, PhD, ... SHOW ALL ... , and Phuoc T. Tran, MD, PhD AUTHORS INFO & AFFILIATIONS

Outcome	MDT Median Time to Event, months (95% CI)	Observation Median Time to Event, months (95% CI)	HR (95% CI)	P
PFS	11.9 (8 to 18.3)	5.9 (3.2 to 7.1)	0.44 (0.29 to 0.66)	< .001
rPFS	18.3 (12 to 36)	17 (13 to 22.8)	0.81 (0.50 to 1.29)	.37
CRPC	NR (62 to NR)	63 (53.9 to NR)	0.67 (0.34 to 1.31)	.24
OS	NR (84 to NR)	NR (73 to NR)	0.53 (0.13 to 2.11)	.36



Deek MP et al. J Clin Oncol. 2022

Metachron oligometastasiertes HSPC

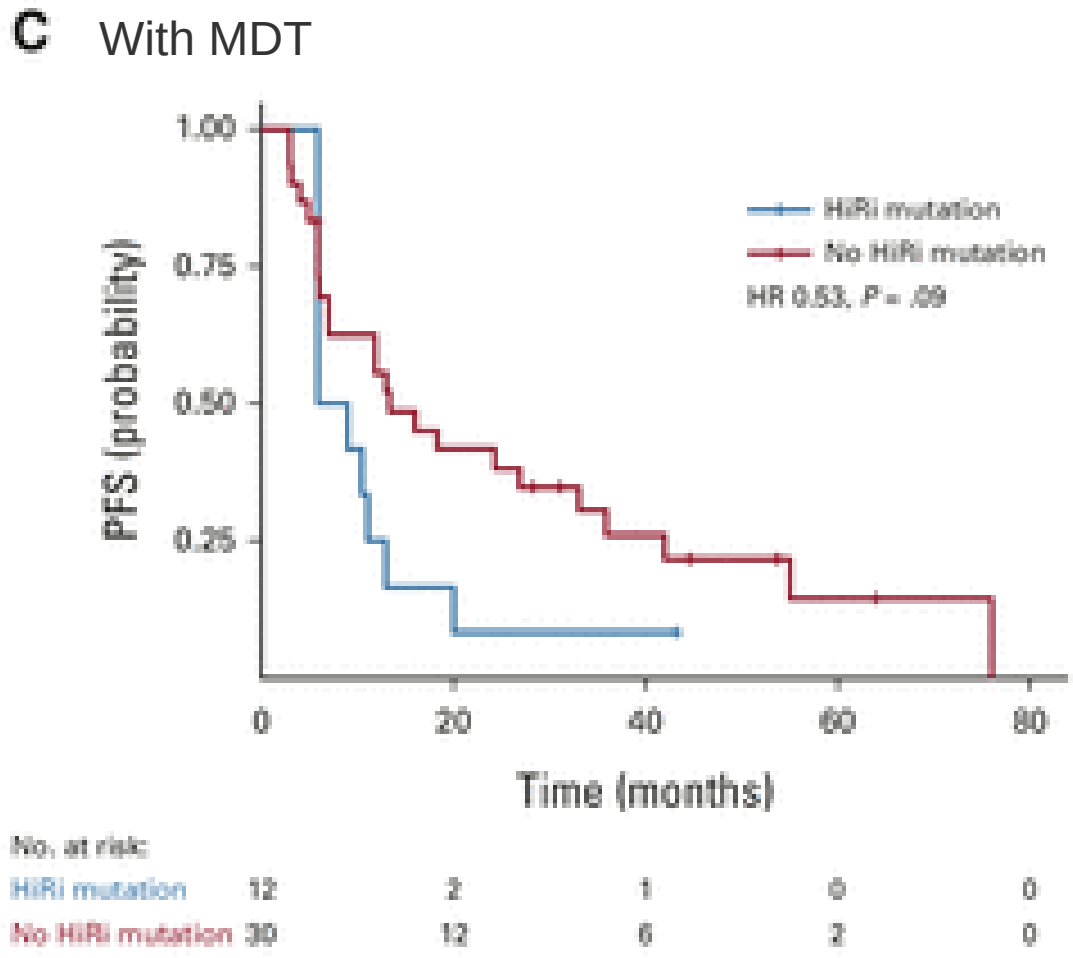


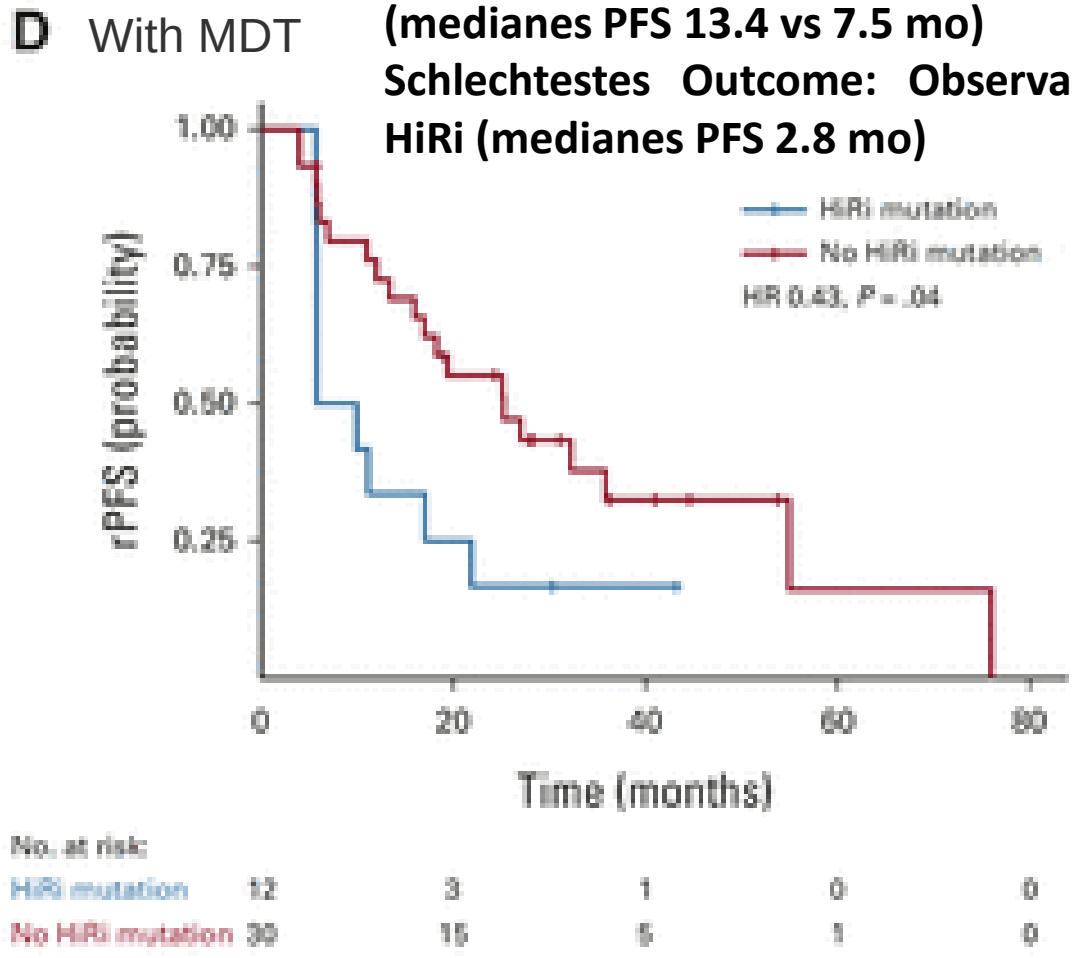
HiRi: *ATM*, *BRCA1/2*, *Rb1*, or *TP53*

Deek MP et al. J Clin Oncol. 2022

Metachron oligometastasiertes HSPC

Bestes Outcome: MDT ohne HiRi (medianes PFS 13.4 vs 7.5 mo)
Schlechtestes Outcome: Observanz mit HiRi (medianes PFS 2.8 mo)





HiRi: *ATM*, *BRCA1/2*, *Rb1*, or *TP53*

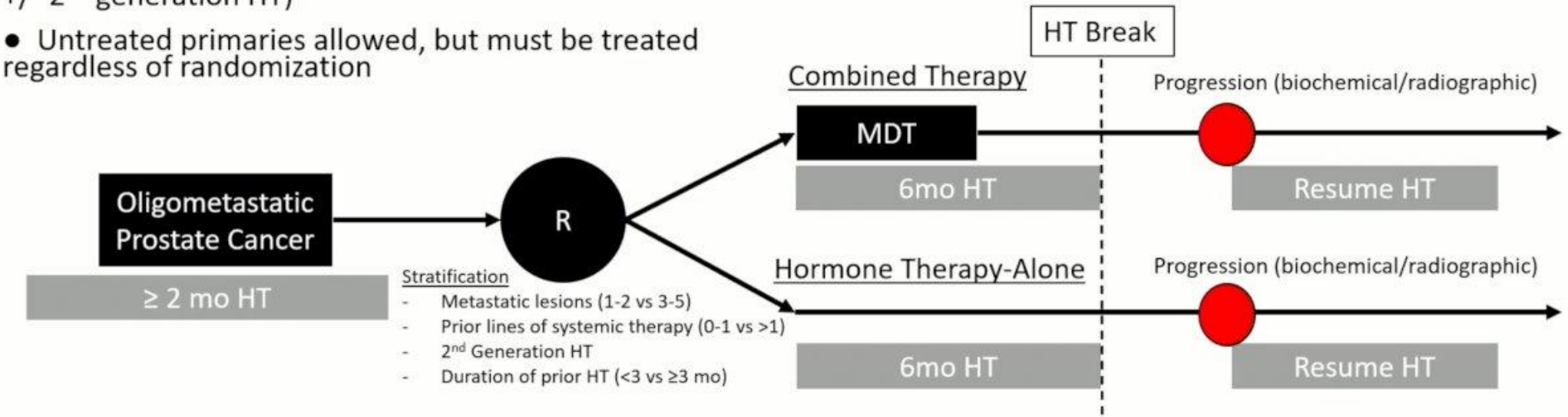
Deek MP et al. J Clin Oncol. 2022

Metachron oligometastasiertes HSPC

EXTEND intermittent prostate cancer

RCT Phase II
- **87 oligorecurrent men mostly mHSPC** (>90%)
- Randomization 1:1: **intermittent ADT** *vs* **ADT + MDT**
- **≤ 5 metastases** (mostly conventional imaging 75%; fluciclovine PET/CT 25%)
- ≥ 2 mo prior HT (ADT ± ARPI) (~35% ARPI)
- Median FU: 22 mo

Major Inclusion Criteria
- Histologic diagnosis of prostate cancer
- ≤5 metastases
- ≥2 months of prior HT (either GNRH agonist/antagonist +/- 2nd generation HT)
- Untreated primaries allowed, but must be treated regardless of randomization



Tang C et al. JAMA Oncol 2023

Metachron oligometastasiertes HSPC

JAMA Oncology

RCT: Addition of Metastasis-Directed Therapy to Intermittent Hormone Therapy for Oligometastatic Prostate Cancer

POPULATION

87 Men

Adults with oligometastatic prostate cancer at ≤5 metastatic sites

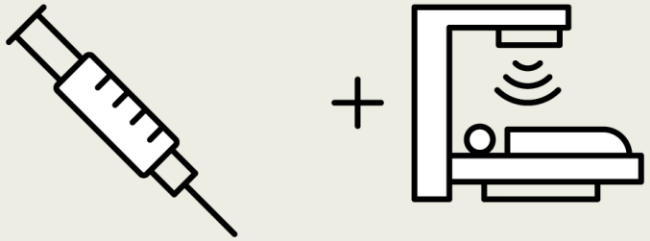
Median age, 67 y

SETTINGS / LOCATIONS

3 Tertiary care centers in US

INTERVENTION

87 Participants randomized



44 Hormone therapy alone
Intermittent hormone therapy

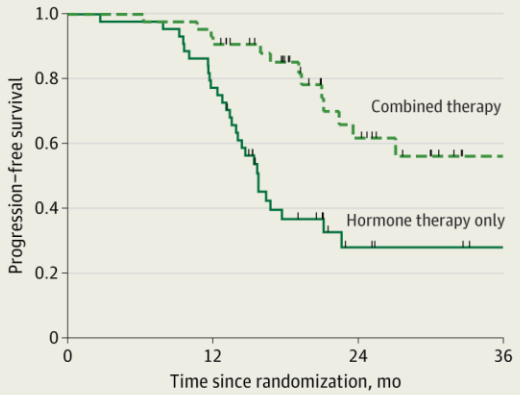
43 Combined therapy
Metastasis-directed therapy combined with intermittent hormone therapy

PRIMARY OUTCOME

Progression-free survival (PFS), defined as time from randomization to radiographic progression per RECIST 1.1 criteria, clinical progression, increasing prostate-specific antigen level, or death

FINDINGS

PFS was significantly improved with combined therapy compared with hormone therapy alone



Hazard ratio, 0.25 (95% CI, 0.12-0.55)
Median PFS: hormone therapy alone, 15.8 mo; combined therapy, median PFS not reached

MDT + ADT ± ARPI (intermit.) verbessert PFS

Tang C et al. JAMA Oncol 2023

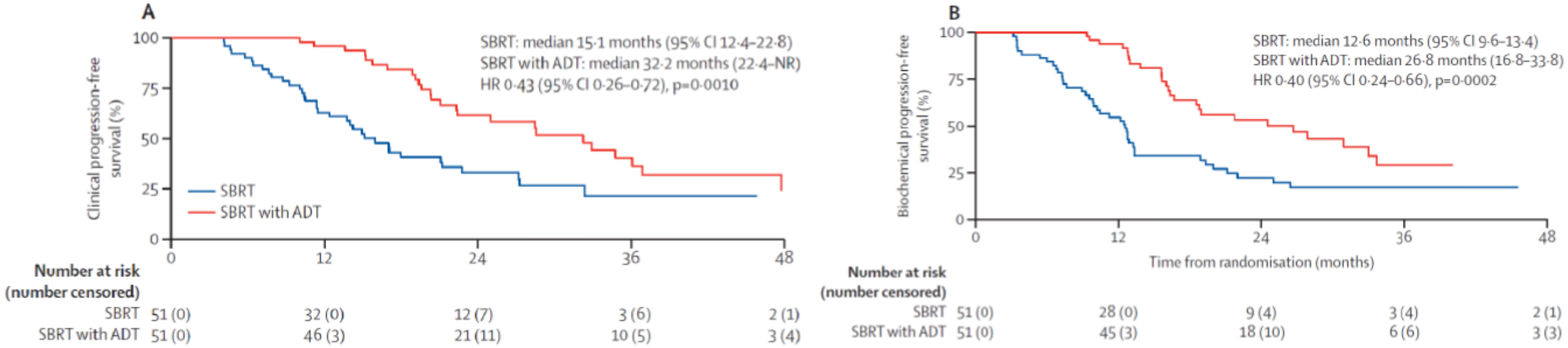
Metachron oligometastasiertes HSPC

ADT with SBRT versus SBRT alone for hormone-sensitive oligorecurrent prostate cancer (RADIOSA): a randomised, open-label, phase 2 clinical trial

Giulia Marvaso, Giulia Corrao*, Mattia Zaffaroni, Maria Giulia Vincini, Chiara Lorubbio, Sara Gandini, Cristiana Fodor, Sofia Netti, Dario Zerini, Stefano Luzzago, Francesco Alessandro Mistretta, Konstantinos Venetis, Giulia Cursano, Tiziana Burla, Ketti Mazzocco, Federica Cattani, Giuseppe Petralia, Nicola Fusco, Gabriella Pravettoni, Gennaro Musi, Ottavio De Cobelli, Chad Tang, Piet Ost, David A Palma, Roberto Orecchia, Barbara Alicja Jereczek-Fossa*

Marvaso G et al. Lancet Oncol. 2025

Metachron oligometastasiertes HSPC



MDT + 6 Monate ADT verbessert bRFS und PFS (vs. MDT)

Marvaso G et al. Lancet Oncol. 2025

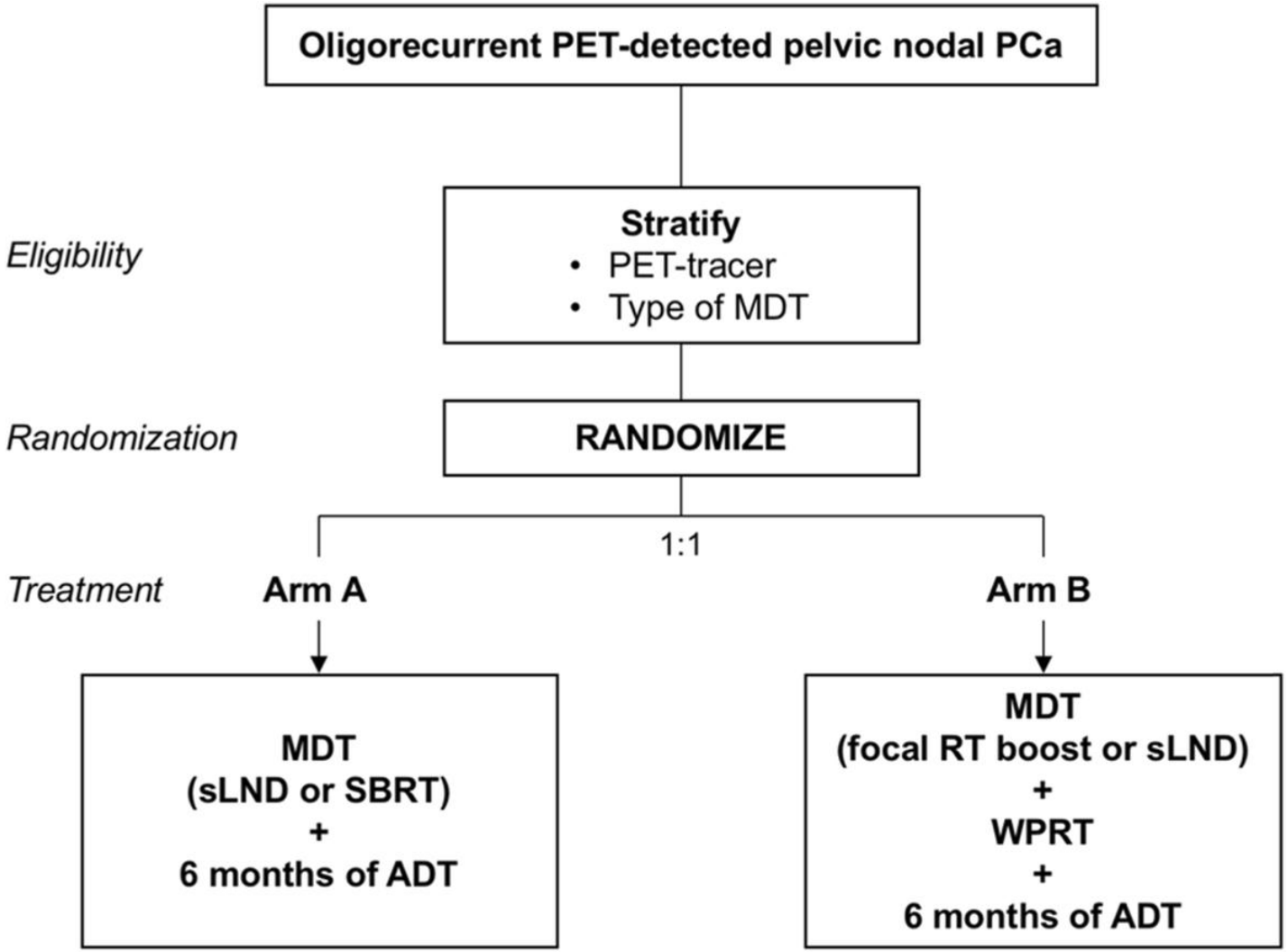
Metachron oligometastasiertes HSPC

Salvage metastasis-directed therapy versus elective nodal radiotherapy for oligorecurrent nodal prostate cancer metastases (PEACE V–STORM): a phase 2, open-label, randomised controlled trial

Piet Ost, Shankar Siva, Sigmund Brabrand, Piet Dirix, Nick Liefhooghe, François-Xavier Otte, Alfonso Gomez-Iturriaga, Wouter Everaerts, Mohamed Shelan, Antonio Conde-Moreno, Fernando López Campos, Alexandros Papachristofilou, Matthias Guckenberger, Marta Scorsetti, Almudena Zapatero, Ana-Elena Villafranca Iturre, Clara Eito, Felipe Couñago, Paolo Muto, Wim Duthoy, Nicolas Mach, Valérie Fonteyne, Daniel Moon, Kristian Thon, Carole Mercier, Vérane Achard, Karin Stellamans, Els Goetghebeur, Dries Reynders, Thomas Zilli

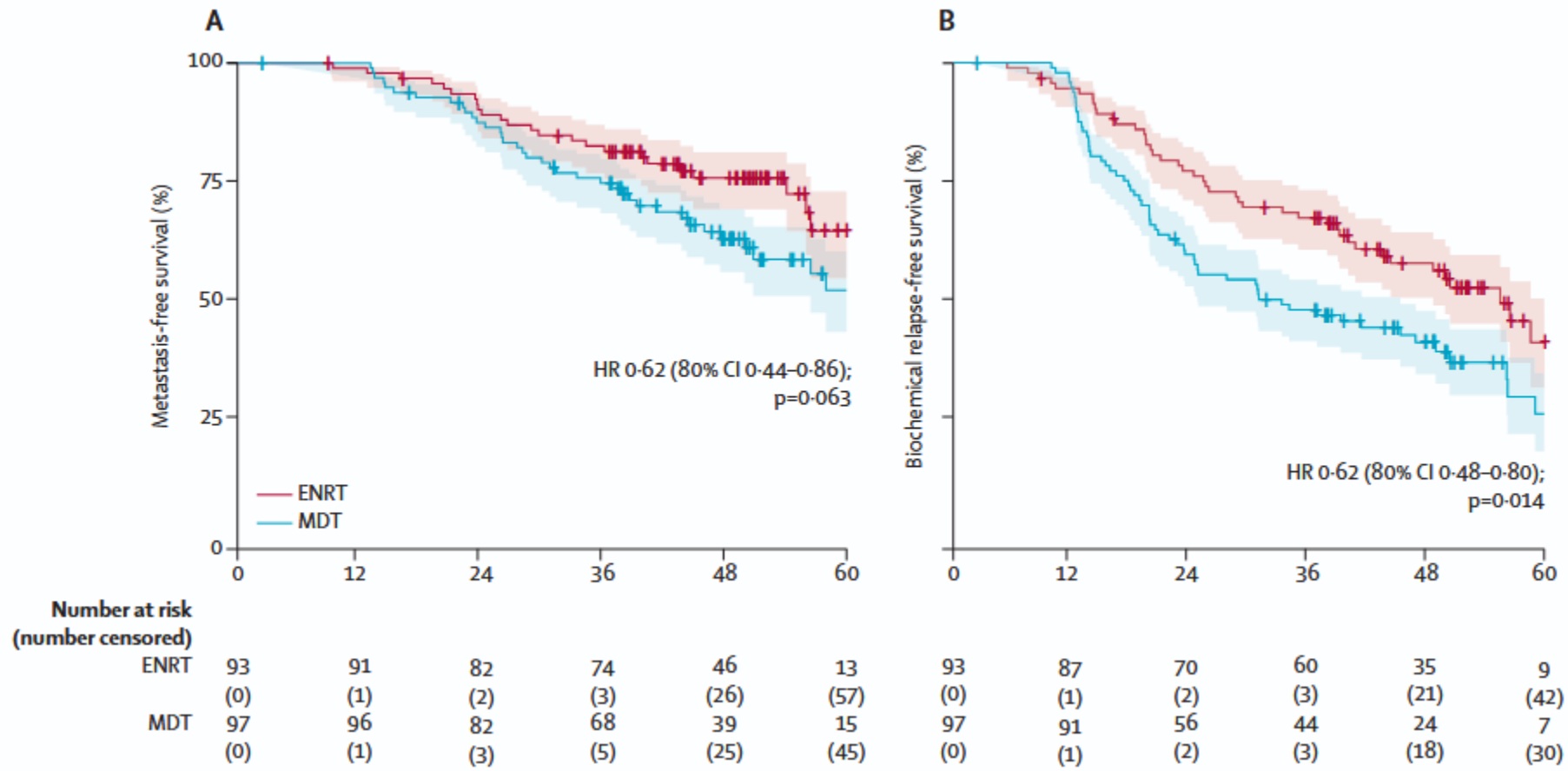
Ost P et al. Lancet Oncol. 2025

Metachron oligometastasiertes HSPC



Ost P et al. Lancet Oncol. 2025

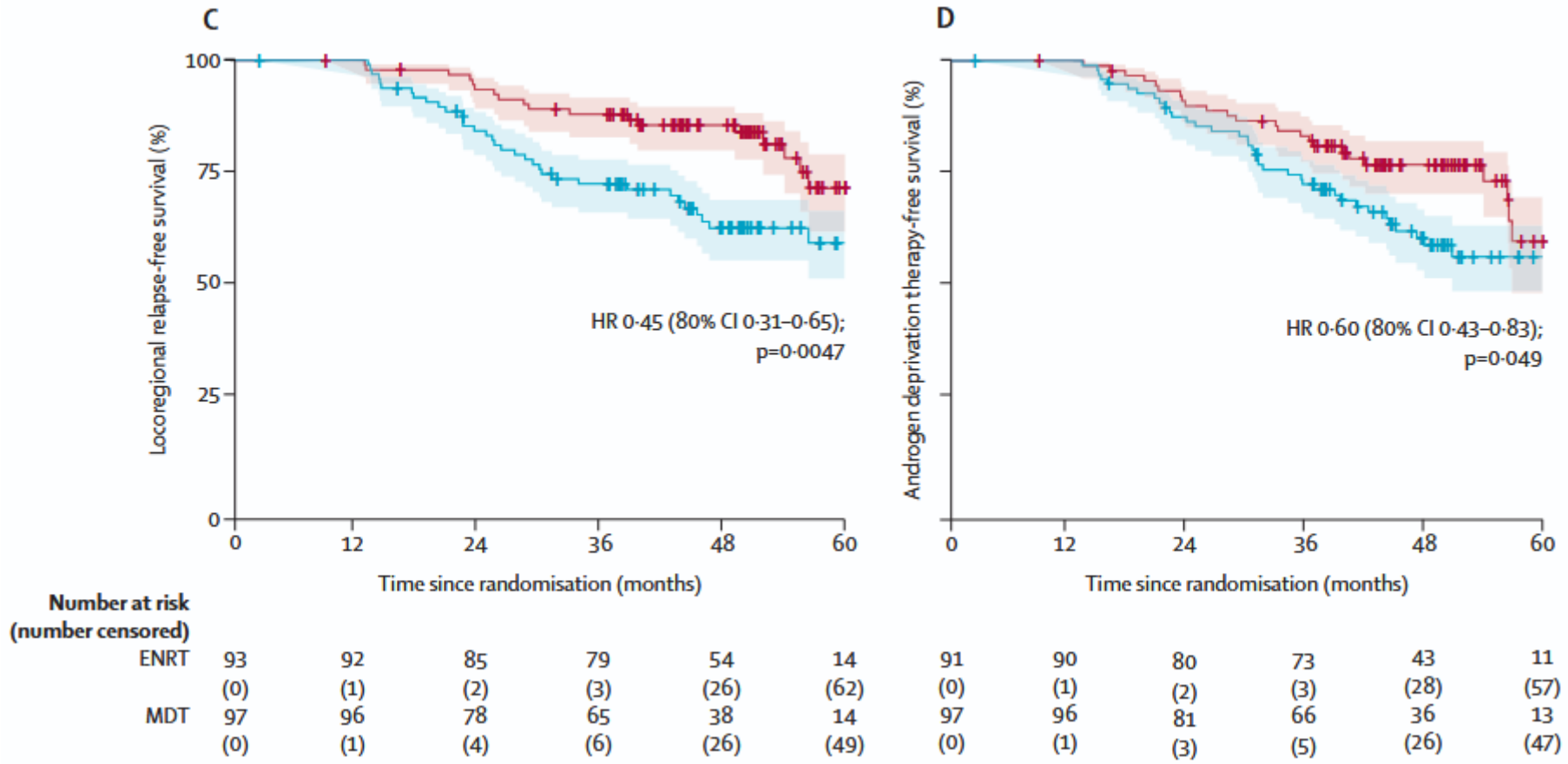
Metachron oligometastasiertes HSPC



Elektive nodale RT + 6 Mo ADT verbessert MFS, bRFS und lokoregionäre Kontrolle (vgl. mit fokaler MDT + 6 Mo ADT)

Ost P et al. Lancet Oncol. 2025

Metachron oligometastasiertes HSPC



Number at risk (number censored)												
ENRT	93	92	85	79	54	14	91	90	80	73	43	11
	(0)	(1)	(2)	(3)	(26)	(62)	(0)	(1)	(2)	(3)	(28)	(57)
MDT	97	96	78	65	38	14	97	96	81	66	36	13
	(0)	(1)	(4)	(6)	(26)	(49)	(0)	(1)	(3)	(5)	(26)	(47)

Elektive nodale RT + 6 Mo ADT verbessert MFS, bRFS und lokoregionäre Kontrolle (vgl. mit fokaler MDT + 6 Mo ADT)

Ost P et al. Lancet Oncol. 2025

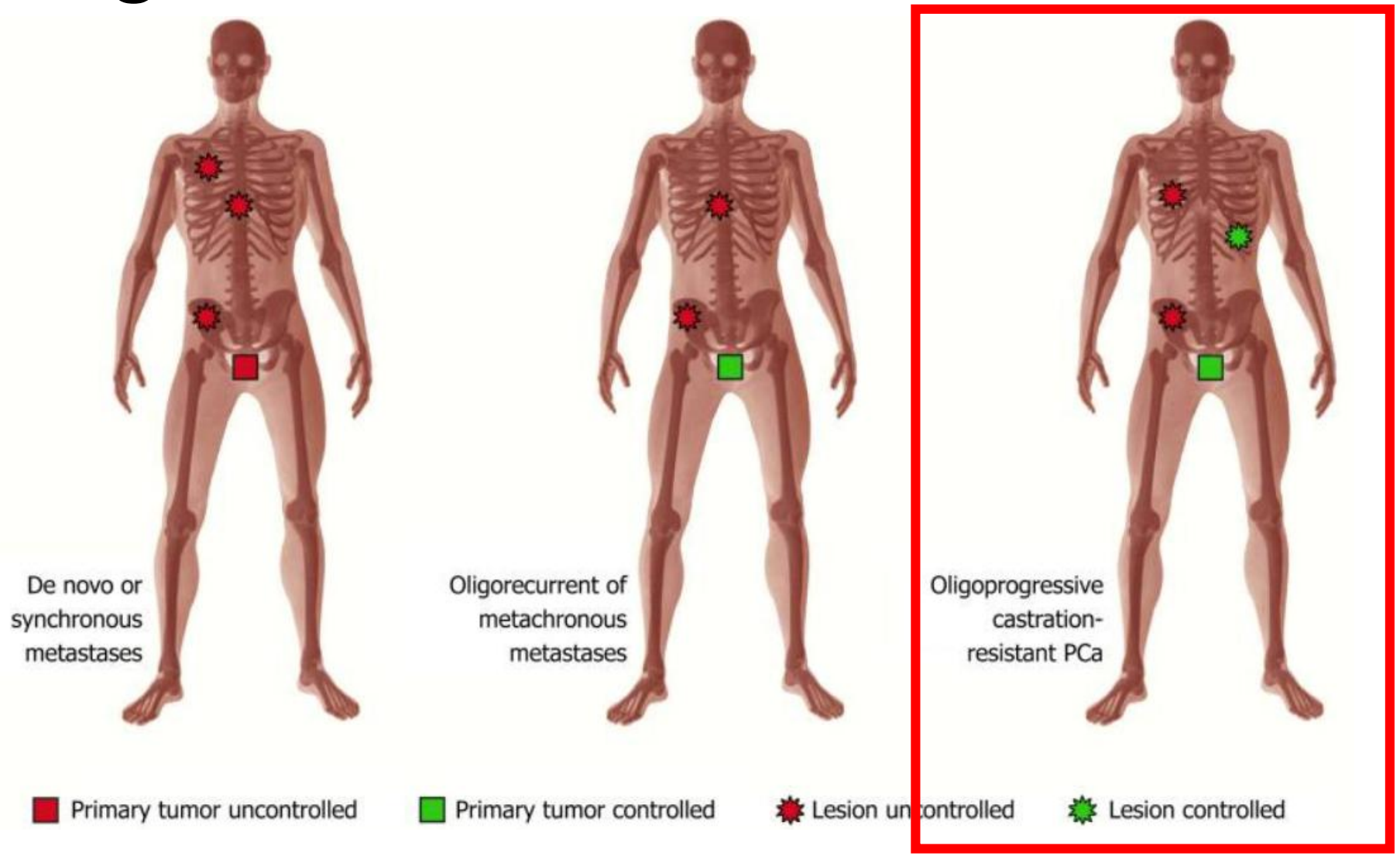
Synchron oligometastasiertes HSPC

Systemic therapy backbone	Timing of metastases	Number of metastases[a]	Intensification approach	Advanced Prostate Cancer Consensus Conference votes in favour[b]
All patients: ADT + ARPI (abiraterone, apalutamide, enzalutamide or darolutamide) or ADT alone for those with a very short life expectancy owing to age or comorbidities	Metachronous	≤3 bone metastases (±non-regional lymph node metastases)	Stereotactic ablative radiotherapy to metastases	68% (91% of respondents chose ADT + ARPI doublet as preferred systemic therapy)
		≥4 bone metastases (visceral metastases rare)	Docetaxel (for patients deemed fit for chemotherapy)	84% (34% recommend the ADT + ARPI + docetaxel triplet for the majority of patients with ≥4 metachronous bone metastases, and 50% recommend this approach for selected patients)
	Synchronous (de novo)	≤3 bone metastases (±non-regional lymph node metastases)	Prostate radiotherapy and stereotactic ablative radiotherapy	82%
		≥4 bone metastases or any liver metastasis	Docetaxel (for patients deemed fit for chemotherapy)	94% (54% recommend ADT + ARPI + docetaxel triplet for the majority of patients with ≥4 synchronous bone metastases, and 40% recommend this approach for selected patients)

ADT, androgen-deprivation therapy; ARPI, androgen receptor pathway inhibitors. [a]Detectable on conventional imaging with CT (including CT as part of prostate-specific membrane antigen PET–CT) and technetium-99m whole-body bone scintigraphy; future refinements to be made based on prostate-specific membrane antigen PET and molecular biomarkers. [b]Advanced Prostate Cancer Consensus Conference votes in favour combines votes for 'in the majority of patients' and 'in selected patients'[131].

Cilento, M.A. et al. Nat Rev Clin Oncol 2026

Oligometastasiertes CRPC

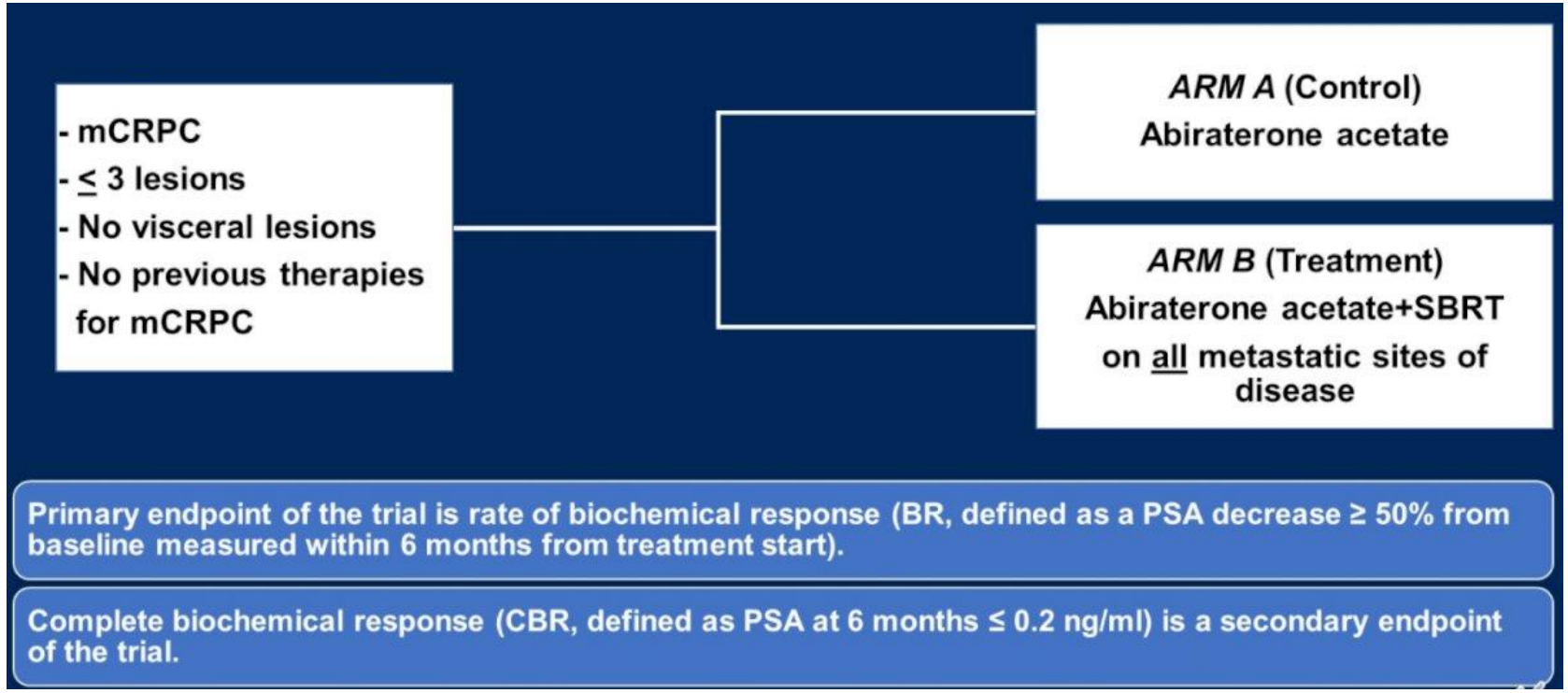


Palacios-Eito A. et al. World J Clin Oncol. 2019

Oligometastasiertes CRPC – ARTO

Stereotactic Body Radiation Therapy and Abiraterone Acetate for Patients Affected by Oligometastatic Castrate-Resistant Prostate Cancer: A Randomized Phase II Trial (ARTO)

Authors: Giulio Francolini, MD , Andrea Gaetano Allegra, MD , Beatrice Detti, MD, Vanessa Di Cataldo, MD , Saverio Caini, MD, Alessio Bruni, MD , Gianluca Ingrosso, MD , ... SHOW ALL ... , on behalf of the ARTO Working Group members | AUTHORS INFO & AFFILIATIONS



157 oligometastatic mCRPC pts
(1-3 non-visceral lesions on NGI)
Phase II RCT:

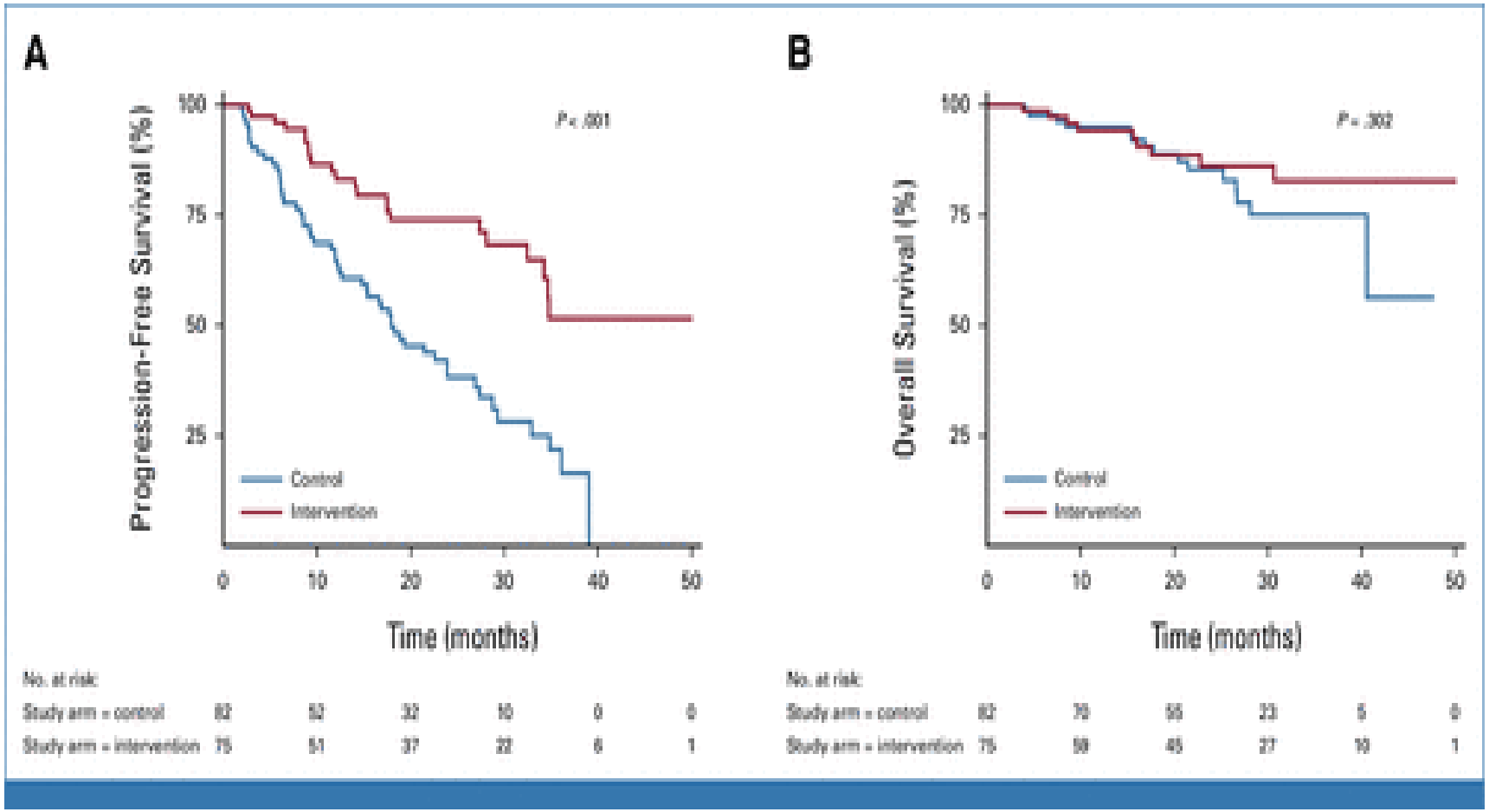
Abiraterone vs Abiraterone + SBRT

Primary endpoint:

PSA response (decrease ≥ 50% at 6 mo)
Secondary endpoints:

Complete biochemical response (PSA <0.2 ng/mL at 6 mo); PFS

Oligometastasiertes CRPC – ARTO

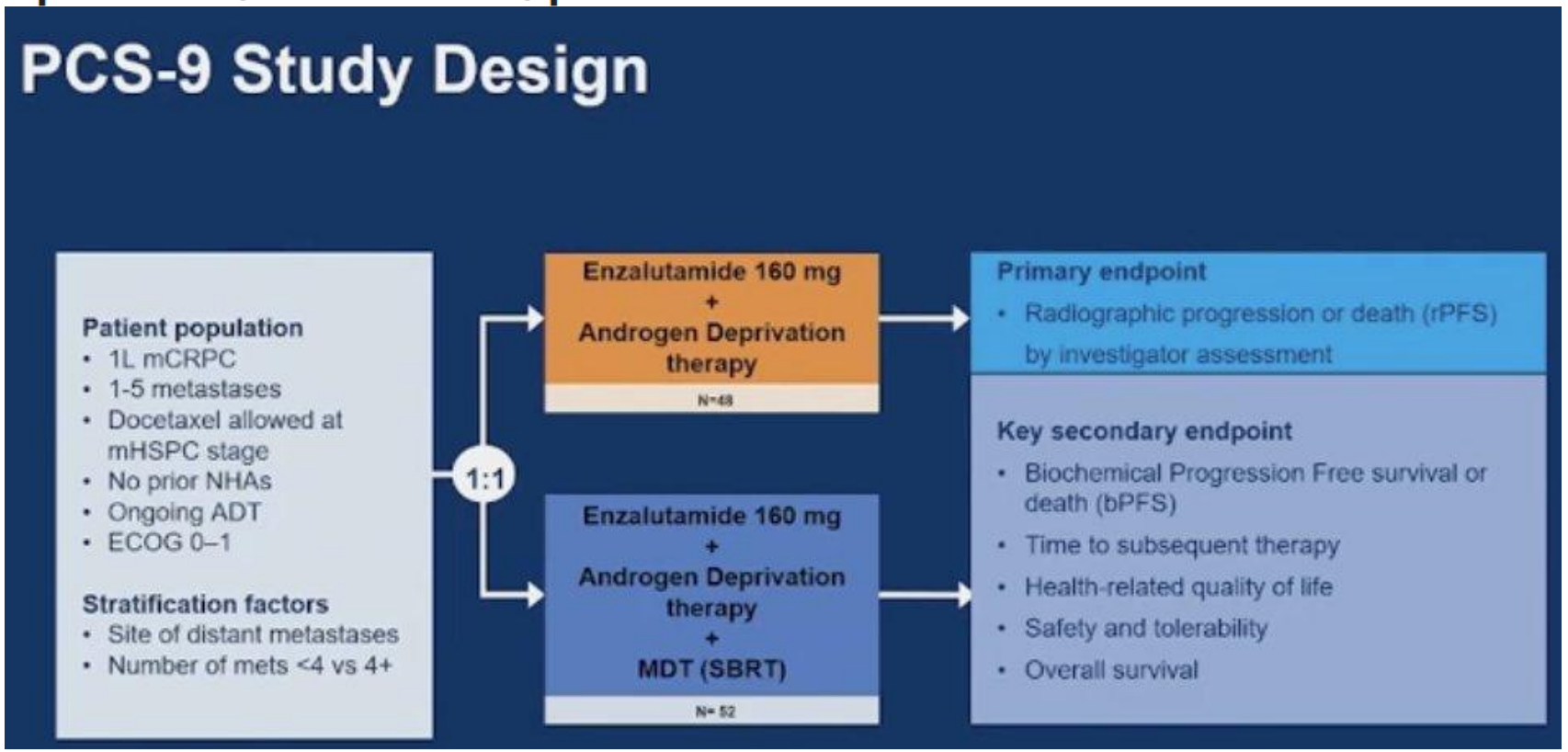


SBRT + Abirateron verbessert biochemische Response und PFS beim oligoprogr. CRPC

Francolini G et al. J Clin Oncol. 2023

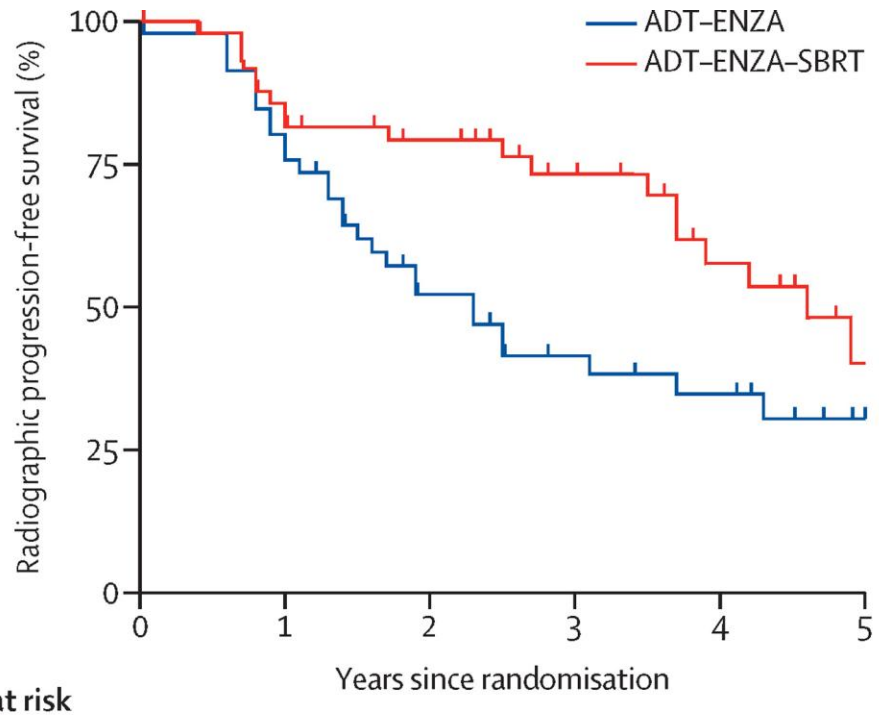
Oligometastasiertes CRPC – GROUQ-PCS 9

Metastases-directed therapy in addition to standard systemic therapy in oligometastatic castration-resistant prostate cancer in Canada (GROUQ-PCS 9): a multicentre, open-label, randomised, phase 2 trial

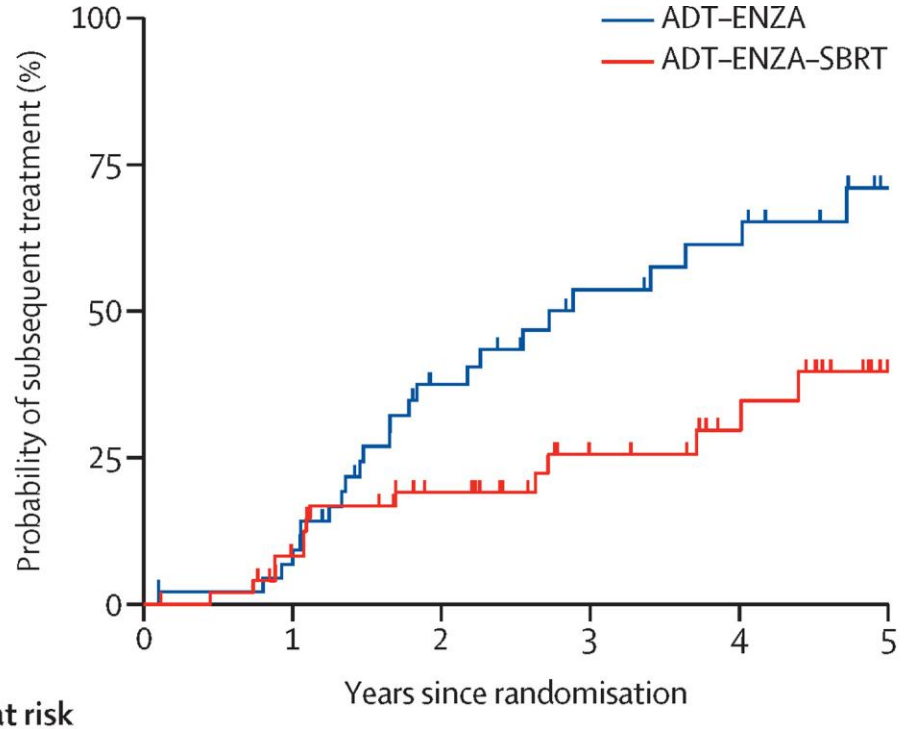


Niazi T et al. Lancet Oncol. 2025

Oligometastasiertes CRPC – GROUQ-PCS 9



Number at risk (censored)						
ADT–ENZA	48 (··)	37 (4)	20 (3)	13 (1)	10 (6)	2 (1)
ADT–ENZA–SBRT	52 (··)	42 (5)	33 (9)	22 (4)	15 (9)	2 (2)



Number at risk (censored)						
ADT–ENZA	48 (··)	39 (5)	21 (3)	13 (1)	10 (6)	2 (1)
ADT–ENZA–SBRT	52 (··)	43 (6)	32 (10)	20 (5)	14 (10)	2 (1)

SBRT + Enzalutamid verbessert rPFS und verzögert Nächstlinientherapie beim oligoprogr. CPRC

Niazi T et al. Lancet Oncol. 2025

SBRT beim oligometastasiertem CRPC

Oligometastatic mCRPC starting ARPI

ARTO trial
→ Phase II randomized: AAP + SBRT vs AAP alone
→ PSA50 92% vs 68%; PFS HR 0.35
→ mRPFS NR vs 34m HR 0.39

GROUQ-PCS 9 trial
→ Phase II randomized: ENZA + SBRT vs ENZA alone
→ mRPFS 4.6 years vs 2.3 years HR 0.48

Oligoprogressive mCRPC on ARPI

TRAP trial
→ Phase II prospective; SBRT to progressing sites on ADT/ARPI
→ Median PFS 6.4 months; acceptable safety
→ Delays next-line therapy

Francolini JCO 2023, Niazi et al. Lancet Oncology 2025, Patel et al Int J Radiat Oncol Biol Phys. 2025

Oligometastasiertes Prostatakarzinom

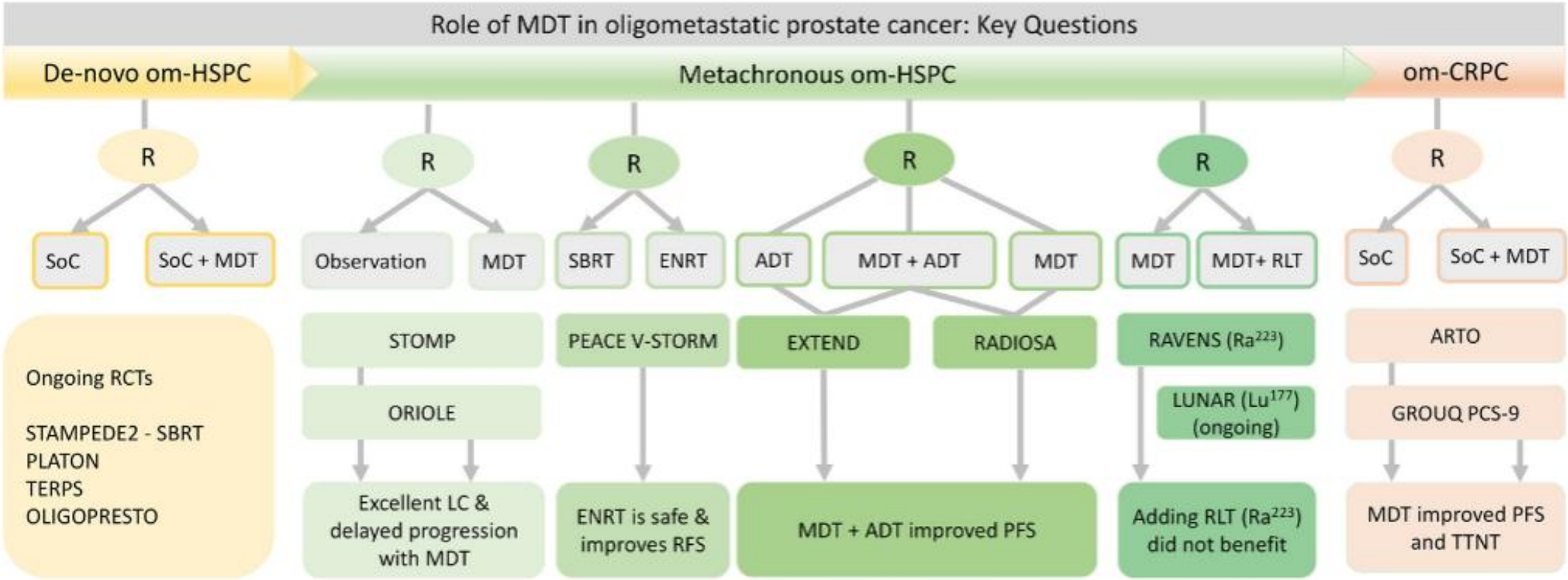
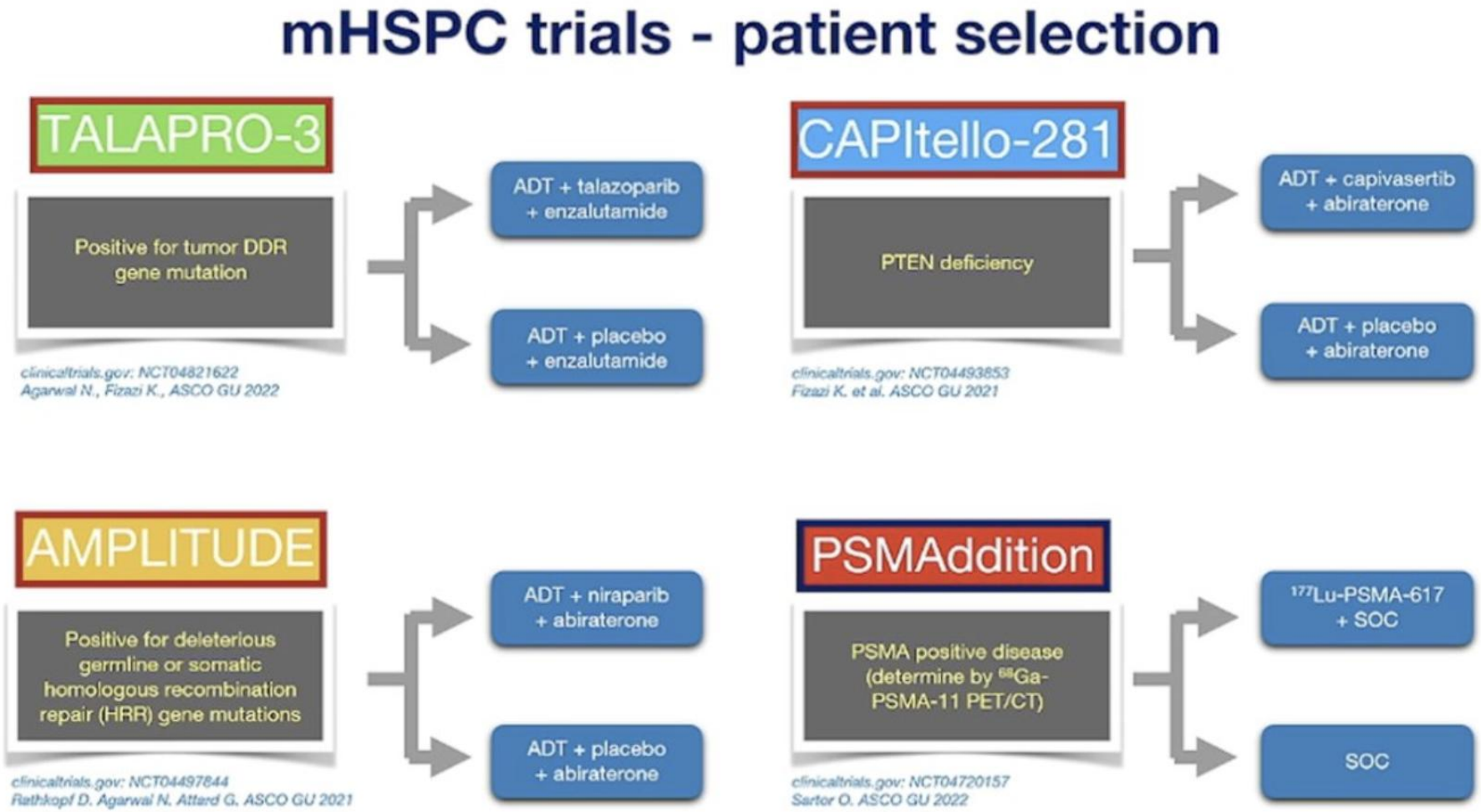


Figure 1 MDT in oligometastatic prostate cancer.

Abbreviations: ADT, androgen deprivation therapy; ENRT, elective nodal radiotherapy; LC, local control; MDT, metastasis directed therapy, om-HSPC; oligometastatic hormone sensitive prostate cancer; om-CRPC, oligometastatic castrate resistant prostate cancer; PFS, progression free survival; RFS, recurrence free survival; RLT, radioligand therapy; SBRT, stereotactic body radiotherapy; SoC, standard of care; TTNT, time to next therapy.

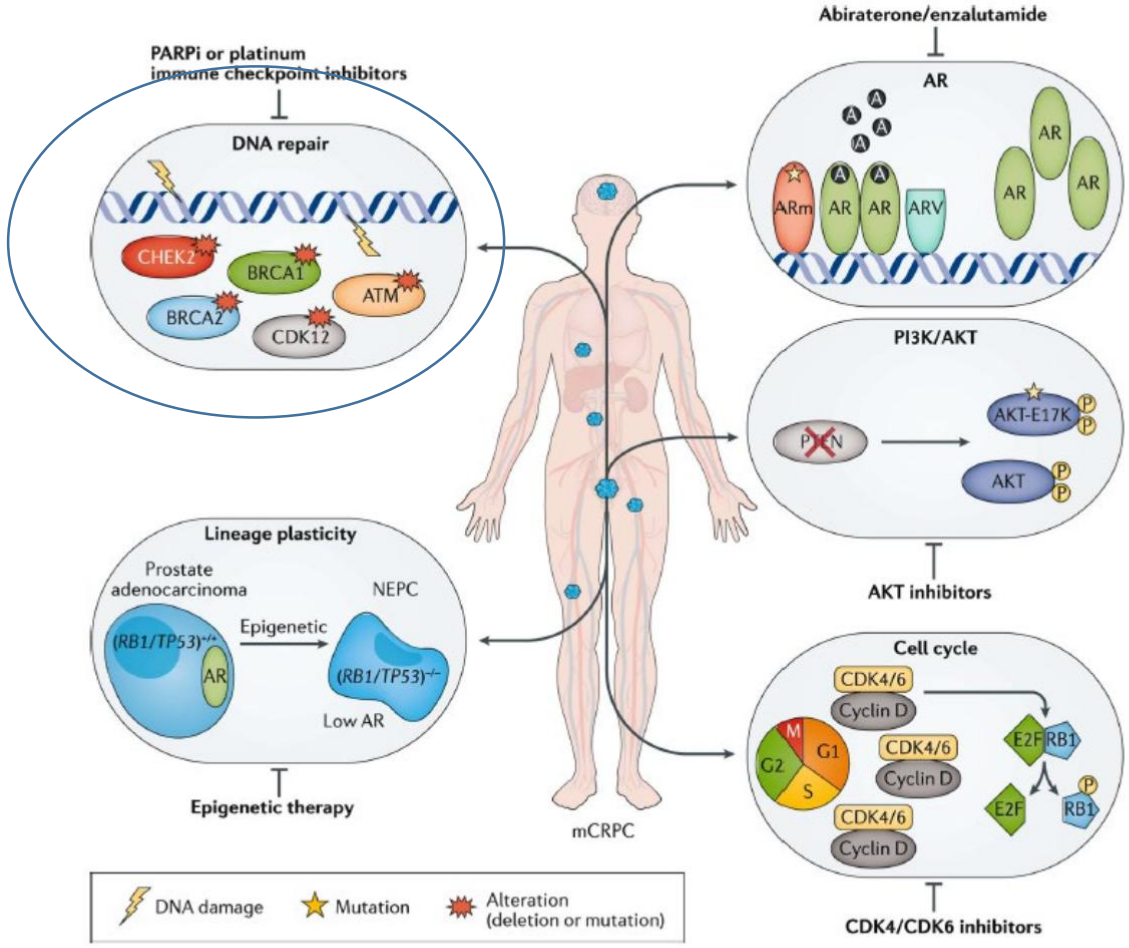
Singh M et al. Semin Radiat Oncol. 2025

Veränderte Therapielandschaft beim mHSPC



M.De Santis EAU 2025

Zielgerichtete Therapien des fortgeschrittenen Prostatakarzinoms: PARPi



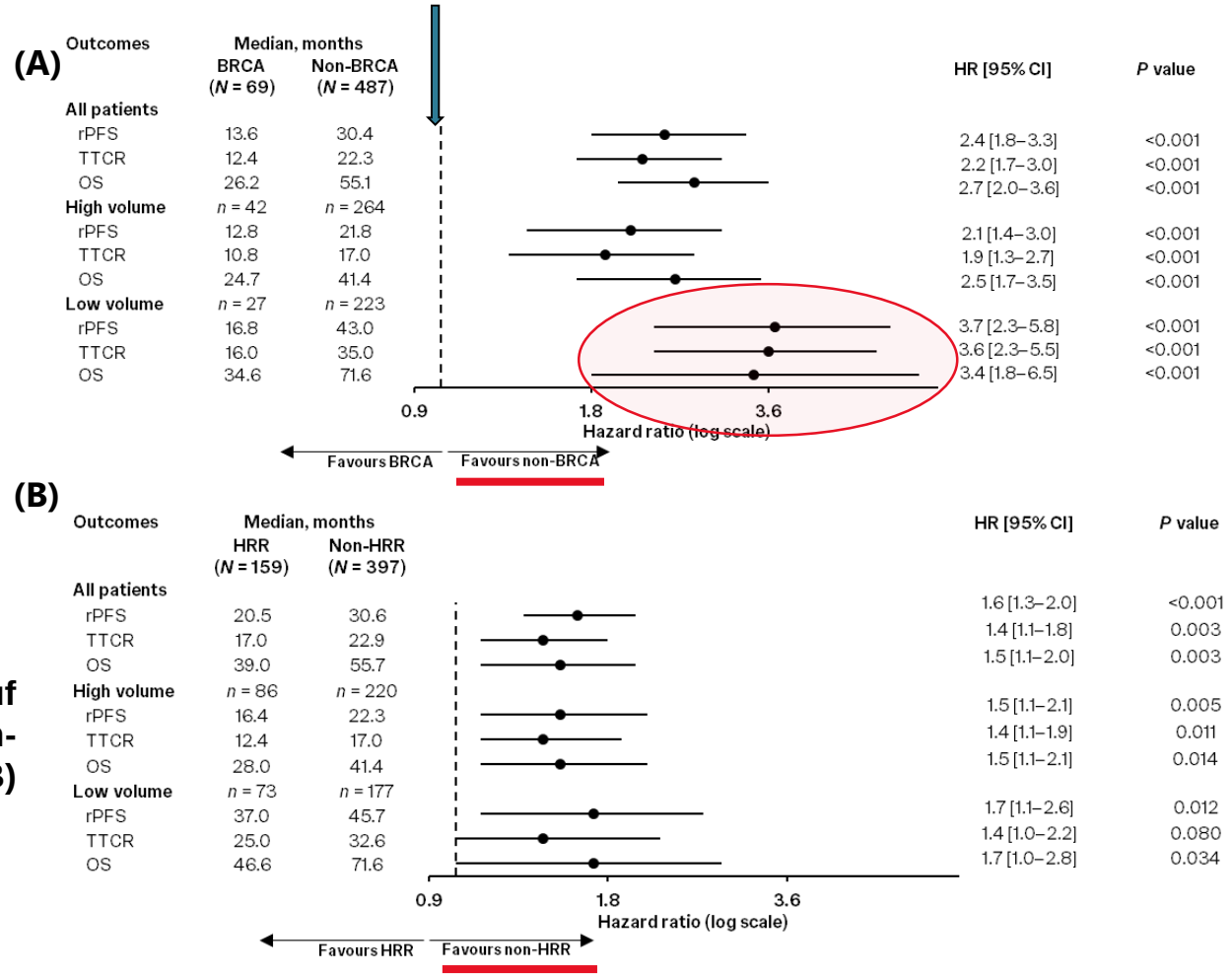
Ku et al, Nat Rev Urol, 2019

CAPTURE: mHSPC und HRR-Alterationen

Comparison of outcomes between mutational subgroups by tumour burden

- **Der Nachweis von BRCA und HRR Alterationen war mit schlechter Prognose in sowohl der low- und der high-Volume Subpopulation assoziiert**
- **Der negative Impact war stärker in der low-Volume Population**

Outcomes in Bezug auf high-volume and low-volume / BRCA versus non-BRCA (A) und HRR versus non-HRR (B)



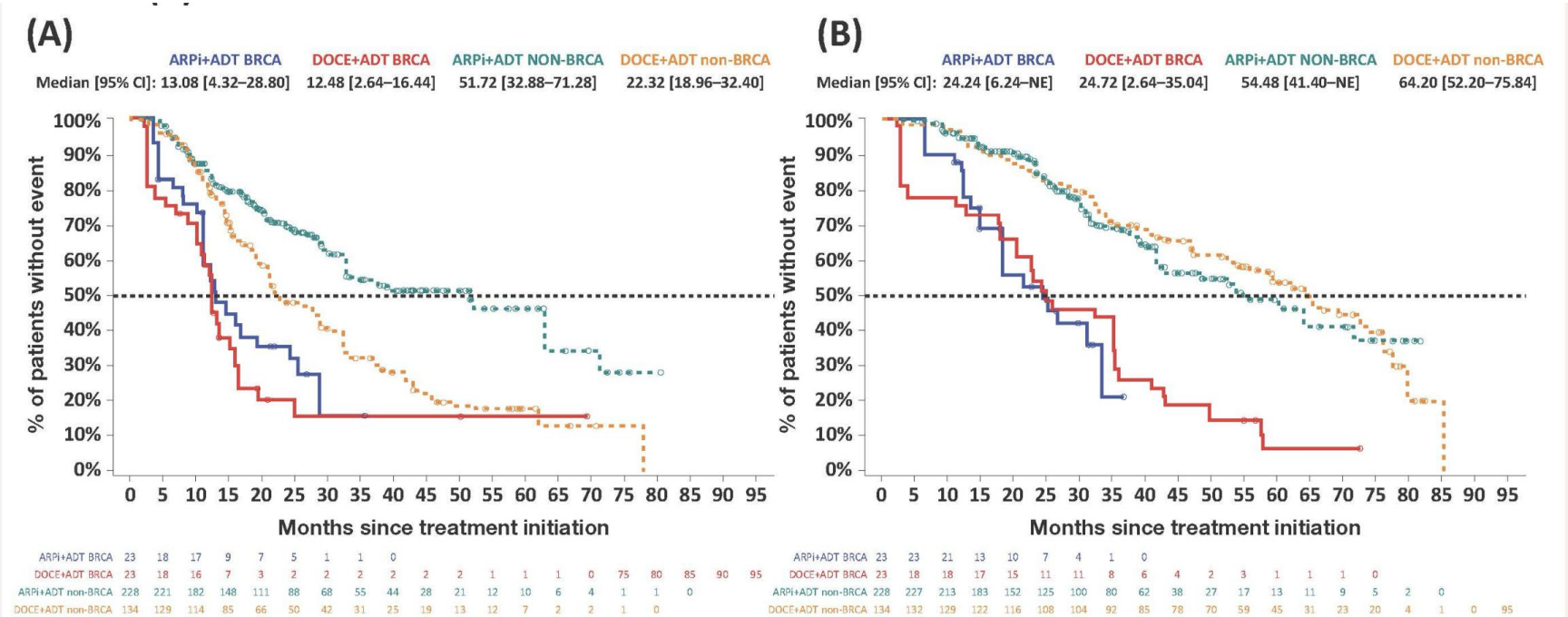
BRCA, BReast CAncer gene; CI, confidence interval; HR, hazard ratio; HRR, homologous recombination repair; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; rPFS, radiographic progression-free survival; TTCR, time to castration-resistant prostate cancer.

1. Olmos D, et al. Ann Oncol. 2024;35:458–472.

CAPTURE: mHSPC und HRR-Alterationen

Vergleich von ADT+ARPi vs ADT+Docetaxel bezogen auf BRCA/non-BRCA für PFS (A) und OS (B)[a,b]

Patienten mit BRCA Alterationen hatten das schlechteste Outcome, unabhängig von der Art der Therapie



[a]Results presented are from IPTW analysis.
[b]Balancing between treatment groups was performed within the BRCA and non-BRCA subgroups separately.

[a]Results presented are from IPTW analysis.
BRCA, BReast CAncer gene; CI, confidence interval; HR, hazard ratio; HRR, homologous recombination repair; IPTW, inverse probability treatment weighting; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; rPFS, radiographic progression-free survival.

1. Olmos D, et al. Ann Oncol. 2024;35:458–472.

AMPLITUDE Phase III Studie: ADT + AAP ± Niraparib

First and final rPFS analysis and first interim analysis of time to symptomatic progression and overall survival. Median follow-up: 30.8 months

Key inclusion criteria:

- mCSPC[a]
- Alteration in ≥1 HRR eligible gene: *BRCA1*, *BRCA2*, *BRIP1*, *CDK12*, *CHEK2*, *FANCA*, *PALB2*, *RAD51B*, *RAD54L*[b]
- ECOG PS 0-2

Key exclusion criteria:

- Any prior
  - PARPi
  - ARPI other than AAP

Prior allowed treatments in mCSPC:

- ADT ≤6 months
- Docetaxel ≤6 cycles[c]
- AAP ≤45 days
- Palliative RT

Randomized 1:1 (N=696)

Nira (200 mg QD) + **AAP** (1000 mg QD + 5 mg QD) + **ADT** (n=348)

PBO + **AAP** (1000 mg QD + 5 mg QD) + **ADT** (n=348)

Primary end point

- rPFS by investigator review

Key secondary end points

- Time to symptomatic progression
- OS
- Safety

Stratification factors:

- *BRCA2* vs *CDK12* vs all other alterations
- Prior docetaxel (yes vs no)
- Disease volume (high vs low)

Clinical data cutoff: January 7, 2025

[a]Patients with lymph node–only disease are not eligible. [b]HRR gene panel was fixed prior to trial initiation based on MAGNITUDE trial and external data from the published literature. [c]Last dose ≤3 months prior to randomization.
ECOG PS, Eastern Cooperative Oncology Group performance status; Nira, niraparib; OS, overall survival; PBO, placebo; RT, radiotherapy; QD, once daily.

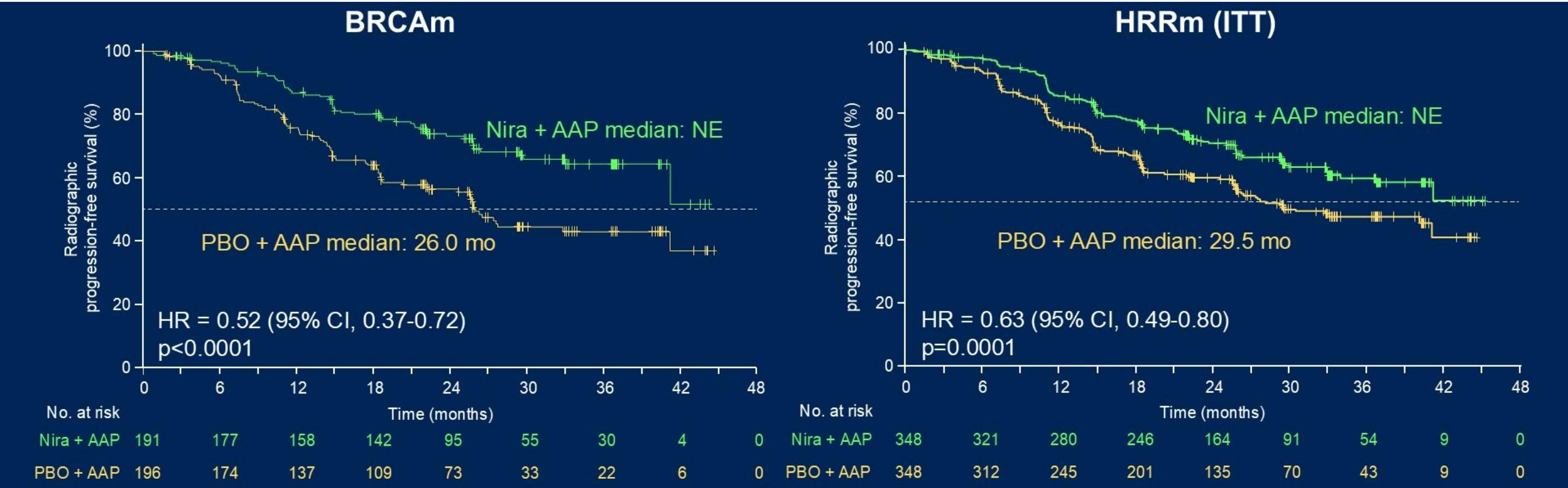
Baseline Characteristics

		Nira + AAP (n=348)	PBO + AAP (n=348)
Median age (range), y		68 (40-88)	67 (40-92)
Median PSA at initial diagnosis (range), ng/mL		112 (0.1-17475)[a]	102 (0.1-15900)[b]
ECOG PS score, n (%)	0 ≥1	242 (70) 106 (30)	218 (63) 130(37)
Gleason score at initial diagnosis, n (%)	≥8	**276 (79)**	**262 (75)**
Metastatic stage at diagnosis, n (%)	M1 (Synchronous)	**301 (86)**	**302 (87)**
Disease volume, n (%)	High	**269 (77)**	**271 (78)**
Prior docetaxel use in mCSPC, n (%)		54 (16)	56 (16)
Site of metastases[c], n (%)	Bone only Visceral Lymph nodes	146 (42) 57 (16) 173 (50)	154 (44)[d] 54 (16)[d] 161 (46)[d]
BRCA alteration, n (%)		191 (55)	196 (56)

- Characteristics were well balanced between treatment groups

[a]n=258. [b]n=275. [c]Non-mutually exclusive. [d]n=347.
PSA, prostate-specific antigen.

AMPLITUDE Phase III Studie: primärer Endpunkt rPFS



AMPLITUDE met the primary end point: Nira + AAP significantly reduced the risk of radiographic progression[a] or death by 48% in BRCAm group and by 37% in HRRm population

[a]rPFS by investigator review; rPFS improvement by blinded independent central review was as large: HR = 0.51 (95% CI, 0.37-0.72) for BRCAm group and 0.61 (95% CI, 0.47-0.79) for HRRm group.
NE, not estimable.

Prespecified Subgroup Analysis of rPFS

Variable	Subgroup	Median, mo		HR (95% CI)	Events/N	
		Nira + AAP	PBO + AAP		Nira + AAP	PBO + AAP
All patients		NE	29.5	0.65 (0.51-0.83)	113/348	151/348
Age	<65 yr	41.2	29.3	0.51 (0.34-0.77)	35/116	62/135
	65-74 yr	NE	NE	0.74 (0.50-1.11)	45/148	52/139
	≥75 yr	NE	26	0.74 (0.46-1.19)	33/84	37/74
ECOG PS at baseline	0	NE	40.2	0.60 (0.44-0.82)	72/242	93/218
	≥1	34	29.5	0.76 (0.51-1.14)	41/106	58/130
Prior docetaxel use	Yes	41.2	NE	0.75 (0.40-1.40)	18/54	23/56
	No	NE	29.5	0.62 (0.48-0.82)	95/294	128/292
Visceral metastases	Yes	NE	18.5	0.57 (0.33-0.99)	22/57	30/54
	No	NE	33.2	0.67 (0.51-0.87)	91/291	121/294
Bone-only metastases at baseline	Yes	NE	41.2	0.71 (0.46-1.10)	36/146	48/154
	No	41.2	25.6	0.60 (0.45-0.81)	77/202	103/194
Metastases stage at diagnosis	M0	NE	NE	0.96 (0.29-3.17)	5/32	6/36
	M1	NE	27.4	0.60 (0.47-0.78)	100/301	142/302
Disease volume at baseline	High	41.2	26.3	0.65 (0.50-0.85)	100/269	130/271
	Low	NE	40.2	0.55 (0.27-1.10)	13/79	21/77
Regions	Asia	36.8	NE	1.11 (0.62-1.97)	26/72	21/63
	Europe	NE	26.3	0.56 (0.40-0.78)	56/168	86/177
	North America	NE	33.2	0.51 (0.25-1.04)	14/45	18/44
	Rest of world	NE	NE	0.65 (0.35-1.20)	17/63	26/64

Benefit from Nira + AAP is generally consistent across prespecified subgroups

Results in small subgroups should be interpreted with caution. Hazard ratios stratified by disease volume (high vs low).

Adverse Events of Special Interest

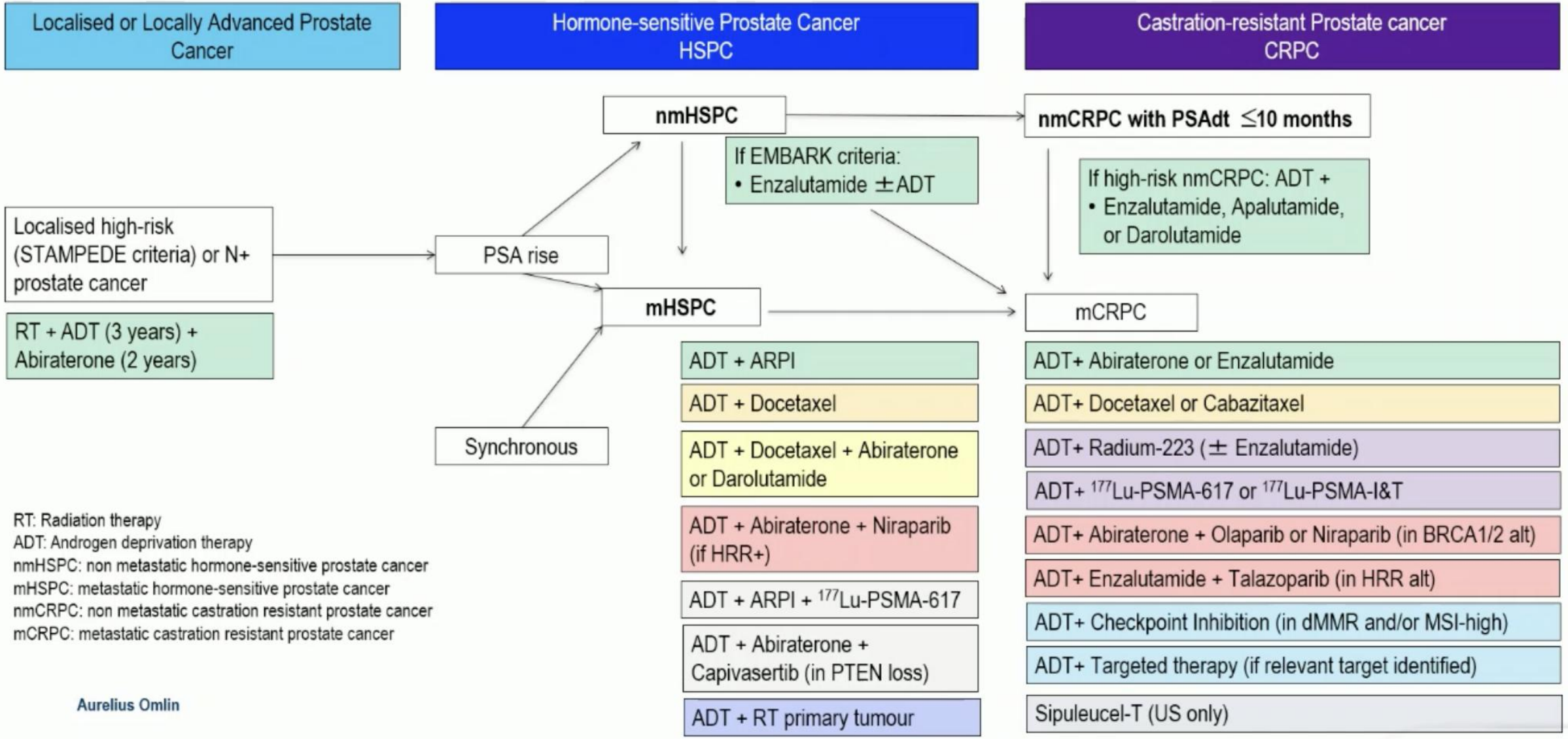
Selected categories of TEAEs of interest, n (%)		Nira + AAP (n=347)		PBO + AAP (n=348)	
		All grades	Grade ≥3	All grades	Grade ≥3
Patients with ≥1 AE of interest		306 (88)	217 (63)	261 (75)	132 (38)
Hematologic	**Anemia**	**179 (52)**	**101 (29)**	**83 (24)**	**16 (5)**
	Neutropenia	76 (22)	33 (10)	28 (8)	7 (2)
	Thrombocytopenia	66 (19)	24 (7)	20 (6)	1 (<1)
	MDS	1 (<1)	1 (<1)	0	0
Cardiovascular	**Hypertension**	**155 (45)**	**93 (27)**	**113 (33)**	**64 (18)**
	Arrhythmia	68 (20)	19 (5)	28 (8)	11 (3)
	Cardiac failure	20 (6)	9 (3)	6 (2)	4 (1)
Other	Hypokalemia	92 (27)	40 (12)	70 (20)	38 (11)
	Hepatotoxicity	46 (13)	8 (2)	71 (20)	19 (5)

- Other common AEs of any grade: constipation (35% vs 16%), nausea (31% vs 14%), fatigue (26% vs 18%), and arthralgia (21% vs 21%) in the Nira +AAP vs placebo + AAP arms, respectively

Patients are counted only once for any given event, regardless of the number of times they actually experienced the event. The event experienced by the patient with the worst toxicity is used. If a patient has missing toxicity for a specific AE, the patient is only counted in the total column for that AE.

PRESENTED BY: Prof. Gerhardt Attard, MD, FRCP, PhD

Fortgeschrittenes Prostatakarzinom Therapieoptionen



RT: Radiation therapy
ADT: Androgen deprivation therapy
nmHSPC: non metastatic hormone-sensitive prostate cancer
mHSPC: metastatic hormone-sensitive prostate cancer
nmCRPC: non metastatic castration resistant prostate cancer
mCRPC: metastatic castration resistant prostate cancer

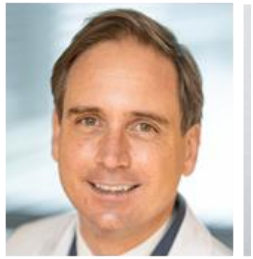
Aurelius Omlin

Präzisionsonkologie / Molekulares Tumorboard

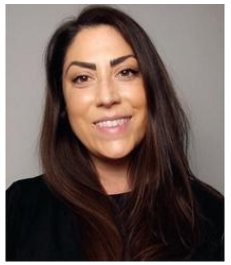
AG Molekulares Tumorboard & AG Uroonkologie

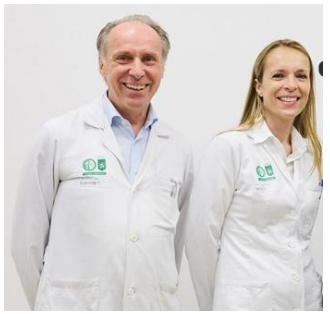
Med Uni Graz

Onkologie







Philipp Jost, Leo Edlinger, Florian Moik, Tamara Esterl, Sam Hasenleithner, Lea Reiter, Karin Groller

Thomas Bauernhofer
Angelika Terbuch
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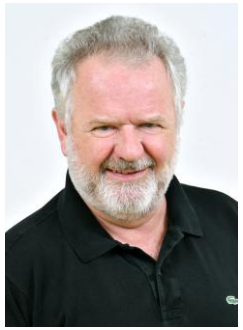
Pathologie




Gerald Höfler, Stephan Jahn, Karl Kashofer, Martin Zacharias

Humangenetik


Jochen Geigl, Ellen Heitzer

UROONKO ARBEITSGRUPPE

Onkologie Graz

Ausblick / laufende Studien

mCRPC

ASCLEPIuS Phase I/II Studie

Androgen suppression with abiraterone acetate, leuprolide, PARP inhibition and stereotactic body radiotherapy (ASCLEPIuS) in high-risk and node positive prostate cancer (PCa)

CAVE: Unabhängig vom HRR-Status!

This Phase I/II trial aimed to determine whether combining biological SBRT with a 6-month treatment of ADT, AAP, and the PARP inhibitor niraparib could offer a shorter, intensified and safe treatment option

Introduction/aim

- Treating high-risk and node-positive prostate cancer with 4–9 weeks of RT alongside 18–36 months of ADT, with or without AAP is an effective approach; however, it may lead to recurrence, varying degrees of side effects, and be inconvenient
- This multicentre investigator-initiated Phase I/II trial aimed to assess whether biological SBRT combined with a 6-month regimen of ADT, AAP and the PARP inhibitor niraparib could provide a shorter, intensified, yet safe and effective treatment option

Study design

Eligibility

At least one risk factor:

- cN1 on conventional or PET imaging
- Grade group 4/5
- Grade group 3 and PSA ≥20 ng/mL
- Grade Group 3 AND PSA ≥10 AND ≥50% positive biopsy core
- High probability of radiographic T3 on MRI AND Grade group ≥2

Baseline assessment

- Tissue from baseline prostate biopsy sent for MiOncoSeq
- EPIC-26
- Blood draw for cfDNA and CTC

Treatment

5–6 fraction SBRT (total dose: 37.5–40 Gy)

+

Concurrent systemic therapy for 6 cycles:

- **Leuprolide** (22.5 mg Q3M) or **ADT**
- Abiraterone acetate (1000 mg daily) + prednisone (5 mg BID)
- Niraparib (follow dose escalation schedule)

CTC/cfDNA during Cycle 3 (pre-SBRT) and during cycle

Post-treatment evaluations

Q3M for year 1, Q4M–Q6M for year 2, Q6M year 3, 4 and 5:

- CTCAE v5.0 toxicity, EPIC-26
- 2-year CTC/cfDNA blood collection or at time of recurrence if sooner
- 2-year post-treatment biopsy

Baseline characteristics (N=54)

- 12.1 months (IQR 9.4–18.9) median follow-up of the Phase I cohort
- 80% (n=43) Grade Group 4–5
- Median PSA 17 ng/mL (range, 1–73)
- 15% (n=8) cN+ disease
- 76% (n=41) received nodal RT

Phase I primary endpoint

MTD of **niraparib** using the time-to-event continuous reassessment method

Jackson WC, et al. ASCO GU 2025. A387.

This study demonstrates that combining biological SBRT with a 6-month treatment of ADT, AAP, and the PARP inhibitor niraparib has a manageable safety profile

Results:
To date there were:

- Zero DLTs
- No grade ≥3 rectal or urinary toxicities
- Five SAEs (anaemia, non-rectal gastrointestinal, syncope, infection, musculoskeletal) possibly attributable to study treatment
- Transient dose reductions/interruptions of AAP or niraparib in 10 and 11 patients, respectively
- No statistically significant declines in patient-reported urinary QoL
- Transient decline in bowel QoL at 6-months ($p<0.01$) that improved by 12 months

Safety and tolerability

Acute toxicity	Overall	Grade 1	Grade 2	Grade 3
GI	112 (17%)	92 (82%)	18 (16%)	2 (1.8%)
GU	67 (10%)	47 (70%)	20 (30%)	0 (0%)
Hot flashes	60 (9.0%)	53 (88%)	7 (12%)	0 (0%)
Fatigue	56 (8.4%)	45 (80%)	11 (20%)	0 (0%)
LFTs	44 (6.6%)	36 (82%)	3 (6.8%)	5 (11%)
Leukopenia	36 (5.4%)	14 (39%)	11 (31%)	11 (31%)
Anaemia	33 (5.0%)	24 (73%)	7 (21%)	2 (6.1%)
Hypertension	25 (3.8%)	3 (12%)	10 (40%)	12 (48%)

Conclusion

The combination of SBRT, ADT, AAP, and niraparib at 200 mg has a manageable safety profile for men with high-risk or node-positive prostate cancer

Jackson WC, et al. ASCO GU 2025. A387.

Ausblick / laufende Studien

Lokalisiertes Prostatakarzinom, BRCA mut, high risk / very high risk

EvoPAR-Prostate02 Phase III Studie

A Randomised, Double-blind, Placebo-controlled, Phase III Study of Adjuvant Saruparib (AZD5305) in Patients with BRCAm Localised High-Risk Prostate Cancer Receiving Radiotherapy with Androgen Deprivation Therapy

REKRUTIERUNG @ ONKOLOGIE

EvoPAR-Prostate02 REKRUTIERUNG @ ONKOLOGIE

Stratification factors

- Primary RT (Y/N)
- At initial diagnosis, N1 on conventional imaging (Y/N)
- At diagnosis (de novo) or at BCR , PSMA PET+ M1 vs. M0 vs. unknown

1:1

Cohort A: Primary RT (high risk) and Salvage RT (high risk) Doublet regimen

R

N=400

- **Saruparib 60 mg + ADT**
- **Placebo + ADT**

Saruparib/placebo x 2 years

Total duration of ADT x 2 years

1:1

Cohort B: Primary RT (very high-risk) Triplet regimen

R

N=300

- **Saruparib 60 mg + ADT + Abiraterone ***
- **Placebo + ADT + Abiraterone ***

Saruparib/placebo x 2 years

Total duration of ADT and abiraterone x 2 years

Stratification factors

- At initial diagnosis, N1 on conventional imaging (Y/N)
- 1 vs. ≥ 2 very high-risk factors
- At diagnosis, PSMA PET+ M1 vs. M0 vs. unknown

Endpoint	Measure
Primary	MFS using standard clinical imaging (conventional imaging or PSMA-PET) by BICR
Secondary	OS (key secondary endpoint) MFS by conventional imaging by BICR MFS by PSMA-PET by BICR Time to biochemical recurrence Prostate cancer-specific survival PFS2 AEs PK PRO (urinary and functional deterioration)

PSA measurement:

- Every 12 weeks from randomization until disease progression

Imaging assessment:

- 48 weeks (midpoint of study treatment)
- At time of biochemical recurrence then every 6 months until progression (MFS)

*** For Cohort B participants:** Abiraterone may be administered as a pre-study regimen with RT (neoadjuvant/concurrent) OR as initiated at time of randomization as an adjuvant only regimen

Zusammenfassung

- **Oligometastasierung durch NextGen-Imgaging häufiger diagnostiziert**
- **Synchron metastasiertes HSPC: Behandlung des Primums und möglicherweise der Metastasen sinnvoll (keine randomisierte Evidenz)**
- **Molekulargenetische Testung bereits beim mHSPC sinnvoll**
- **Metachron metastasiertes HSPC: MDT kann Tumorprogression und den Einsatz einer Langzeit-ADT verzörgern (Phase 2 Evidenz)**
- **Oligoprogr. CRPC: MDT kann PSA Versagen & Nächstlinientherapie verzögern**
- **Diskussion in einem multidisziplinären Tumorboard sowie in einem molekularen Tumorboard sinnvoll**

Med Uni Graz *Pioneering Minds*

Kontakt

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