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Tübingen - Stuttgart

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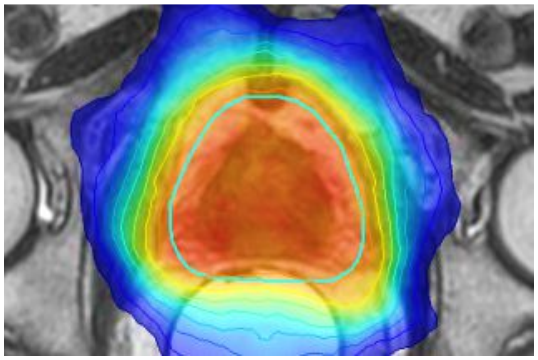

SBRT des oligomet. hormonsensitiven Prostatakarzinoms. Kombination mit ADT oder SBRT zur Vermeidung von ADT

Challenges in SBRT 22.11.2019

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Disclosures

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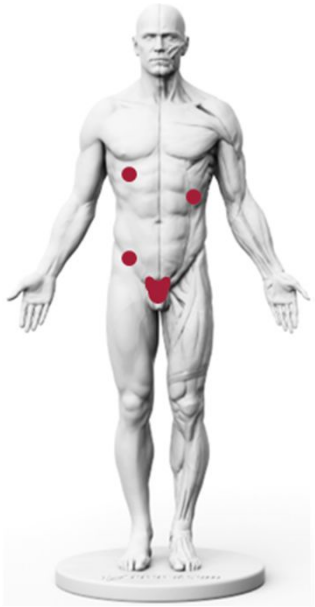
Metachrone Metastasierung nach Lokaltherapie des Primarius

Therapie von nodalen Oligometastasen (N1/M1a)

Therapie von ossären Oligometastasen (M1b)

Allgemeine Terminologie

Oligometastasen



Source: 3dtotal.com

Anzahl (n)	Ort	Zeit
Solitär (n=1)	Intrakraniell (Hirnfiliae)	Metachron / sequentiell (zeitlich versetzt nach der Primärdiagnose
Oligo- (n bis 5 (ggf. bis 10)*		
Diffus (n>5 (ggf. erst ab >10)*	Extrakraniell (alle Läsionen außerhalb des Hirns)	Synchron (gleichzeitig mit der Primärdiagnose)

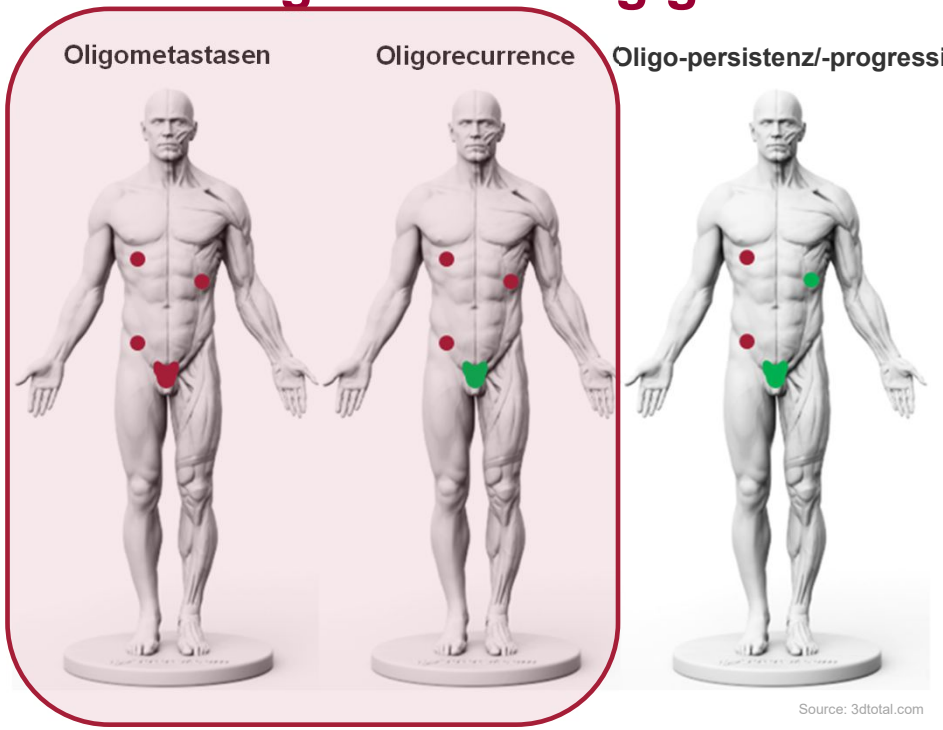
Beim Prostatakarzinom M1:

M1a distante Lymphknoten
M1b Knochenmetastasen
M1c viszerale Metastasen

Heute Fokus auf
hormonsensitives Prostatakarzinom (+/-ADT)

Müller et al. StrOnk 2018

Terminologie in Abhängigkeit von Vortherapie



Oligometastasen - synchron
Oligorecurrence - metachron nach Primärtherapie
Oligopersistenz - Persistenz unter Systemtherapie
Oligoprogression - Progress nach Systemtherapie

Konzept der Oligometastasen:

Weichselbaum & Hellmann JCO 1995:

Intermediate biologic state

Limited number and organ sites of metastases

Transitional state to dissimination

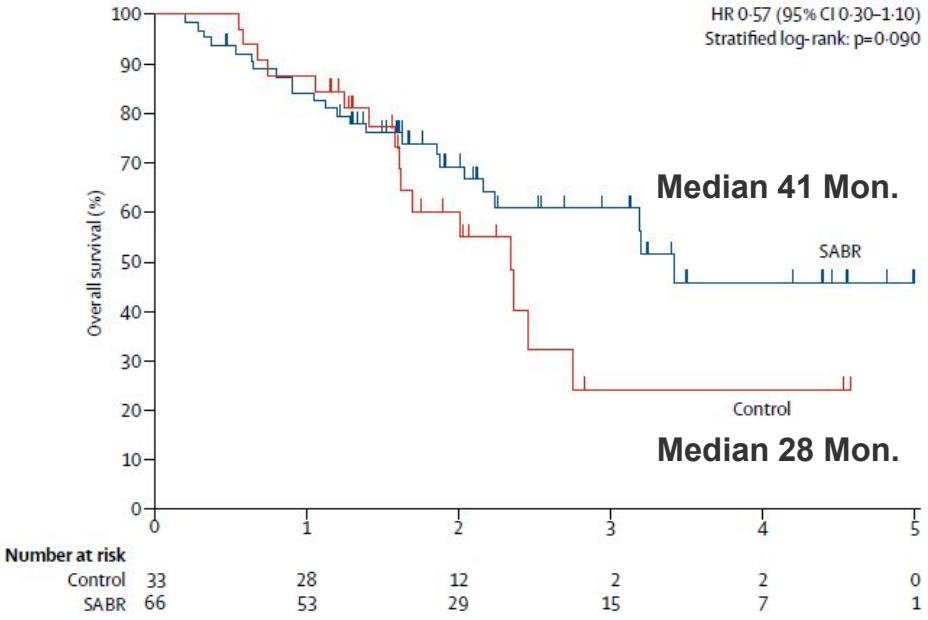
Some patients amenable to curative strategy

nach Palacios-Eito et al. und Campo et al.

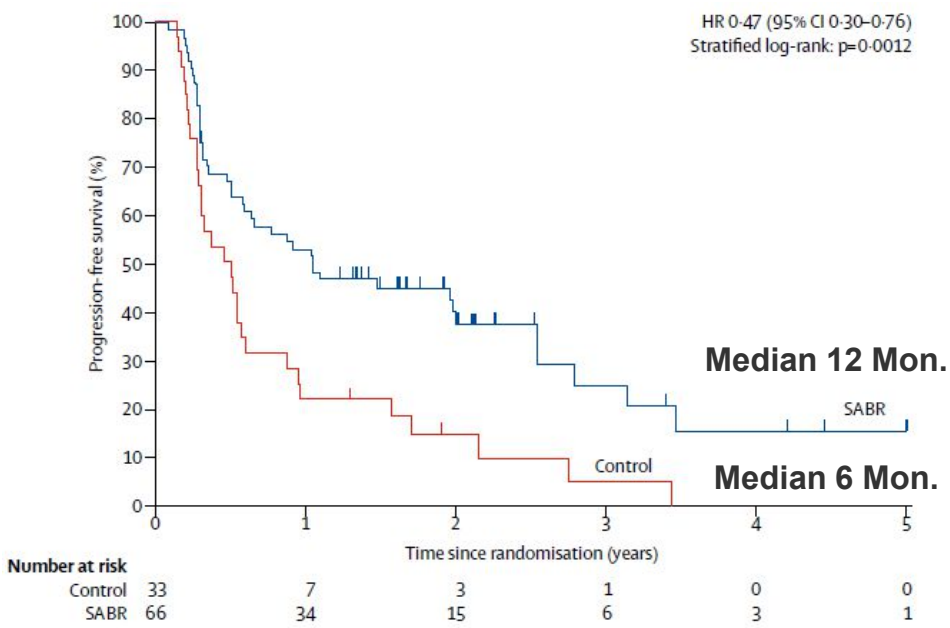
SABR-COMET, Palma et al. Lancet 2019: SABR vs. pall. Therapie

Stereotactic Ablative Radiotherapy for the Comprehensive Treatment of Oligometastases ?!

Gesamtüberleben



PFS



G2+: 9% vs. 29% (p=0,03), QoL idem

Todesfälle (n.s.): 0 vs. 4.5% (Pneumonitis, Lungenabszeß, SAB): **Trotzdem OS +13 Mon.**

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Therapie von ossären Oligometastasen (M1b)

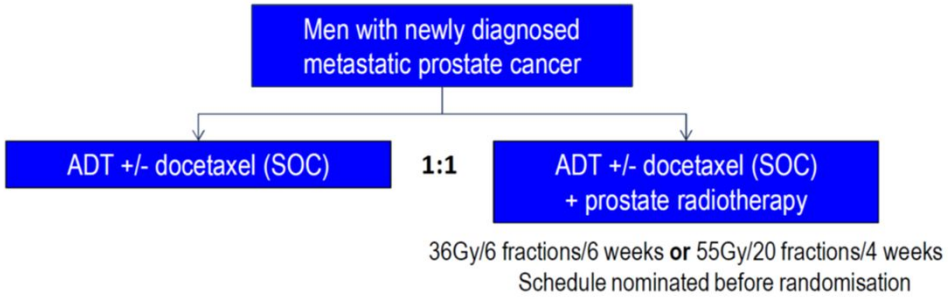
Low burden = Oligo?

„Oligo“ – Abgrenzung „low vs. high volume“ beim Prostatakarzinom

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

Staging: CT + GKS, N1/M1a nicht berücksichtigt, M1c ausgeschlossen

STAMPEDE: SOC +/- Radiotherapie der Prostata = "Zytoreduktion", n=2061

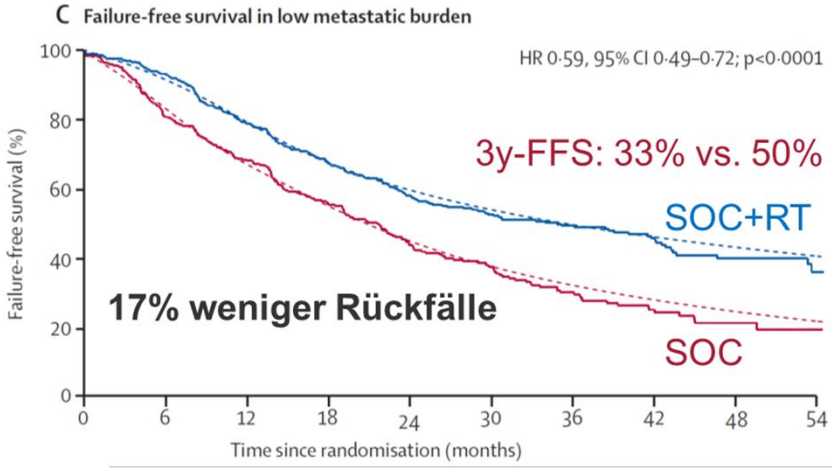


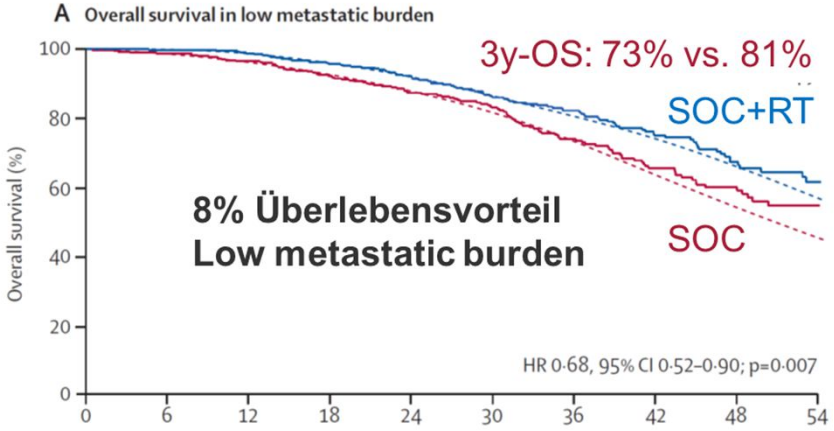
Einschluß: **cT3/4: 90% (>80% GS8+, iPSA=98)**

cN1: 64%
cM1a: 29%
cM1b: 89%
cM1c: 6%

} **Nur systemisch behandelt**

Staging: **GKS + CT-AB (MRI)** CHAARTED Criteria **binnen 12 Wochen nach ADT-Start**





Parker et al., ESTRO/ESMO

Lokale RT bei synchron M1 jenseits von Horrad / STAMPEDE

First author (year)	n	Treatment	Key results	Toxicity/complications	Conclusion
M+ disease					
Jang (2018) [64]	79	ADT vs RP	PFS: 75 vs 28 mo (HR, 0.388; $p = 0.003$)	7.9% Grade I 2.6% Grade II 2.6% Grade IIIa 2.6% Grade IIIb (Clavien-Dindo classification)	Robotic RP is a safe and feasible procedure that improves oncological outcomes Robotic RP prevents urinary tract complications from PCa
Boeve (2018) [47]	432 (unknown number with <5 bone lesions)	ADT ± prostate RT	Addition of prostate RT to ADT was associated with a trend towards improved OS on multivariate analysis: HR, 0.43; 95% CI, 0.17–1.05; $p = 0.063$		Findings suggest possible benefit of adding prostate RT in men with <5 bone lesions
Poelaert (2017) [41]	46	SoC ± cRP	At 3 mo: cRP: 5 (29.4%) pts reported stress urinary incontinence without any further local symptoms SoC: 2 (6.8%), 11 (37.9%), and 2 (6.8%) patients suffered urge incontinence, obstructive voiding needing medical intervention, and ureteric obstruction, respectively	No intraoperative 29.4% Grade I 11.8% Grade II (Clavien-Dindo classification)	Preliminary results of this prospective study show that cRP is safe Patients have more favourable characteristics vs patients treated with SoC only
Gandaglia (2017) [65]	11	RP + extended PLND	Median follow-up for survivor: 63 mo 7-yr clinical progression-free and CSM-free survival rates: 45% and 82%, respectively	18% Grade I 18% Grade II 9% Grade IIIa 9% Grade IIIb (Clavien-Dindo classification)	Findings support the safety and effectiveness of RP in a highly selected cohort of PCa pts with bone metastases and long-term follow-up
O'Shaughnessy (2017) [40]	20	ADT, RP + PLND, and SBRT [a]	Each treatment modality contributed to the outcome: 95% of pts achieved undetectable PSA with multimodal treatment, 25% of pts after ADT alone Additional 50% and 20% after surgery and SBRT, respectively	Intraoperative: 1 grade 3 Postoperative: 2 grade 3 (Clavien-Dindo classification)	Findings support a multimodal strategy aimed at treating all sites of disease
Loppenberg (2017) [45]	15 501	ADT + local therapy (RP or RT) vs no RP/RT	Local therapy vs no RP/RT: OS at 3 yr: 69% vs 54% ($p < 0.001$)		mPCa at diagnosis benefits from local therapy in terms of OM; those with a relatively low tumour risk and good general health may benefit most
Leyh-Bannurah (2017) [66]	474 1896	RP/RT vs no local therapy	RP/RT results in lower CSM (sub-HR, 0.40; 95% CI, 0.32–0.50) Lower mortality after RP than RT GS ≤7, ≤cT3, and M1a: most benefit from RP/RT		Pts with PCa that spreads outside of the prostate might still benefit from prostate-directed treatments such as RT or RP
Parikh (2017) [67]	6051	RP/RT vs no local therapy	5-yr OS: 45.7% vs 17.1% ($p < 0.01$) Use of local therapy (RP or RT) associated with OS (HR, 0.47; 95% CI, 0.31–0.72; $p < 0.01$)		Use of local therapy is associated with improvements in OS
Steuber (2017) [68]	43 vs 40	RP vs best systemic therapy	No significant castration resistance–free survival ($p = 0.92$) No significant OS ($p = 0.25$) Locoregional complication: 7% vs 35% ($p < 0.01$)		Potential selection bias in previous retrospective study RP benefits from a significant reduction in locoregional complications
Rusthoven (2016) [46]	6382	ADT ± prostate RT	Median follow-up: 5.1 yr Addition of prostate RT to ADT was associated with improved OS on univariate ($p < 0.001$) and multivariate analyses (HR, 0.624; 95% CI, 0.551–0.706; $p < 0.001$)		Men with mPCa receiving prostate RT and ADT lived substantially longer than men treated with ADT alone
Sooriakumaran (2016) [43]	106	RP + PLND	No complications in 79.2% of pts At median follow-up of 22.8 mo, 94/106 (89%) were still alive	4/5 no complication More complications only related to extension of lymphadenectomy	RP for men with locally resectable, distant mPCa has acceptable tolerability in expert hands for meticulously selected pts
Satkunasivam (2015) [69]	4069	ADT + local therapy (RP or RT) vs no RP/RT	RP: 52% reduction in risk of PCSM (HR, 0.48; 95% CI, 0.27–0.85) IMRT: 62% reduction in risk of PCSM (HR, 0.38; 95% CI, 0.24–0.61) Conformal RT: not associated with improved survival		Local therapy with RP and IMRT but not with conformal RT was associated with a survival benefit
Fossati (2015) [70]	8197	RP/RT vs no local therapy	Median follow-up: 36 vs 31 mo ($p < 0.0001$) 3-yr PCSM higher for RP/RT if PCSM risk <40% No difference if PCSM risk >50%		Potential and beneficial impacts of local treatment depend on tumour characteristics and pt selection
Heidenreich (2015) [42]	23	ADT + RT vs ADT + RP	Median follow-up: 34.5 mo CPFS: 38.6 vs 26.5 mo ($p = 0.032$) CSS: 95.6% vs 84.2% ($p = 0.043$)	Grade I: 17.4–18.4% Grade II: 8.7–10.4% Grade IIIa: 8.7–5.2% Grade IIIb: 4.3–23.7% (Clavien-Dindo classification)	RP is feasible in selected men with mPCa who respond well to neoadjuvant ADT
Gratzke (2014) [71]	1538	ADT ± RP	5-yr OS: RP: 55% No RP: 21% ($p < 0.01$)		Data suggest a survival benefit for pts undergoing RP for newly diagnosed mPCa
Culp (2014) [72]	8185	ADT + local therapy (RP or BT) vs no RP/RT	5-yr OS and predicted CSS: RP: 67% and 76% BT: 53% and 61% No RP/RT: 23% and 49% ($p < 0.001$)		Findings suggest that definitive treatment of the prostate improves survival in patients with newly diagnosed mPCa
Antwi (2014) [73]	7858	RP/RT	RP: 73% lower risk of death from all causes 72% lower risk of PCSM BT: 57% lower risk of death from all causes 54% lower risk of PCSM		Findings suggest that definitive local therapy improves survival in men with mPCa at diagnosis
Qin (2012) [74]	146	ADT ± TURP	TURP vs no TURP: Lower PSA nadir (median 0.15 vs 0.82 ng/ml; $p = 0.015$) Longer time to PSA nadir (11.2 vs 6.4 mo; $p < 0.001$) Improved CSS and OS (24.4 vs 24.1 mo and 24.4 vs 22.9 mo; NS)	No serious complications reported	TURP resulted in a better and more prolonged response to HT; tendency towards improved CSS and OS
Thompson (2002) [37]	1286	ADT ± RP	Previous RP in pts with mPCa was associated with a statistically significant decrease in the risk of death (HR, 0.77; 95% CI, 0.53–0.89) relative to those who did not undergo earlier RP		Control of the primary tumour may impact outcomes in pts with advanced PCa

Battaglia EAU 2019

Lokale RT bei synchron M1 jenseits von Horrad / STAMPEDE

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ADT +/-Lokaltherapie:

Radiotherapie
Brachytherapie
Operation
TURP

Retrospektiv OS/PCSM-Benefit

Großer Selektionsbias (retrospektiv)
RND=STAMPEDE=SOC

www.alamy.com, www.hundeferienhauser.de

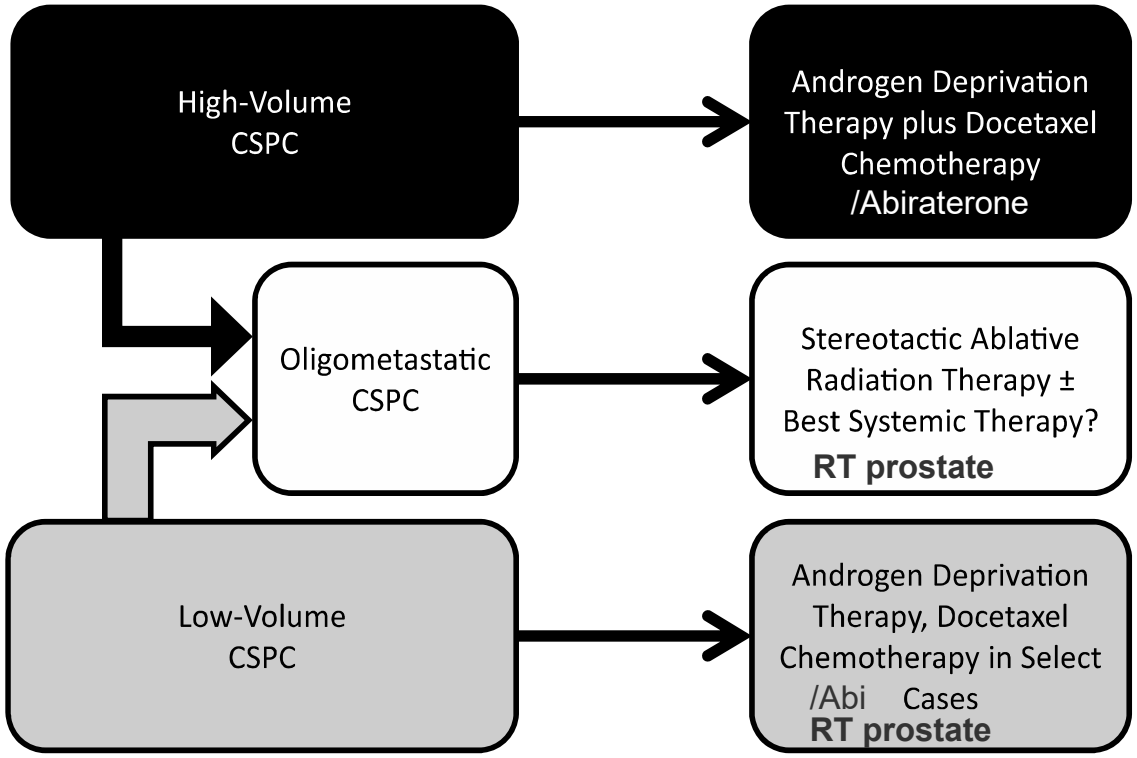
Low burden = $_{any}TNM_{1a}$ + $M_{1b\text{-}Oligo}$

Lokale RT des Primarius entspricht einer „Zytoreduktion“ +/- immunol. Effekte?

Low burden = Palliativtherapie

RT +ADT => OS↑

Zukünftige Strategie in Primärsituation mit synchron M1?



Sajula et al. Urol Oncol 2015

Doch was ist Oligomet. beim Prostatakarzinom genau?

Table 1. Definitions of Oligometastatic Prostate Cancer Used in Ongoing Clinical Trials

Study Group (ClinicalTrials.gov Identifier/ISRCTN Number)	Number of Metastases	Site of Metastases	Imaging Modality
University of Florida (NCT01859221)	NS	Any except brain or CNS	—
Sunnybrook Health Sciences Centre (NCT02563691)	≤ 5	Outside the prostate and pelvic LNs	—
Sidney Kimmel Comprehensive Cancer Center (NCT02489357)	≤ 4	Extrapelvic	—
Mayo Clinic (NCT01777802)	≤ 3	NS	—
Grupo de Investigación Clínica en Oncología Radioterapia (NCT02192788)	≤ 4	Bone, LN	—
University Hospital, Ghent (NCT01558427)	≤ 3	NS (N, M1a/b)	—
Technische Universität Dresden (NCT02264379)	≤ 5	NS	—
City of Hope Medical Center (NCT00544830)	≤ 5	NS (N1–3, M1)	—
Memorial Sloan Kettering Cancer Center (NCT02020070)	≤ 10	Bone, LN	—
Sidney Kimmel Comprehensive Cancer Center (ORIOLE) (NCT02680587)	≤ 3	Bone, LN	—
MD Anderson Cancer Center (NCT01751438)	NS	Any except brain or CNS	Bone scan, CT scan, and/or MRI
Martini-Klinik am UKE GmbH (NCT02454543)	≤ 5	Bone, LN	—
Oxford University Hospitals (ISRCTN15704862)	NS	Bone, LN	—
University Hospital, Ghent (NCT02138721)	NS	Any except brain or CNS	—

CNS = central nervous system; LN = lymph node; NR = not reported; NS = not specified.

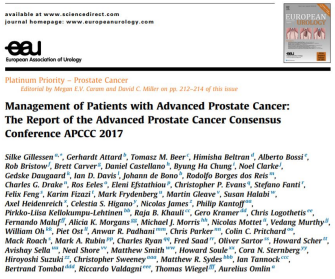
Table 2. Definitions of Oligometastatic Prostate Cancer Used in the Published Literature

Studies	n	Number of Metastases	Site of Metastases	Imaging Modality
Tabata et al[81]	35	≤ 5	Bone only; each site < 50% size of vertebral body	Bone scan
Ahmed et al[82]	17	≤ 5	NS	^{11}C-choline PET/CT, MRI, biopsy, CT, and ^{11}C-choline PET/CT + MRI
Berkovic et al[83]	24	≤ 3	Bone, LN	Bone scan + ^{18}F-FDG PET/CT, bone scan + ^{11}C-choline PET/CT
Schick et al[84]	50	≤ 4	NS	Bone scan + ^{18}F-choline PET/CT, bone scan + ^{11}C-acetate PET/CT
Decaestecker et al[85]	50	≤ 3	Bone, LN	^{18}F-FDG PET/CT, ^{18}F-choline PET/CT
Ost et al[66]	119	≤ 3	Any	^{18}F-FDG PET/CT, ^{18}F-choline PET/CT

FDG = fluorodeoxyglucose; LN = lymph node; NS = not specified; PET = positron emission tomography.

Ahmad et al. Oncology 2017:

Anzahl: **3-5 Läsionen**
Site: **LK, M1a, M1b**



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eau European Association of Urology

Platinum Priority – Prostate Cancer
Editorial by Megan E.V. Coram and David C. Miller on pp. 212-214 of this issue

Management of Patients with Advanced Prostate Cancer: The Report of the Advanced Prostate Cancer Consensus Conference APCCC 2017

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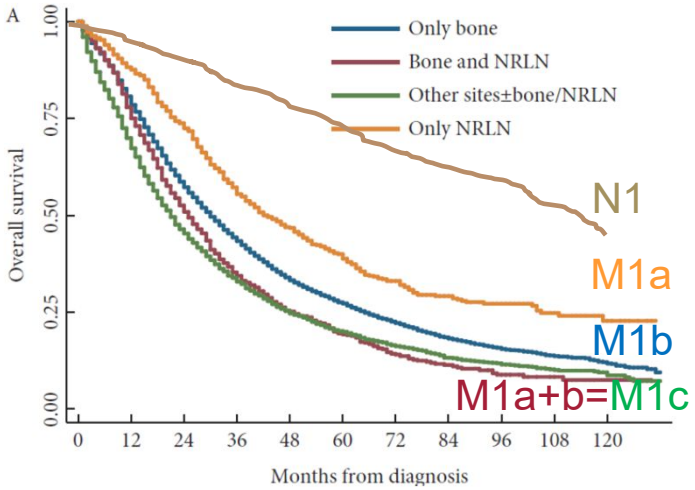
EAU kein Consensus:

Anzahl: **2** **3** **5**

Ort: **LK** **Knochen** **LK + Knochen** **„any location“**

Welche Definition ist sinnvoll? – persönliche Sicht

Trennung in prognostisch unterschiedliche Gruppen



Ali et al 2019 (n=17.167)

Rusthoven et al. 2014

Staging: **(PSMA-)PET-CT**

Anzahl: **PET-limited: n=5**

Ort: **Nicht M1a-b Kombination**
Nicht M1c, Nodes separat

Biomarker?

Limited N1	
Limited N1 oligo M1a	**anyN1? oligo M1a**
Limited N1 oligo M1b	**anyN1? oligo M1b**

Übersicht

Oligometastasen

Definition und Hintergrund

Synchrone Metastasierung

Lokale Therapie des Primarius **Plus ADT**

Therapie von nodalen Oligometastasen (N1/M1a) plus Primarius

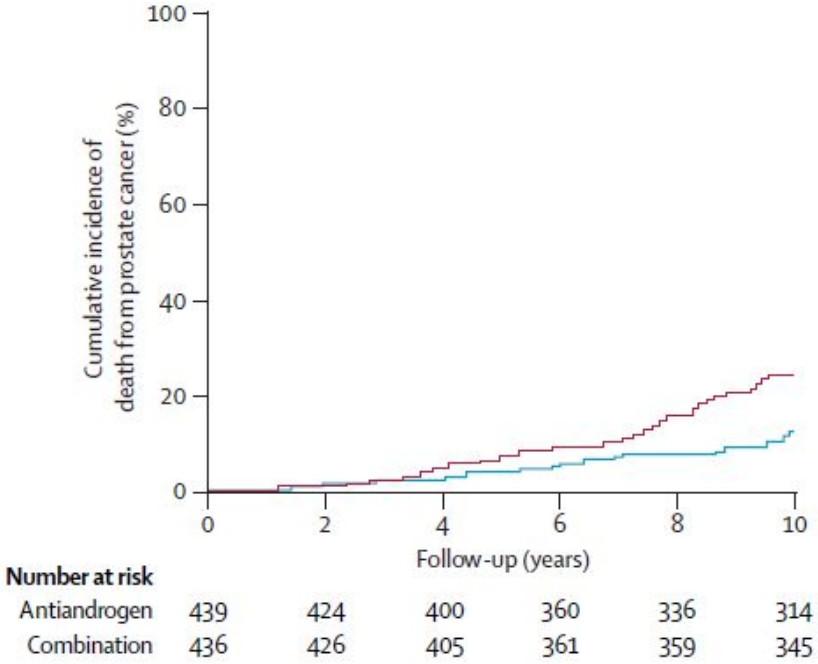
Therapie von ossären Oligometastasen (M1b) plus Primarius

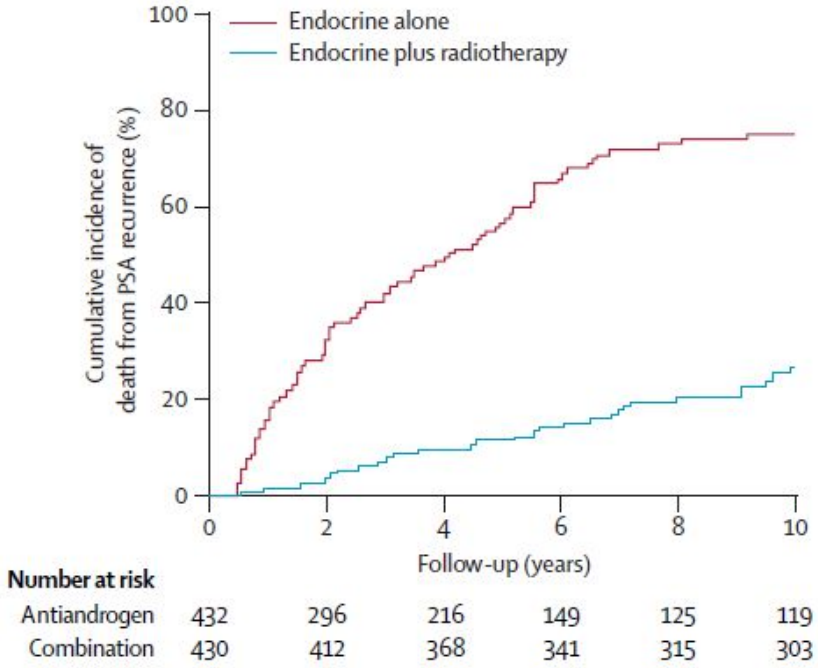
Metachrone Metastasierung nach Lokaltherapie des Primarius

Therapie von nodalen Oligometastasen (N1/M1a)

Therapie von ossären Oligometastasen (M1b)

ADT+/- RT Prostata bei Pat. mit „unknown nodal status“SPCG-7/SFUO-3



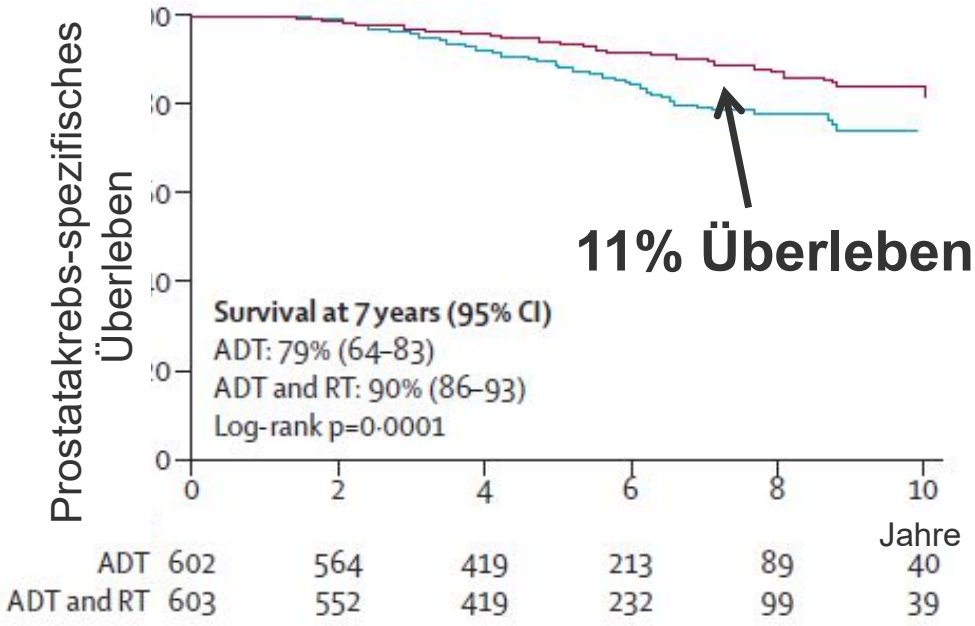


cT1b-3 und PSA<70 any GS (Staging GKS+RöThorax+DRU)
LHRH +/- RT: Prostate RT (Minipelvis obturator nodes) 50 Gy + Boost 20Gy: **GD 70Gy**

10yOS Benefit: 10% (OM: 39.4 vs. 29.6%), 10yBCR 74.7% vs. 25.9%

Widmark P et al., Lancet 2009

ADT +/- RT Becken mit „unknown nodal status“ NCIC PR.3/ MRC UK PR07



Pelvic lymph nodes were not imaged unless the planned radiation area was to the prostate only and was negative for nodal involvement. Surgical staging was allowed, but if done pelvic nodes had to be histologically confirmed free of disease.

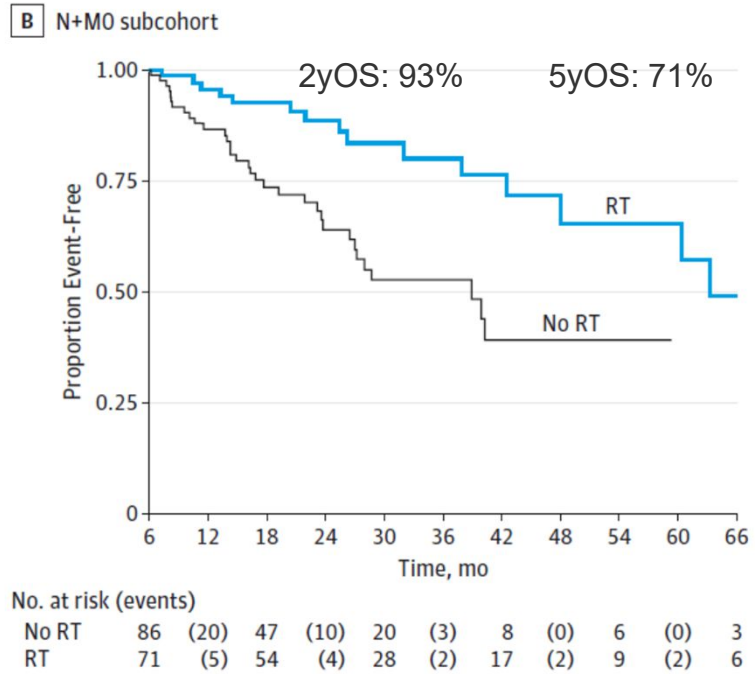
T3-4 oder T2&PSA>40 oder T2+GS8-10 + PSA>20: WPRT (45Gy) bis GD 64-69Gy

Grad3-Nebenwirkungen: Durchfall 1%, rektale Blutung <1%, Blase 2%

Warde P et al., Lancet 2011; 378: 2104–11

STAMPEDE 2016: T1-4 N1 M0 Subgruppe n=177

Randomized Patient Characteristic	No. (%)[a] Full M0 Cohort October 5, 2005, to May 1, 2014 (N = 721)	Radiotherapy NOMO Subcohort Before November 15, 2011 None Planned (n = 59)	Planned (n = 121)	N+M0 Subcohort at Least 1 Year Before Data Freeze None Planned (n = 80)	Planned (n = 97)
Age group, y					
<60	133 (19)	13 (22)	31 (26)	17 (21)	21 (22)
60-64	145 (20)	10 (17)	26 (21)	22 (28)	27 (28)
65-69	189 (26)	11 (19)	34 (28)	16 (20)	30 (31)
≥70	254 (35)	25 (42)	30 (25)	25 (31)	19 (20)
Age at randomization, median (IQR), y	66 (61-72)	68 (61-73)	65 (59-69)	65 (60-71)	65 (60-68)
Gleason Sum Score					
<8	156 (22)	15 (25)	29 (24)	21 (26)	18 (19)
≥8	535 (74)	44 (75)	91 (75)	56 (70)	76 (78)
Unknown	30 (4)	0	1 (1)	3 (4)	3 (3)
World Health Organization performance status					
0	611 (85)	47 (80)	114 (94)	69 (86)	85 (88)
≥1	110 (15)	12 (20)	7 (6)	11 (14)	12 (12)
Nodal stage					
N0	434 (60)	59 (100)	121 (100)	0	0
N+	286 (40)	0	0	80 (100)	97 (100)
NX	1 (0.1)	0	0	0	0
PSA before ADT, median (IQR)					
ng/mL	43 (18-88)	90 (58-164)	45 (22-75)	40 (17-98)	28 (15-67)
Log-transformed	3.8 (2.9-4.5)	4.5 (4.1-5.1)	3.8 (3.1-4.3)	3.7 (2.8-4.6)	3.3 (2.7-4.2)



RT 46-50Gy Pelvis
Boost 74Gy
IMRT ggf. nodal boost

FFS: HR=0,48 (CI 0,29-0,79) für SOC+RT

the data suggest that the benefits of RT extend to men with N+M0

James 2016

STAMPEDE: 2/3 N1

6.1.2 Standard-Of-Care (M0) Prostate RT

6.1.2.A N0M0 Participants

Investigators should give standard radiotherapy (RT) to participants with node negative, non-metastatic disease (N0M0), in accordance with data from the PR07 and SPCG trials. If there is an intention to omit radiotherapy (e.g. RT is contraindicated for the participant) in participants with N0M0 disease this must be discussed with the STAMPEDE trial team before randomisation to confirm eligibility. See Section 6.7 for further details of radiotherapy administration.

6.1.2.B N+M0 Participants

For participants with node-positive, M0 disease there are no randomised data on whether radiotherapy is indicated or not. However the NCIC PR.3 / MRC PR07 trial included participants with unknown nodal status who received whole pelvic radiotherapy (12) and demonstrated a large overall benefit. Additionally, non-randomised data from the STAMPEDE control arm suggests that the benefit observed in participants with N0M0 disease can be extended to those with pelvic nodal involvement. Therefore the STAMPEDE TMG recommends that pelvic nodal radiotherapy be considered for participants with node-positive, M0 disease at the discretion of the treating clinician (13).

6.1.2.C Planned Use Of SOC RT

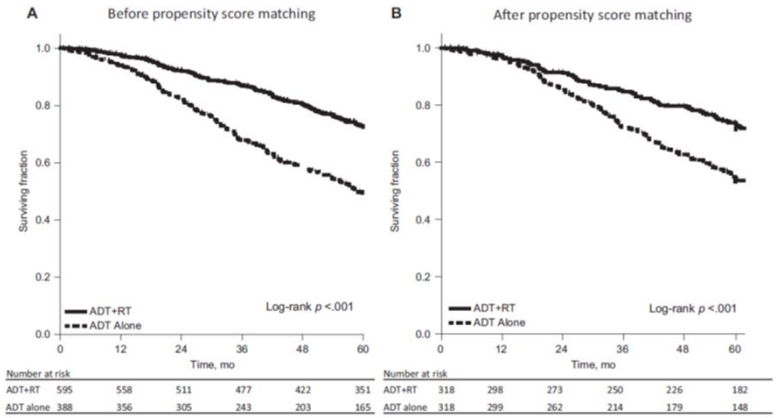
Suitability for radiotherapy is assessed by the treating clinicians. Investigators will be asked to state their intention with regards to planned radiotherapy in this group at randomisation. Intention to give radiotherapy (or not) for **all** participants must be stated at randomisation to ensure that there is no bias towards particular combinations of systemic therapy with radiotherapy.

SOC radiotherapy is not a core part of the trial, therefore we intend to collect minimal data about the radiotherapy administered. It is accepted that some participants will develop progressive disease before radiotherapy can be administered and if this occurs the reasons for non-delivery of treatment must be recorded on the Radiotherapy Detail CRF.

It is well known that prostate radiotherapy improves survival for men with locally advanced (T3–4 N0 M0) prostate cancer.[22] We have now found that prostate radiotherapy also improves survival for men with a low metastatic burden (T_{any} N_{any} M1) prostate cancer. It therefore seems safe to conclude that radiotherapy would also improve survival for men with pelvic node-positive prostate cancer (T_{any} N1 M0). This is important, because it is not feasible to do randomised trials specifically in men with non-metastatic node-positive prostate cancer and because such men often receive systemic treatment alone. In the current study, roughly 60% of patients were N1 in both the high and low metastatic burden subgroups.

Empfehlung zur pelvinen RT bei N1

cN1 – retrospektive Daten



5-Jahres Überleben:

Vorteil 18% (n=983)

71,5%vs. 53,2%

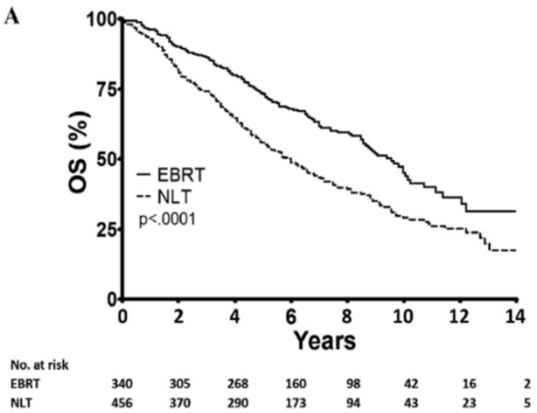
ADT+RT vs. ADT allein
Propensity Score (b)

Table 4. Multivariable Cox proportional hazards analyses of five-year overall mortality, stratifying by age at diagnosis, clinical T stage, Gleason Score, and PSA level*

Stratified subset	ADT alone, No. (%) dead within 5 y	ADT plus RT, No. (%) dead within 5 y	Adjusted HR (95% CI) †	P‡
Age < 65 y	50 (37.9)	24 (16.4)	0.25 (0.14 to 0.45)	<.001
Age ≥ 65 y	89 (47.9)	59 (34.3)	0.64 (0.44 to 0.95)	.03
T1-T2	74 (38.5)	37 (19.6)	0.40 (0.26 to 0.62)	<.001
T3-T4	65 (51.6)	46 (35.7)	0.62 (0.38 to 1.01)	.05
GLS ≤7	33 (33.3)	16 (17.2)	0.49 (0.23 to 1.01)	.05
GLS ≥8	94 (48.0)	63 (30.6)	0.55 (0.38 to 0.79)	.001
PSA < 20 ng/mL	56 (38.6)	35 (24.3)	0.60 (0.35 to 1.04)	.07
PSA ≥ 20 ng/mL	74 (48.1)	45 (29.0)	0.44 (0.28 to 0.68)	<.001

Lin JNCI 2015

cN1 SEER



10-Jahres Überleben:

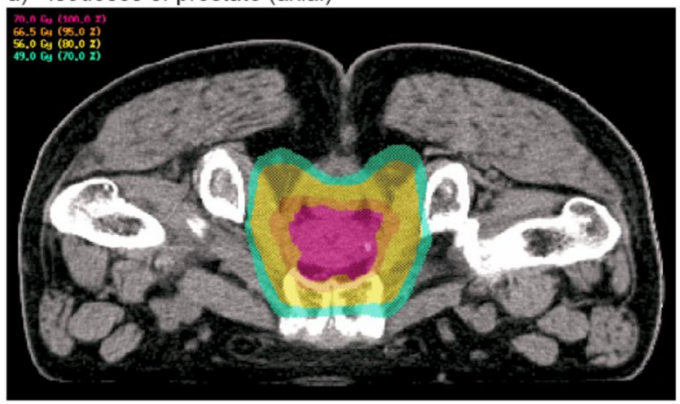
Vorteil 16% (n=796)

45%vs. 29%

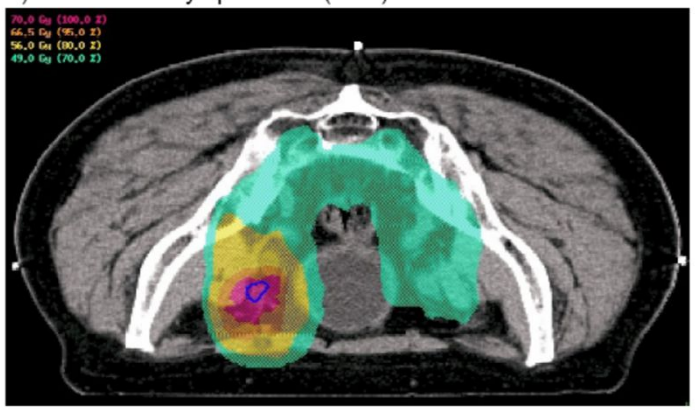
Rusthoven IJRBOP 2014

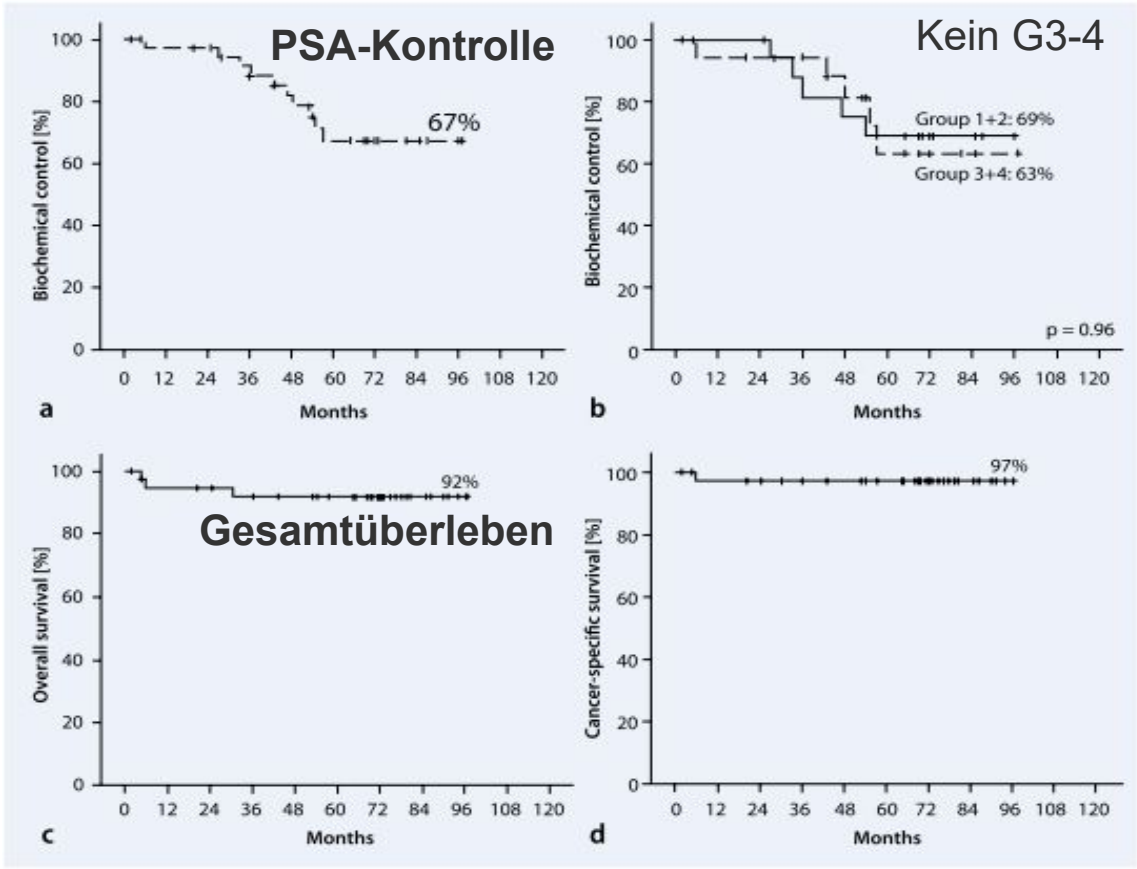
Stadium IV (cN1): Exemplarisch definitive RT (LK-Boost 70Gy)+ ADT

a) Isodoses of prostate (axial)



b) Isodoses of lymph nodes (axial)





Müller et al.

Stadium IV (cT+cN1): SBRT+Pelvis? (cave Bauman et al.)

Patient characteristics at diagnosis

Age: Median (range)	68 (44–89)	
Clinical T stage		
	T2a	1 (2%)
	T2b	2 (3%)
	T2c	15 (23%)
	T3a	12 (17%)
	T3b	22 (32%)
	T4	16 (23%)
Clinical N stage		
	N0	27 (46%)
	N1	37 (54%)
Risk grouping		
	High risk	20 (29%)
	Very high risk	11 (17%)
	Node positive	37 (54%)
ADT		
	Medical	54 (79%)
	Surgical	14 (21%)
Duration of ADT: median (IQR)	15 months (12–24 months)	
Radiotherapy volumes		
	Prostate only	31 (45%)
	Prostate + gross node	3 (5%)
	Prostate + gross node + pelvic nodal region	3 (5%)
	Primary + pelvic nodal region	31 (45%)
Radiotherapy dose to prostate + gross nodes		
	37.5 Gy in 5 fractions	12 (18%)
	35 Gy in 5 fractions	56 (82%)
Pelvis	25 Gy in 5 fractions	
TURP		
	Yes	12 (17%)
	No	56 (83%)

ADT, androgen deprivation therapy; IQR, interquartile range; TURP, transurethral resection of prostate.

Murphy et al. 2018

Constraints used for organs at risk

	V14 (Gy)	V17.5 (Gy)	V28 (Gy)	V31.5 (Gy)	V35 (Gy)
Rectum (%)	–	40	15	8	3
Bladder (%)	–	20	–	–	3
Bladder in N+ (%)	40	27	–	–	–
Femur head	5	–	–	–	–

V14, volume receiving 14 Gy; V17.5, volume receiving 17.5 Gy; V28, volume receiving 28 Gy; V31.5, volume receiving 31.5 Gy; V35, volume receiving 35 Gy; N+, node positive.

n=68 NCCN high/very high/ node-positive)

Median ADT 15 Mon. (12-24)
Neoadj ADT-Start: 7 Mon.

Medianer FU: 18 M.:

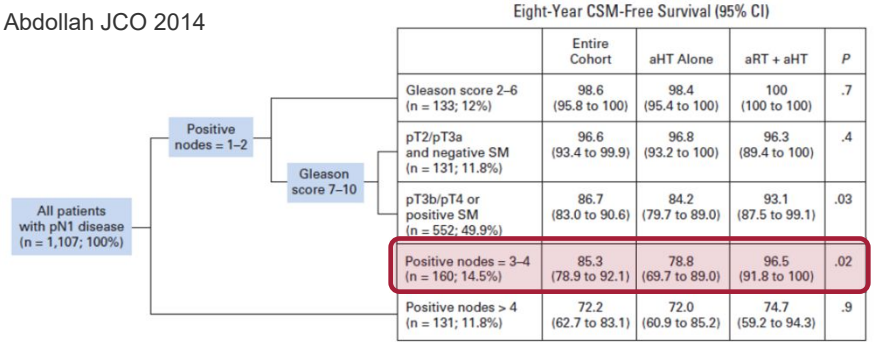
OS: 97%
BCC: 94%

PTV 5mm (Rectum 3mm), IPSS<15
IMRT (FFF), CBCT+Arzt
Toxizität: 2.5% G3 GU, sonst 8.5% G2 GU/GI

Author	Total no. of patients (no. of HR)	Median FU (mo)	Dose (Gy)	Field Size	bRFS (%)	Toxicity	
						Grade 2, 3 GI (%)	Grade 2, 3 GU (%)
Murthy[14]	68 (31)	18	35-37.5/5 fx	P + SV ± LN	94*	Acute: 4, 0 Late: 4, 0	Acute: 12, 0 Late: 4.5, 2.5
Masunuru[12]	30	25	40/5 fx	P + SV ± LN	NR	Acute: 3.3, 0 Late: 32, 0	Acute: 46.7, 0 Late: 52, 0
Pinitpatcharalert	(19)	18	37.5-40/5 fx	P + SV + LN	95.7	Acute: 0, 0 Late: 9.1, 0	Acute: 36.4, 4.5 Late: 27.3, 4.5

Stadium IV (pN1): S3-Leitlinie: ADT 3 Jahre +/- RT Becken

Abdollah JCO 2014

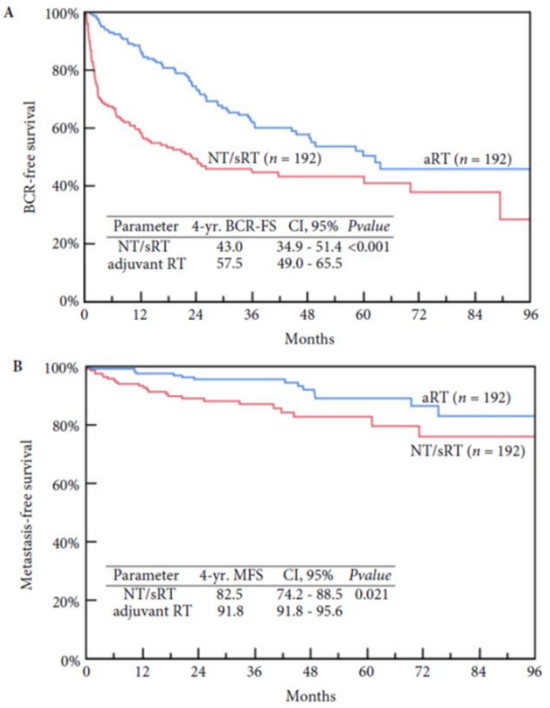


Eight-Year CSM-Free Survival (95% CI)

	Entire Cohort	aHT Alone	aRT + aHT	P
Gleason score 2–6 (n = 133; 12%)	98.6 (95.8 to 100)	98.4 (95.4 to 100)	100 (100 to 100)	.7
pT2/pT3a and negative SM (n = 131; 11.8%)	96.6 (93.4 to 99.9)	96.8 (93.2 to 100)	96.3 (89.4 to 100)	.4
pT3b/pT4 or positive SM (n = 552; 49.9%)	86.7 (83.0 to 90.6)	84.2 (79.7 to 89.0)	93.1 (87.5 to 99.1)	.03
Positive nodes = 3–4 (n = 160; 14.5%)	85.3 (78.9 to 92.1)	78.8 (69.7 to 89.0)	96.5 (91.8 to 100)	.02
Positive nodes > 4 (n = 131; 11.8%)	72.2 (62.7 to 83.1)	72.0 (60.9 to 85.2)	74.7 (59.2 to 94.3)	.9

CSM-Nutzen: pT3bN1 u. any pTpN1(n=3-4)

5.62	Empfehlung	neu 2017
Empfehlungsgrad 0	Bei Patienten mit lymphknotenpositivem Prostatakarzinom nach radikaler Prostatektomie und Lymphadenektomie kann eine adjuvante Bestrahlung der pelvinen Lymphabflusswege in Kombination mit einer hormonablativen Therapie von mindestens 24 Monaten, besser 36 Monaten Dauer angeboten werden.	
Level of Evidence 2–	Literartur: [da Pozzo et al. 2009; Briganti et al. 2011; Abdollah et al. 2014; [Tilki et al. 2016; Jegadeesh et al. 2017]	
	Gesamtabstimmung: 78 %	



Adjuvant besser als Salvage v.a. PSA<0,5 bei RT-Start progn. günstig

Tilki et al. 2017

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Therapie von nodalen Oligometastasen (N1/M1a) plus Primarius	**Plus ADT**

1.	Lokale Therapie (T_{any}+N1):	RT Becken +/- Boost (PC +/-nodes) OP (pN1): adj. RT Becken
2.	Systemtherapie:	(2-) **3 Jahre ADT** (pN1 1-2LK zurückhaltend)
3.	**SBRT:**	bei pelviner Mitbehandlung => **Studien**

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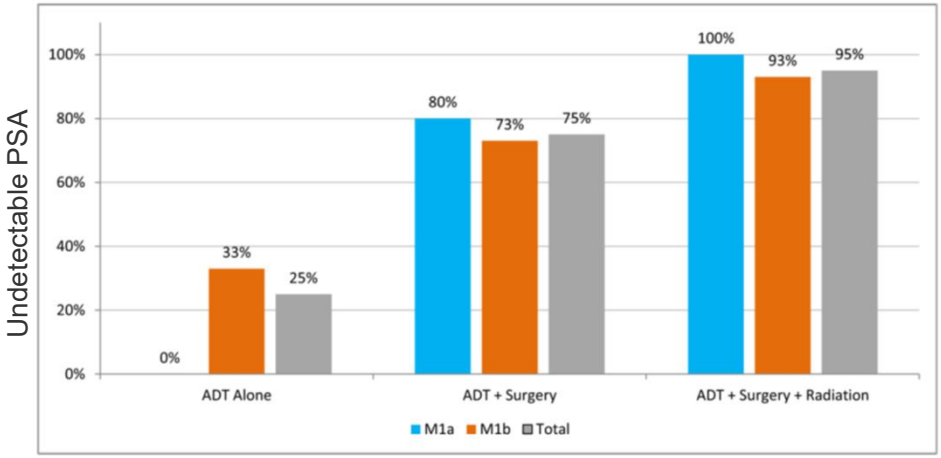
Therapie von ossären Oligometastasen (M1b)

Synchrone ossäre Metastasierung: Case report level

Synchronous or metachronous oligometastases					
Schick (2013) [17]	50	High-dose EBRT	3-yr follow-up bRFS, 54.5%; clinical failure-free survival, 59%; OS: 92% bRFS significantly associated with the number of metastases 66.5% vs 36.4% (1 and >1 metastatic lesion)	No >grade 2 acute or late toxicity	OMPCa may be treated successfully with short-term ADT and high-dose irradiation to the metastatic lesions; high dose improves bRFS
Tabata (2012) [49]	35	RT	3-yr OS: 77% 88% of pts who had pain were improved 1 mo after RT Median duration of pain relief: 12 mo		RT of bone oligometastases in PCa was effective for long-term pain relief
O'Shaughnessy et al.	20	ADT/OP/SBRT			

n=7/50

Battaglia 2019



Datenbasis limitiert
=> STAMPEDE (SOC + X)

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Therapie von ossären Oligometastasen (M1b) plus Primarius	**Plus SOC**

Therapie analog STAMPEDE, individuell (TuKo) mehr (RT Becken/LK/M1a/b)

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Therapie von ossären Oligometastasen (M1b)

Oligorecurrent nodes & SBRT

Table 3 – Site (pelvic or extrapelvic) of nodes treated with SBRT.

	Total no. of patients treated with SBRT	Total no. of nodes treated with SBRT	Pelvic (no. of pts/no. of nodes)	Extrapelvic (no. of pts/no. of nodes)
Casamassima et al (2011) [12]	18	18	15 (pelvic and/or extrapelvic)/NR	3 (mediastinal)/NR
Jereczek-Fossa et al (2012) [13]	18	18	16/16	2/2
Ahmed et al (2013) [14]	1	1	0	1/1
Decaestecker et al (2014) [15]	27	27	25/25	2/2
Detti et al (2015) [16]	30	39	NR/27	NR/12
Muldermans et al (2016) [17]	5	6	NR	NR
Pasqualetti et al (2016) [18]	NR	25	NR/18	NR/7
Ingrosso et al (2016) [19]	40	47	35/40	5/7
Ost et al (2016) [20]	72	89	53/NR	19/NR

NR = not reported; pts = patients; SBRT = stereotactic body radiotherapy.

Median FU (mo)	ADT	No. of pts in ADT	Median duration of ADT (mo)
29	No	–	–
21.9; 13.7 [b]	Yes	14 (78%)	17.5; 12 [b]
4.4	Yes	1 (100%)	NR
24	Yes	35 (70%)	1
12	Yes	14 (46%)	NR
16	NR	NR	NR
11.5	No	–	–
23.8	Yes	19 (47%)	NR
36	Yes	31 (43%)	1

Ponti et al. EAUFocus 2017

N=114/235 Pat. mit ADT / (N1/M1a)
Cholin-PET-CT, SBRT (BED>100Gy)

Lokale Kontrolle: 98%
PFS: 22.5 Mon (11-30 Mon.)
Tox. Gering

Feasibility Daten (ADT Dauer 1-17 M.)

Study	Median PFS (mo)	b-RFS (mo)	Toxicity scale	FU evaluation	In-field recurrence	ADT-FS (mo)	RECIST criteria	No. of pts with acute and/or late toxicity (grade ≥ 2)
Casamassima et al (2011) [12]	24	NR	RTOG	PSA every 3 mo, choline-PET at 2 mo	No	NR	NR	0
Jereczek-Fossa et al (2012) [13]	>30; 11 [a]	NR	RTOG	PSA every 3 mo and choline-PET (timing not reported)	No	NR	Yes	1 (acute); 2 (late)
Ahmed et al (2013) [14]	NR	NR	CTCAE 3.0	PSA every 3 mo and imaging at 3 mo	No	NR	Yes	0
Decaestecker et al (2014) [15]	19	NR	CTCAE 3.0	PSA every 3 mo and choline-PET at PSA progression	No	25	Yes	3 (late)
Detti et al (2015) [16]	NR	8.1	CTCAE 4.0	PSA every 3 mo and imaging at PSA progression	No	NR	Yes	1 (acute)
Muldermans et al (2016) [17]	NR	NR	CTCAE 4.0	PSA every 3 mo and choline-PET at 3–6 mo	No	NR	Yes	0
Pasqualetti et al (2016) [18]	NR	NR	CTCAE 4.0	PSA every 3 mo and choline-PET at 3–6 mo	No	39.7	Yes	0
Ingrosso et al (2016) [19]	15.5	24	RTOG	PSA every 3 mo and choline-PET at PSA progression	Yes (1 pt)	26 (mean)	Yes	1 (acute); 1 (late)
Ost et al (2016) [20]	21	NR	CTCAE 4.0	PSA every 3 mo and choline-PET at 3–6 mo	Yes (3 pts)	44	Yes	3 (late)

ADT-FS = androgen deprivation therapy-free survival; b-RFS = biochemical relapse-free survival; FU = follow-up; NR = not reported; PET = positron emission tomography; PFS = progression-free survival; PSA = prostate-specific antigen; pts = patients; RECIST = response evaluation criteria in solid tumors; RTOG = Radiation Therapy Oncology Group.
[a] Two patients with retroperitoneal node metastasis.

Oligorecurrent nodes & ADT 12 Mon.

Synchronous or metachronous oligometastases					
Schick (2013) [17]	50 **n=43**	High-dose EBRT	3-yr follow-up bRFS, 54.5%; clinical failure-free survival, 59%; OS: 92% bRFS significantly associated with the number of metastases 66.5% vs 36.4% (1 and >1 metastatic lesion)	No >grade 2 acute or late toxicity	OMPCa may be treated successfully with short-term ADT and high-dose irradiation to the metastatic lesions; high dose improves bRFS

Battaglia 2019

40.5% N1 23% M1a 31.5% M1b

Becken mit 50.4Gy und Boost LK (54-74Gy)
ADT: median 12 Mon. (3-34)

50% nach median 14.4 Mon. (21/25 Pat. multitop) rez.

3ybRFS: 65% and 41.8% **(>64 Gy** vs. weniger)

Trend M1b schlechter: **3y bRFS 65.3% (**N1/M1a**)** versus 32.4%

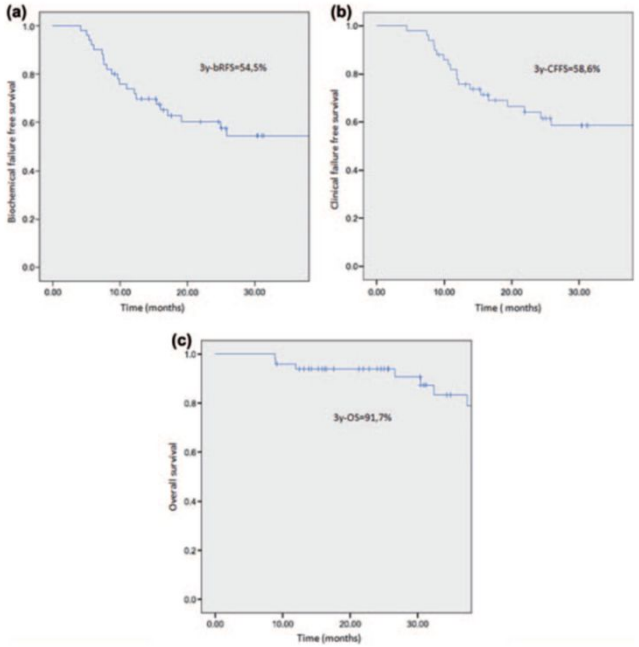


Figure 2. (a) Biochemical relapse free survival. (b) Clinical failure free survival. (c) Overall survival.

Oligorecurrent nodes & ADT 2 Mon.

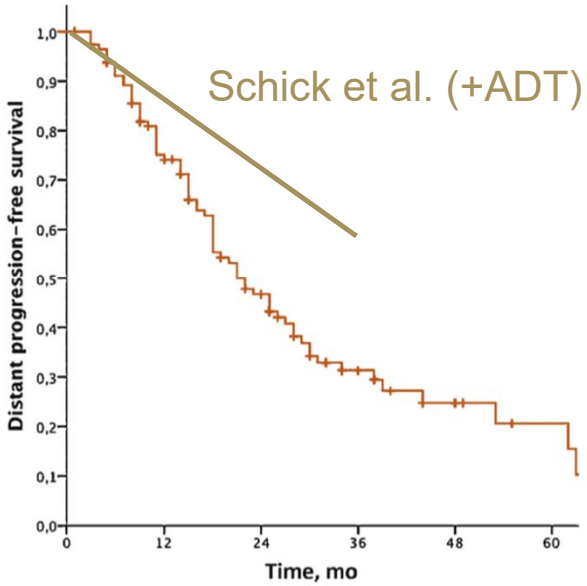
Progression-free Survival Following Stereotactic Body Radiotherapy for Oligometastatic Prostate Cancer Treatment-naive Recurrence: A Multi-institutional Analysis

Piet Ost [a,], Barbara Alicja Jereczek-Fossa [b], Nicholas Van As [c], Thomas Zilli [d], Alexander Muacevic [e], Kenneth Olivier [f], Daniel Henderson [c], Franco Casamassima [g], Roberto Orecchia [b], Alessia Surgo [b], Lindsay Brown [f], Alison Tree [c], Raymond Miralbell [d], Gert De Meerleer [a]*

Gepoolte Analyse
(teilweise Metaanalyse von Ponti et al. enthalten)

n=119 (163 Met.)
v.a. Cholin PET
60% N1/M1a

Primary site of metastases, *n* (%)	
Lymph nodes	72 (60)
Pelvic	53 (45)
Obturator	12 (10)
Internal iliac	9 (8)
External iliac	17 (14)
Presacral	2 (2)
Common iliac	6 (5)
Combination of nodal sites	7 (6)
Extrapelvic	12 (10)
Both	7 (6)
Bones, *n* (%)	43 (36)
Axial	22 (18)
Appendicular	17 (14)
Both	4 (3)
Viscera, *n* (%)	
Liver	1 (1)
Lung	1 (1)
Node and/or bone and/or viscera, *n* (%)	2 (2)



Lokale Kontrolle n. 3 J.: BED>100 Gy (99%) vs. BED<100Gy: 79%

Kurz-Zeit ADT 2 Mon. (n=60) range 1-8 Mon.
DPFS: 25 vs. 18 Mon (p=0,09)
Anderes Rezidivmuster: 70% oligorezidiviert (n=1-3)
⇒ 35x Salvage SBRT, 2xOP, 33x ADT 2x CTX
⇒ ADT freie Zeit 28 Mon.

Ost EAU 2016

Oligo-stage IV (N1, M1a-c) nach OP: AG STX DEGRO

available at www.sciencedirect.com
journal homepage: www.europeanurology.com/eufocus

Prostate Cancer

Prostate-specific Membrane Antigen Positron Emission Tomography–detected Oligorecurrent Prostate Cancer Treated with Metastases-directed Radiotherapy: Role of Addition and Duration of Androgen Deprivation

Stephanie G.C. Kroeze[a,], Christoph Henkenberens[b], Nina Sophie Schmidt-Hegemann[c], Marco M.E. Vogel[d], Simon Kirste[e,f], Jessica Becker[g], Irene A. Burger[h], Thorsten Derlin[i], Peter Bartenstein[j], Matthias Eiber[k], Michael Mix[l], Christian la Fougère[m], Hans Christiansen[b], Claus Belka[c,n], Stephanie E. Combs[d,o], Anca L. Grosu[e,f], Arndt Christian Müller[g], Matthias Guckenberger[a]*

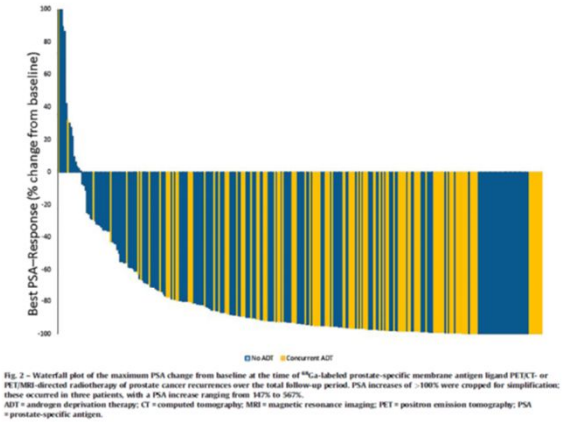
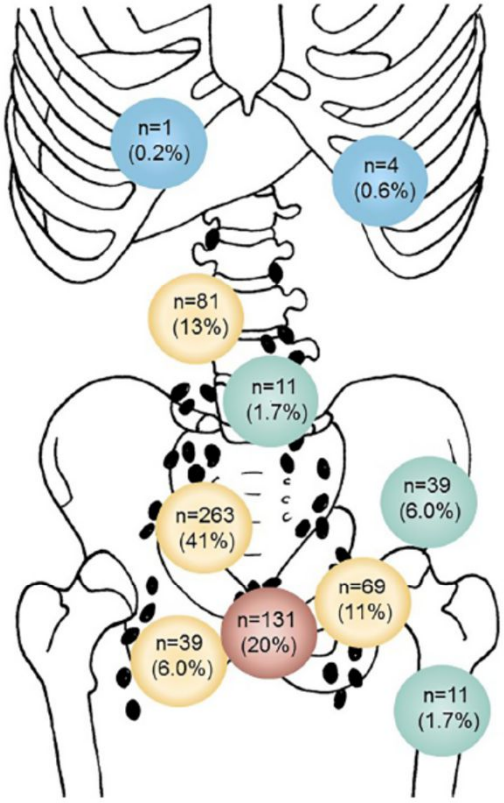


Fig. 2 – Waterfall plot of the maximum PSA change from baseline at the time of ^{68}Ga-labeled prostate-specific membrane antigen ligand PET/CT- or PET/MRI-directed radiotherapy of prostate cancer recurrences over the total follow-up period. PSA increases of >100% were cropped for simplification; these occurred in three patients, with a PSA increase ranging from 147% to 567%.
ADT = androgen deprivation therapy; CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography; PSA = prostate-specific antigen.

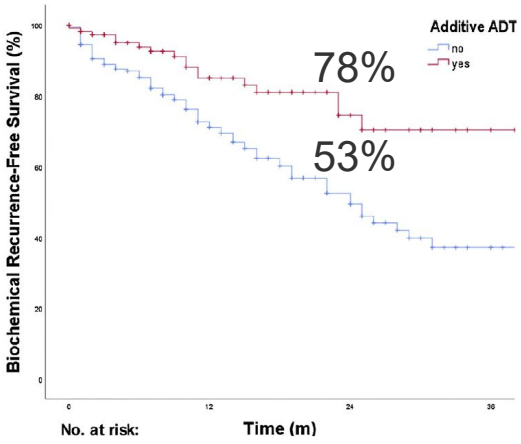
BCR nach OP (SRT erlaubt) im PSMA-PET 1-5 Oligomet.
n=305 (ADT:115)
FU 16 Mon.

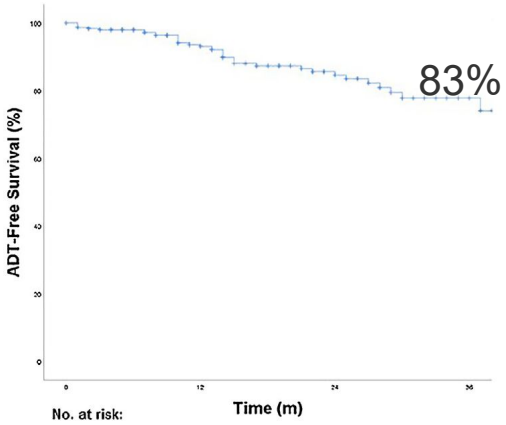
	Overall	No ADT	ADT	*p* value
Median PSA at time of MDT, ng/ml (range)	1.05 (0.04–47.5)	0.88 (0.05–47.5)	1.42 (0.04–40.13)	0.137
PSMA PET–positive recurrences, *n* (%)				0.0001
Prostate bed alone	74 (24.3)	53 (27.9)	21 (18.3)	
N1	165 (54.1)	82 (43)	83 (72)	
M1a	29 (9.5)	14 (7.4)	15 (13)	
M1b	48 (15.7)	34 (17.9)	14 (12.2)	
M1c	3 (2)	2 (1.1)	1 (0.9)	

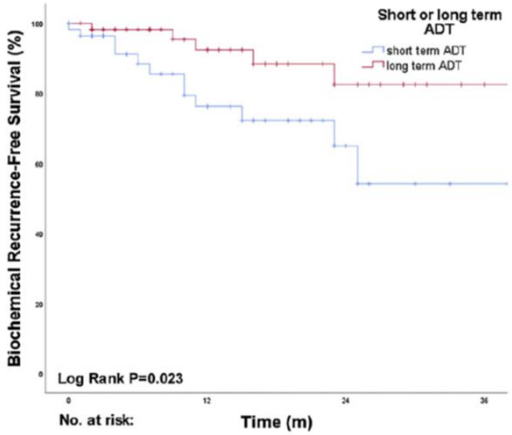


Kroeze… Müller… et al.

Oligo-stage IV (N1, M1a-c) nach OP: AG STX DEGRO







Variable	p value		HR (95% CI)
	Univariate	Multivariate	
Initial PSA (≤10 vs 10–20 vs >20 ng/ml)	0.0882	–	–
Initial T status (<3a vs ≥3a)	0.0126	–	–
Initial N status	0.0179	–	–
Initial risk score	0.3291	–	–
Gleason score (<7a vs ≥7a)	0.1076	–	–
PSA nadir ≤0.0.1 ng/ml	0.0291	–	–
Resection margins (R0 vs R1)	0.9798	–	–
Biochemical recurrence (≤1 vs >1 yr)	0.0126	0.0374	0.55 (0.31–0.97)
Local prostate recurrence only	0.0413	–	–
N status at time of recurrence	0.8492	–	–
M status at time of recurrence	<0.00001	0.0006	1.36 (1.14–1.63)
PSA at time of MDT (≤0.5 vs >0.5 ng/ml)	0.0126	–	–
Concurrent ADT	0.0006	<0.0001	0.28 (0.16–0.51)

ADT = androgen deprivation therapy; CI = confidence interval; HR = hazard ratio; MDT = metastases-directed treatment; PSA = prostate-specific antigen.

Zeit bis zum BCR

M-Status

Simultane Langzeit ADT
Aber Kombination mit elective pelvis!

Kroeze… Müller… et al.

Oligo-stage IV (N1/M1a): Elective nodal RT or SBRT?

De Bleser EAU 11/2019

Multiinstitionelle Analyse n= 506 Pat.
(SBRT 309, ENRT: 197)

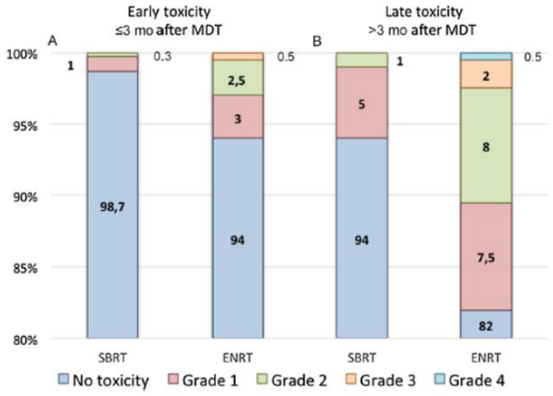
SBRT= ED>5Gy max 10 Frx
ENRT GDmin=45Gy 25 Frx +/- Boost

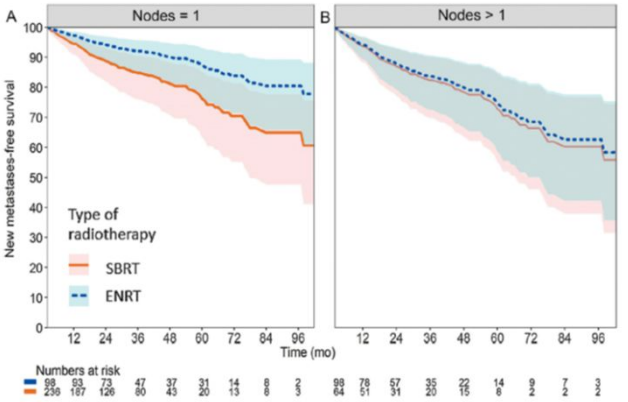
FU 36 Mon.
Initial OP+/-RT/RT (8% initial WPRT!)

Weniger Rezidive nach ENRT
SBRT: 57.3% ENRT: 37.6%
3yDMFS 68% vs. 77% (ENRT) sig.

Mehr Spättox. nach ENRT
3yCRPC-FS ~ 88% idem
Cave: Mehr ADT bei ENRT

Patient characteristic	SBRT (*n* = 309, 61%)	ENRT (*n* = 197, 39%)
Metastatic site, *n* (%)		
Pelvic	222 (72)	143 (73)
Extrapelvic	69 (22)	29 (15)
Pelvic + extrapelvic	18 (6)	25 (13)
No. of positive nodes at imaging, *n* (%)		
1 metastasis	243 (79)	98 (50)
2 metastases	50 (16)	55 (28)
3 metastases	13 (4)	23 (12)
4 metastases	2 (1)	13 (7)
5 metastases	1 (<1)	8 (4)
Adjuvant ADT at time of recurrence, *n* (%)		
No	237 (77)	78 (40)
Yes	71 (23)	119 (60)
Unknown	1 (<1)	0 (0)
Median duration of ADT, mo (IQR)	6 (3–11)	6 (6–9)





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Lokale Therapie des Primarius

Therapie von nodalen Oligometastasen (N1/M1a) plus Primarius

Therapie von ossären Oligometastasen (M1b) plus Primarius

Metachrone Metastasierung nach Lokaltherapie des Primarius

Therapie von nodalen Oligometastasen (N1/M1a)

Zielvolumen überdenken

BFS besser mit ADT (Verdoppelung)
Lokale Kontrolle gut ohne ADT

Elective nodal RT/prostatic fossa RT
ADT vs. Rezidivmuster (mehr diffus)?

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Therapie von nodalen Oligometastasen (N1/M1a)

Therapie von ossären Oligometastasen (M1b)

Wu et al. 2016: ADT+RT bei M1b

n=30, 53 Metastasen (Knochen)

RT Kurz (5x4/10x3Gy) vs.
Lang (37.5/15F bis 40Gy/20F, 50Gy/25F)

Med. FU 32.5 Mon.

3y PFS: 23% (alle mit pall RT)

3yOS: 69% (alle !)

Überlebensvorteil für höherdosierte RT: 76% vs. 44%

3yPFS für Langzeit RT leider nicht berichtet…

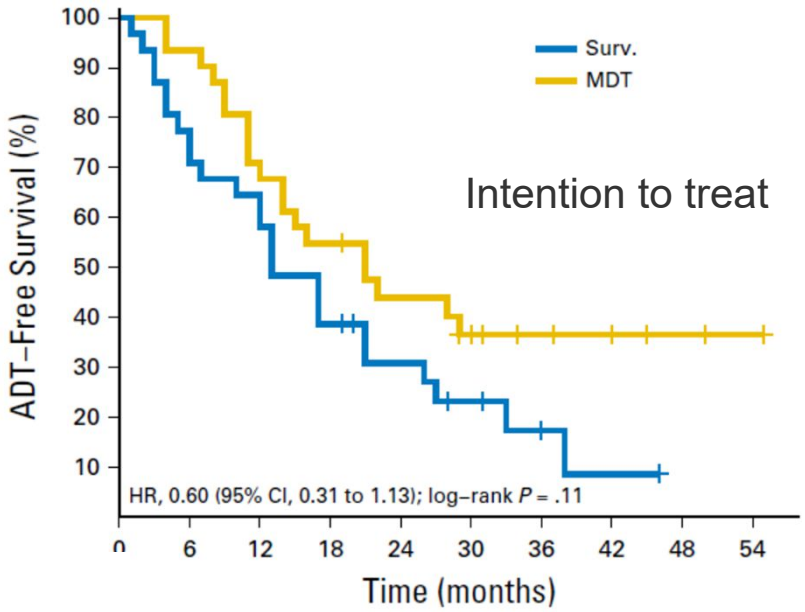
Metachronous oligometastases					
Ost (2018) [14]	62	Surgery/SBRT vs surveillance	3-yr follow-up: Median ADT-free survival: 21 vs 13 mo	17% (6/36) grade 1 in MDT arm, no grade 2–5	In this prospective study, ADT-free survival was longer with MDT than with surveillance alone
Habl (2017) [53]	15	SBRT	Median PSA PFS: 6.9 mo (range 1.1–28.4) Local PFS after 2 y: 100%	No acute or late toxicities	SBRT of bone metastases offers high local cancer control rates in PCa and has an excellent risk-benefit profile
Wu (2016) [54]	30	ADT + RT	3-yr PFS and OS: 23% (95% CI, 13–38%) and 69% (95% CI, 52–81%) Long-course RT was associated with superior 3-yr OS vs short-course RT (76% vs 44%; $p = 0.03$)	3 (10%) acute toxicity: two grade 1, one grade 2	Long-course RT combined with ADT was effective and well tolerated in PCa pts with bone oligometastases after curative RT for PCa
Ponti (2015) [21]	16	SBRT	Local control and a decrease in serum PSA in 94% of pts Mean time delay to ADT: 23.7 mo (range 2.5–51 mo) OS at 19 mo: 94%	1 G2 acute gastrointestinal toxicity 1 G3 late gastrointestinal toxicity	SBRT has an acceptable safety profile, is effective, and is minimally invasive to eradicate limited LN recurrence from OMPCa
Decaestecker (2014) [55]	50	SBRT	Median PFS: 19 mo (95% CI, 13–25 mo) Median ADT-free survival: 25 mo (95% CI, 20–30 mo) 2- and 5-yr CSS: 96% and 90%, respectively	10 (20%) 7 grade I 3 grade II (according to National Cancer Institute Common Terminology Criteria for Adverse Events [CTCAE] v3.0)	Repeated SBRT for OMPCa postpones palliative ADT
Jereczek-Fossa (2014) [20]	69	SBRT	3-yr in-field PFS, PFS, and OS: 64%, 12%, and 50%, respectively	2 grade 3 acute 1 grade 4 late	SBRT is feasible for single abdominal LN recurrence, excellent in-field tumour control, low-toxicity profile
Picchio (2014) [56]	83	HTT with SIB	94 HTT treatments: cBR after 66 treatments, partial response after 12, stable disease after 1, disease progression after 15	2 grade 3 acute genitourinary	High-dose hypofractionated HTT with SIB is well tolerated and associated with a high early BR rate in pts with LN-only relapse
Ahmed (2013) [22]	17	SBRT	Median follow-up 6 mo Local control: 100%; PSA nadir undetectable in 9 pts (53%) 6- and 12-mo CSS estimates: 100%	No acute grade ≥3 No late toxicity (according to National Cancer Institute CTCAE v3.0)	Excellent local control with SBRT in OMPCa; >50% of pts achieved undetectable PSA after SBRT
Berkovic (2013) [13]	24	SBRT	Median ADT-free survival: 38 mo 2-yr local control and clinical PFS: 100% and 42%,repectively	8% acute grade 2 genitourinary 6% acute grade 2 gastrointestinal No late grade 3	Repeated salvage SBRT is feasible and well tolerated, and defers palliative ADT
Muacevic (2013) [57]	40	Single-session SRS	6, 12, and 24 mo local tumour control rate: 95.5%		Single-fraction robotic SRS is a safe, feasible, and patient-friendly treatment option in selected patients with bone metastases of PCa
Casamassima (2011) [18]	71	SBRT	3-yr OS, DFS, and local control rates: 92%, 17%, and 90%, respectively		SBRT was effective in disease eradication of limited nodal recurrences from PCa, avoiding or postponing systemic treatments

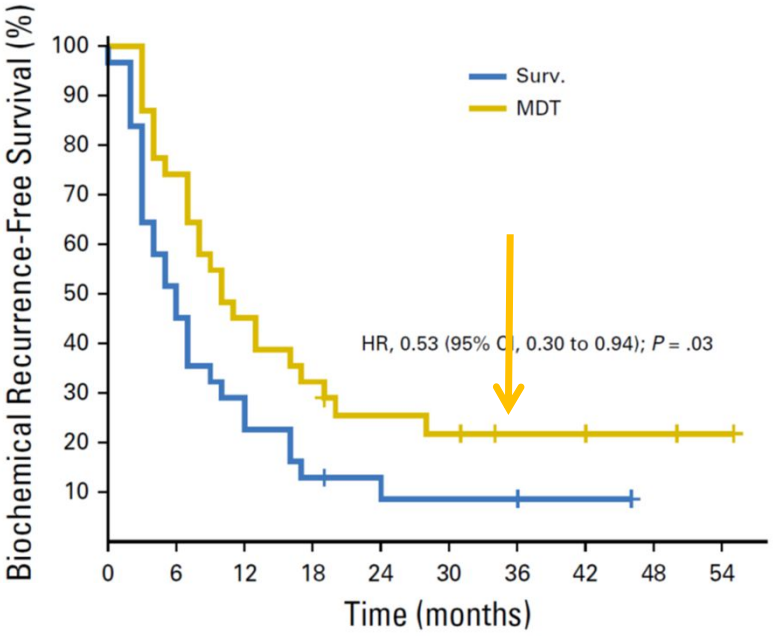
12%

17%

Battaglia et al EAU 2019

Oligo-N1/M1: Choline-PET-CT => Verzögerung der ADT (n=62) um 8 Mon.





Patienten nach OP/RT (58-70% nach RP+sRT), **25% rN1**

iPSA 6.3ng/ml; ADT-Indikation (+ ≥3 Filiae), symptomatischer Progress, Oligoprogress)

SBRT(30Gy/3Frx.) / OP verzögern ADT bei Oligometastasierung (n=3) **21 vs. 13 Mon.,** kein G2+

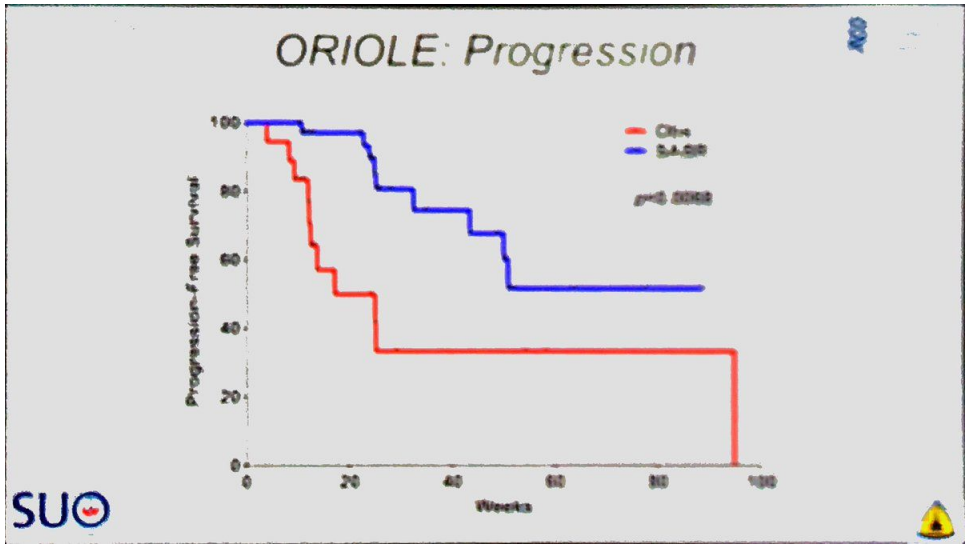
Ost et al. JCO 2018

(Ost JCO 2018)

Oriole Trial on Observation vs. SABR in OMPC ohne ADT

Phase-II-Studie : n=54

Biochem. Rezidiv nach OP/RT
⇒ RND 2:1 SABR vs. OBS
(conv. Imaging, PET blinded)
Oligo= M1b oder soft tissue (M1a?)



Wenn Baseline PET-findings = conv. Staging
⇒ alle Läsionen behandelt
⇒ weniger neue Metastasen
(16% vs 63%, *p* = .006)
⇒ **PSMA-PET prognostisch!**

Ergebnisse: Toxizität: G1-2

6 Monats BCR: SABR: 19% OBS: 61%

DMFS: 29 vs. 6 Mon. (sig.)

Lokale Metastasentherapie => noch kein SOC

Patienten in klinische Studien einbringen

Feasibility: 3y OS: ~90% (RT)
Meiste Arbeiten retrospektiv

Table 3 – Ongoing prospective studies of metastasis-directed therapy in oligometastatic prostate cancer

Study (ClinicalTrials.gov ID)	Phase	Design	Intervention	Primary outcome measure	Estimated completion
Oligorecurrent disease					
IMRT in treating patients undergoing ADT for metastatic PCa (NCT00544830)	II	Open-label, single group assignment	ADT + IMRT	Time to PSA relapse	July 2017
Monitoring anti-PCa immunity following SBRT in OMPCa (NCT01777802)	NA	Observational, cohort	SBRT	Induction of anti-PCa immunity	January 2018
CROP: stereotactic RT for OMPCa (NCT02563691)	I/II	Open-label, single group assignment	Stereotactic RT	Incidence of late RT toxicities	November 2018
Phase II study of SBRT as treatment for oligometastases in PCa (NCT02192788)	II	Open-label, single group assignment	SBRT	[illegible] progression treated by SBRT	
Percutaneous high-dose RT in OMPCa (NCT02264379)	NA	Observational, case control	Stereotactic RT (hypo- or normofractionated)	Toxicity	November 2019
RT for OMPCa (NCT01859221)	II	Nonrandomised, open-label, parallel assignment	SBRT/SHRT	Improvement in median PFS in pts with metastatic PCa over historic control rates	January 2020
SBRT for oligometastatic castration-refractory PCa (NCT02816983)	NA	Observational, case only	SBRT	PSA PFS; OS	June 2020
ORIOLE: SBRT for OMPCa (NCT02680587)	II	Randomised, open-label, parallel assignment	SBRT	Time to progression	March 2021
CORE: conventional care versus radioablation (SBRT) for extracranial oligometastases (NCT02759783)	II/III	Randomised, open-label, parallel assignment	SBRT	PFS	October 2021
PCS IX: management of CRPC with oligometastases (NCT02685397)	II/III	Randomised, open-label, parallel assignment	GnRHa + ENZA vs GnRHa + ENZA + SBRT	Radiographic PFS	April 2025
OLIGOPELVIS: salvage RT combined with hormonotherapy in oligometastatic pelvic node relapses of PCa (NCT02274779)	II	Open-label, single group assignment	RT + ADT	Biochemical or clinical relapse-free survival at 2 yr	July 2026

ADT = androgen deprivation therapy; CRPC = castrate-resistant prostate cancer; ENZA = enzalutamide; GnRHa = gonadotrophin-releasing hormone agonist; IMRT = intensity-modulated radiation therapy; NA = not applicable; OMPCa = oligometastatic prostate cancer; OS = overall survival; PCa = prostate cancer; PFS = progression-free survival; PSA = prostate-specific antigen; pts = patients; RT = radiotherapy; SBRT = stereotactic body radiotherapy; SHRT = stereotactic hypofractionated radiotherapy.

Table 5 – Ongoing prospective trials of prostate-targeted therapy in synchronous (oligo)metastatic prostate cancer

Study (ClinicalTrials.gov ID)	Phase	Design	Primary outcome measure	Estimated completion
Safety and early efficacy of RP for newly diagnosed very-high-risk locally advanced PCa and OMPCa (NCT02971358)	I/II	Open-label, single group assignment	Rate of perioperative complications within 90 d from surgery (Clavien-Dindo)	November 2016
Combining ipilimumab, degarelix, and RP in men with newly diagnosed metastatic castration-sensitive PCa, or ipilimumab and degarelix in men with biochemically recurrent castration-sensitive PCa after RP (NCT02020070)	II	Nonrandomised, open-label, parallel assignment	Undetectable PSA (time frame at 12 and 20 mo) from the start of treatment	December 2017
BST or BST plus definitive treatment (RT or surgery) of the primary tumour in mPCa (NCT01751438)	II	Randomised, open-label, parallel assignment	PFS	March 2018
Cytoreductive prostatectomy in patients with newly diagnosed mPCa (NCT03233711)	I	Open-label, single group assignment	Rate of major perioperative complications (Clavien-Dindo ≥III) within 90 d of surgery	August 2018
[illegible] with RT and axitinib in previously untreated PCa patients with [illegible] oligometastasis	II	Randomised, open-label, parallel assignment	Participants progression free 12 mo after surgery	August 2018
ADT or ADT plus definitive treatment (RT or surgery) in OMPCa patients (NCT02742675)	II	Randomised, open-label, parallel assignment	PFS	March 2019
LoMP: local treatment with RP for newly diagnosed mPCa (NCT02138721)	II	Nonrandomised, open-label, parallel assignment	Castration-refractory PCa PFS; time to first disease-related event (time frame for either: up to 10 yr)	May 2019
g-RAMPP: impact of RP as primary treatment in patients with PCa with limited bone metastases (NCT02454543)	III	Randomised, open-label, parallel assignment	Cancer-specific survival (time frame: 5 yr)	April 2020
TRoMbone (Testing Radical prostatectomy in men with prostate cancer and oligoMetastases to the bone): a randomised controlled feasibility trial (ISRCTN15704862) [50]	II	Randomised, open-label, parallel assignment	Feasibility to randomise (measured at 6 mo)	Completed April 2017
PEACE1: a phase III study of ADT ± docetaxel ± local RT ± abiraterone acetate in metastatic hormone-naïve PCa patients (NCT01957436)	III	Randomised, open-label, parallel assignment	Survival (time frame: 5.5 yr) OS and PFS	October 2023
HORRAD: a randomised study about the effect on survival of HT versus HT plus local external RT in patients with primary diagnosed metastasised PCa (ISRCTN06890529)	III	Randomised active-controlled parallel-group trial	Survival	Completed accrual
STAMPEDE (Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy) new research arm (arm H): RT treatment to newly diagnosed metastatic disease [51]	III	Multiarm multistage randomised controlled parallel assignment trial	Overall survival Safety and efficacy of novel therapeutic strategies against the current standard of care	No longer recruiting for arm H

ADT = androgen deprivation therapy; BST = best systemic therapy; HT = hormonal therapy; ISRCTN = International Standard Randomised Controlled Trial Number; LN = lymph node; mPCa = metastatic prostate cancer; OMPCa = oligometastatic prostate cancer; OS = overall survival; PCa = prostate cancer; PFS = progression-free survival; PSA = prostate-specific antigen; RP = radical prostatectomy; RT = radiotherapy.

Bataglia EAU 2019

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Therapie von nodalen Oligometastasen (N1/M1a)

Therapie von ossären Oligometastasen (M1b)

Unklar ob frühe ADT langfristig besser ist

Indikation (Vermeidung ADT) vs. SOC +/-SBRT entscheidend, Lok. von M1b

Fazit 1:

Oligometastasen

Definition und Hintergrund — **n=3-5, Lokalisation: N1, M1a, M1b (nicht M1c oder M1a+b)**

Synchrone Metastasierung

Lokale Therapie des Primarius	**Plus ADT**
Therapie von nodalen Oligometastasen (N1/M1a) plus Primarius	**Plus ADT/elektiv LN**
Therapie von ossären Oligometastasen (M1b) plus Primarius	**Plus SOC/Stampede Indiv. mehr (Tuko)**

Metachrone Metastasierung nach Lokaltherapie des Primarius

Therapie von nodalen Oligometastasen (N1/M1a)	**ZV überdenken, ADT (2xBFS, Rez.muster?) LC ohne ADT gut**
Therapie von ossären Oligometastasen (M1b)	**Unklar ob frühe ADT langfristig besser ist**

Indikation (Vermeidung ADT) vs. SOC +/-SBRT entscheidend, Lok. von M1b rel.?

Fazit 2: SBRT von Oligometastasen

Was kommt nach 2-4 Jahren?

Kuration?

20%

Wären wir mit **~20 %** Kuration **zufrieden?**

Bis zu welchem **M-Muster** ist eine „maximale Therapie“ **kurativ & verträglich?**

Kurationschance ⇧

Oligo-Rez/Progr.?

X%

Wie effektiv ist eine **erneute SBRT?**

Dann aber **+ ADT?** **+ elektiv RT?**

N1=beste prog. Gruppe elective regions

ADT-Dauer

Kurz **Lang**

Diffuser Progress?

X%

Wie effektiv ist eine verzögerte ADT? **AG STX klären**

Biomarker für diese aggressive Variante? **Oriole (CTC)**

Falls positiv dann Kombinationstherapie oder Nihilismus (BSC)?

Wir stehen erst am Anfang