Klinikum rechts der Isar
Technische Universität München

Operative Therapie beim primär oder sekundär (oligo)-metastasierten Prostatakarzinom

Jürgen E. Gschwend, München

Prostatakrebs

Vorsorge – Diagnostik – Therapie

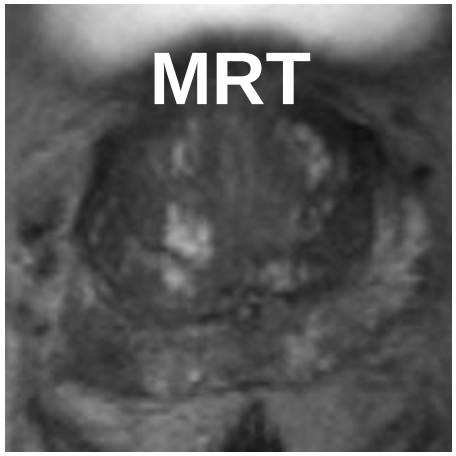
PROSTATUM

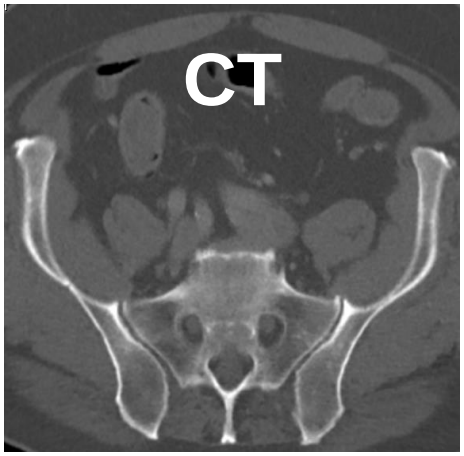
CCC MÜNCHEN
COMPREHENSIVE
CANCER CENTER
KLINIKUM RECHTS DER ISAR
TECHNISCHE UNIVERSITÄT MÜNCHEN

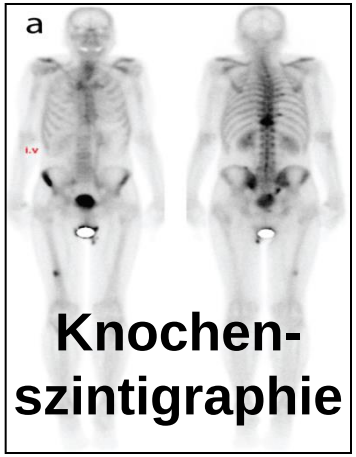
Warum brauchen wir Ausbreitungsdiagnostik?

- Behandlung hängt wesentlich vom Erkrankungsstadium ab:

lokalisiert	lokal fort-geschritten	lokoregionale Metastasen	**oligo-metastatisch**	metastatisch







Agenda

- **Bildgebung beim Prostatakarzinom**
  - Wie definieren wir „nicht-metastasiert“?
  - Wie definieren wir „oligo-metastasiert“?
- **Wie behandeln wir gestern und heute?**
  - **Therapie des sekundär oligo-metastasierten PC**
  - Therapie des primär oligo-metastasierten PC

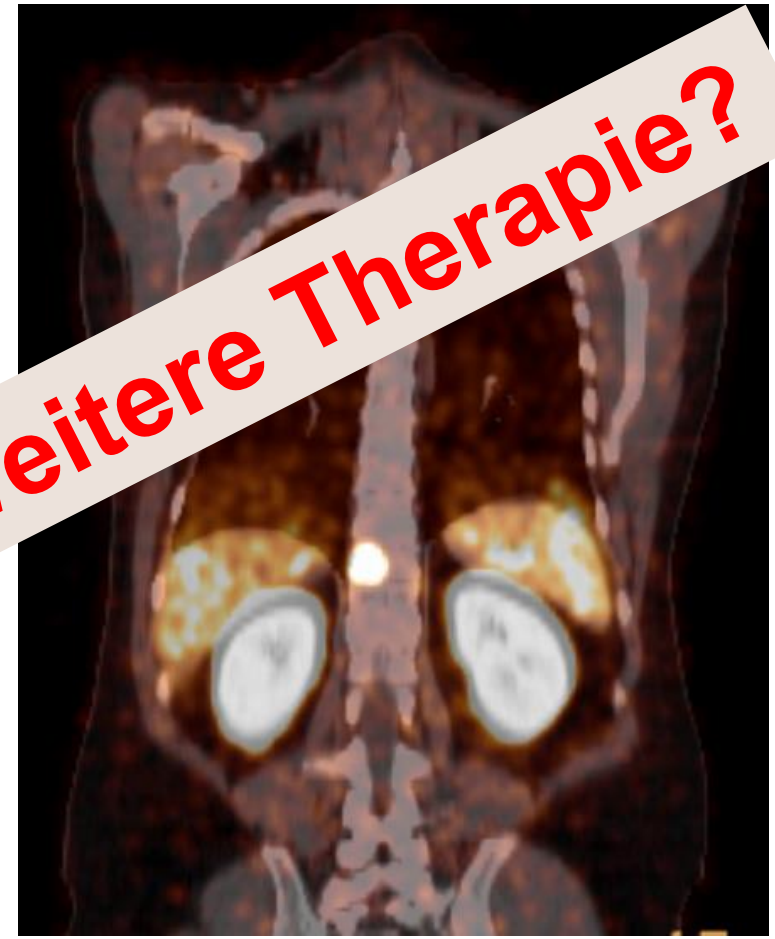
Patient M.V., * 1945

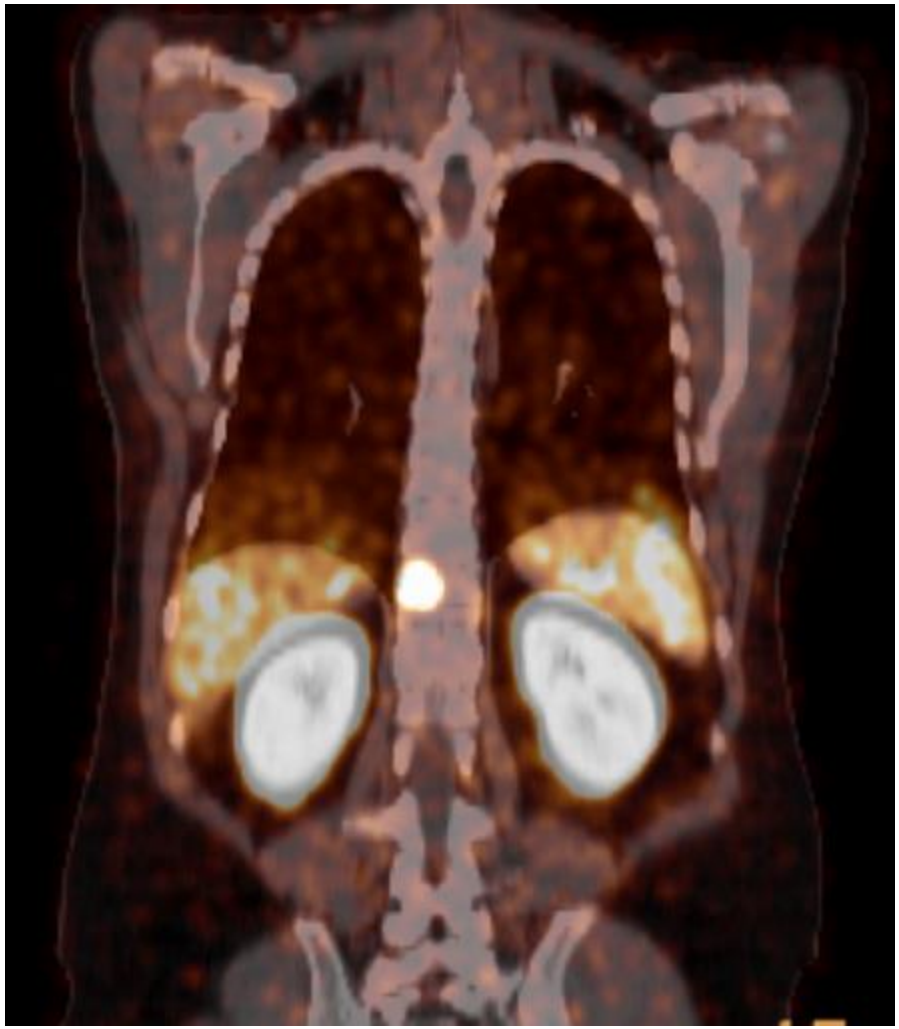
- 12/13: RP
- pT3b pN1 R1 L0 V0
- Gleason 4+4

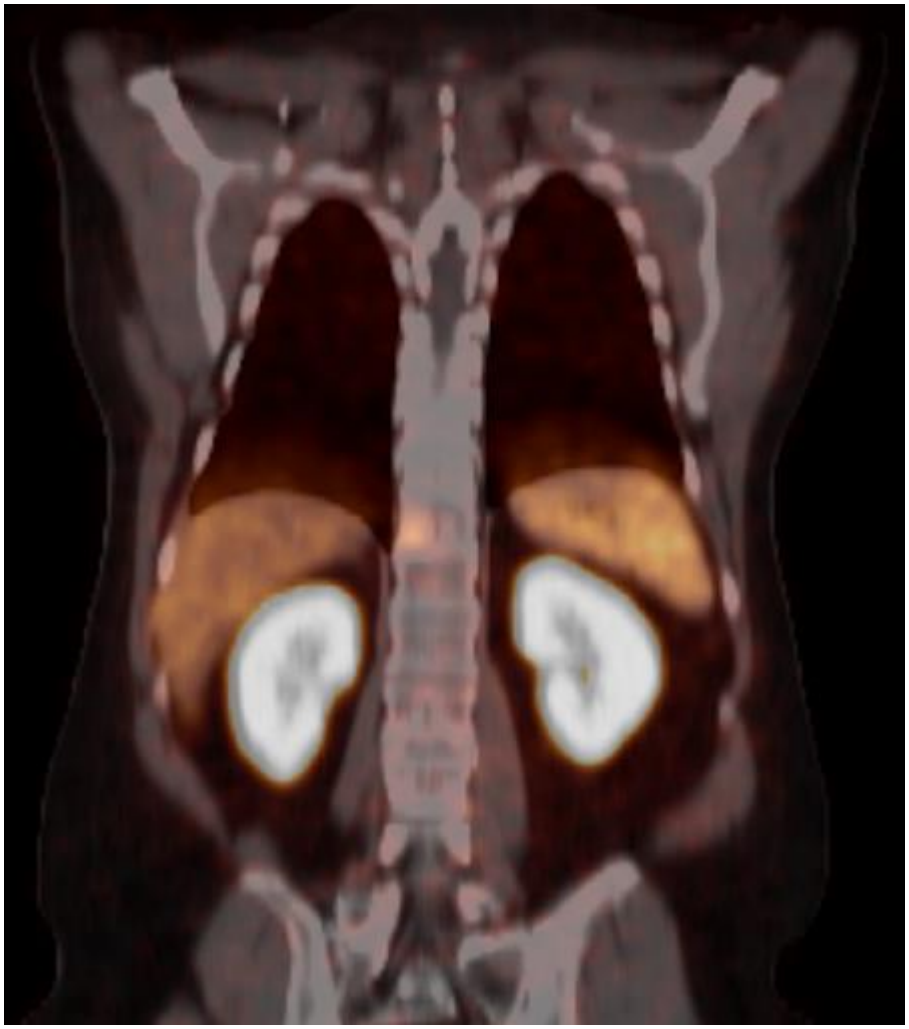
- Präoperativ: PSA 133 ng/ml
- Postoperativ: PSA Nadir 1.3 ng/ml
- 2/14: Beginn mit LHRH-Antagonist
- 8/14: PSA-Nadir 0,04 ng/ml

Patient M.V., * 1945

- 11/17: PSA-Anstieg auf 3,7 ng/ml
- Testosteron 0,2 ng/ml
- Geringe Schmerzen LWS
- CT-Abdomen/Thorax/KS negativ
- PSMA-PET-CT







PSMA-PET beim PSA-Rezidiv?

4.29	Evidenzbasierte Empfehlung	geprüft 2018
Empfehlungsgrad 0	a. Im Rahmen einer Rezidivdiagnostik (nach primär kurativer Therapie, s. Empfehlung 6.2 und 6.3) kann primär eine PET Hybrid-Bildgebung mit radioaktiv markierten PSMA-Liganden zur Beurteilung der Tumorausdehnung erfolgen, falls sich aus dem Befund eine therapeutische Konsequenz ergibt.	
Empfehlungsgrad A	b. Ein negatives PSMA-PET soll eine frühe Salvage-Therapie nicht verzögern.	
Level of Evidence 2+ bis 3 b: 4	a. Literatur: [196-201] b. Expertenkonsens	
	Gesamtabstimmung: 93 %	

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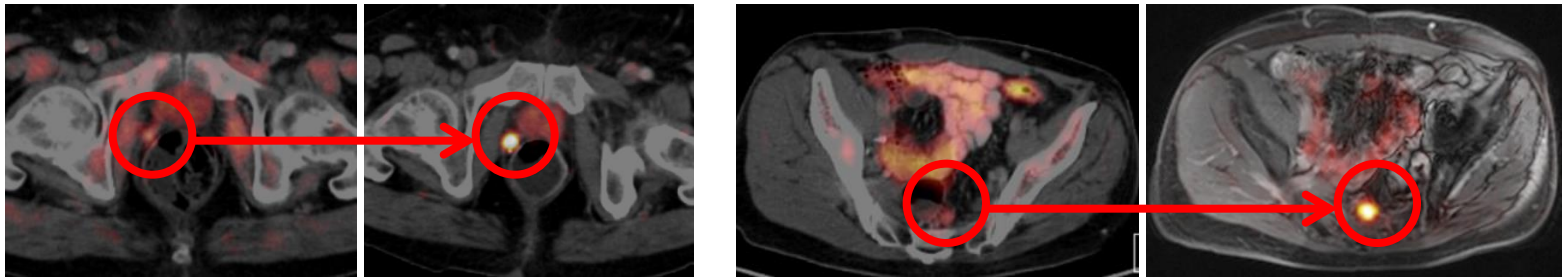
^{68}Ga-PSMA PET vs. ^{11}C-Cholin PET ?



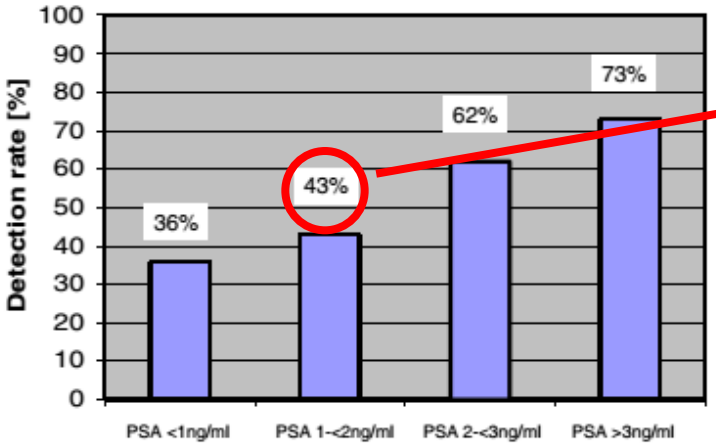
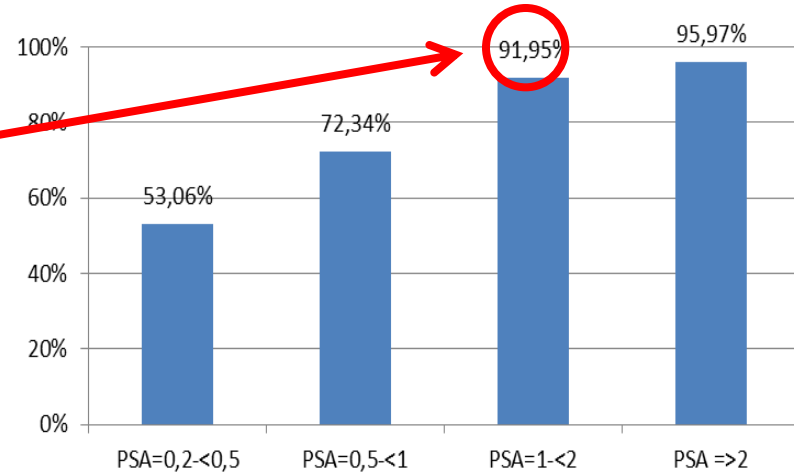


Fig. 1 Detection rate of [^{11}C]Choline-PET/CT plotted against the PSA-value for recurrent prostate cancer

Krause et al., *EJNMMI* 2008



Eiber et al., J Nucl Med. 2015 May;56(5):668-74

Rezidivstaging bei BCR nach RRP (PSA bis 1ng/ml)

PSA (ng/mL)	Pts. (n)	No. of positive ^{68}Ga-PSMA PET/CT scans	Detection rate (mean (95% CI))
All pts.	272	176	64.3 (58.3-70.0)
0.2 – 0.5	134	74	**55.2** (46.4-63.8)
>0.5 – 1.0	138	102	**73.9** (65.8-81.0)

→ Detektionsrate erhöht sich mit höheren PSA-Werten

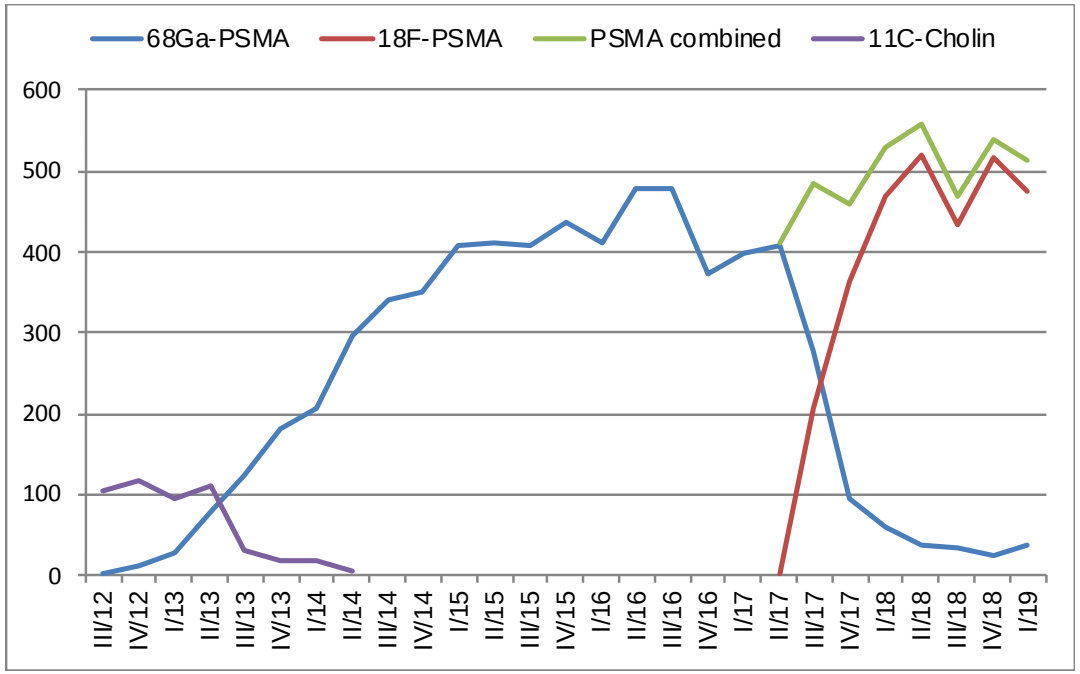
PSA (ng/mL)	Pts. (n)	Local	LN pelvic / retroperitoneal	Bone	LN supra-diaphragmal	Visceral / Others
0.2 – 0.5	134	37.0%	45.2%	**24.7%**	**6.8%**	**4.1%**
>0.5 – 1.0	138	41.2%	54.9%	**29.4%**	**6.9%**	**2.0%**

→ Auch bei niedrigen PSA-Werten finden sich Fernmetastasen!

Rauscher et al., Eur Urol 2018

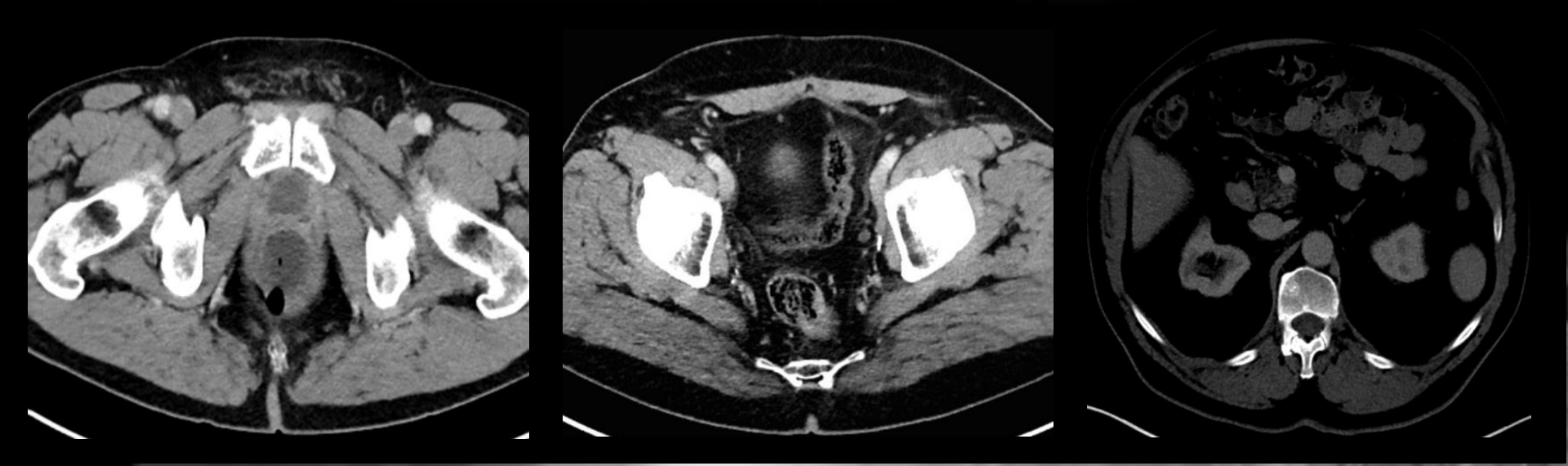
Status quo in Deutschland: § 13.2b AMG

High demand and availability

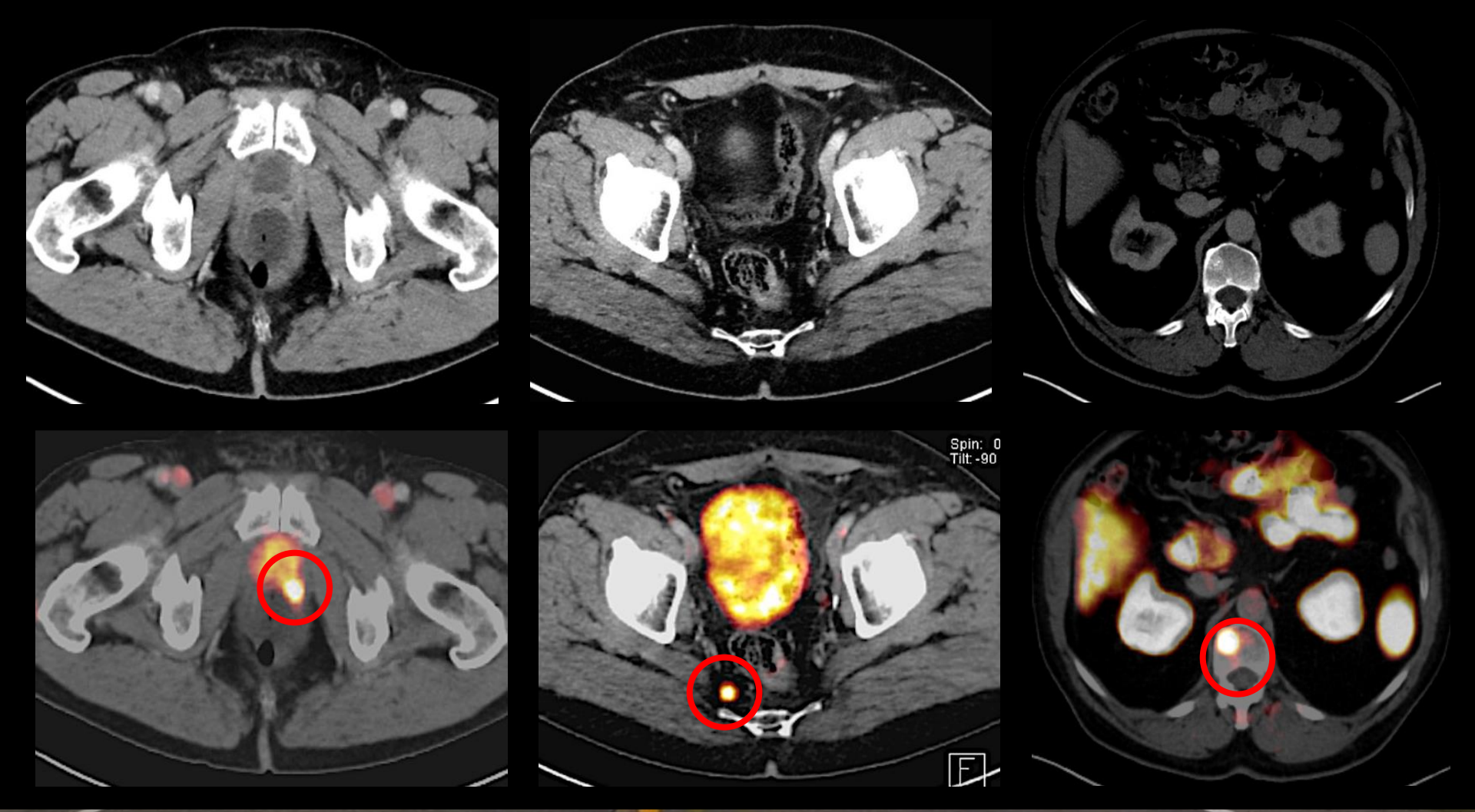


PCa PET-Scans an der TUM/Quartal

(accessed 04/18/2018)



Rauscher et al., Eur Urol 2018



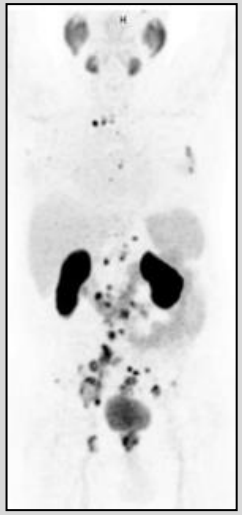
Rauscher et al., Eur Urol 2018

PSMA-PET basierte operative Therapie von lokalisierten Rezidiven mittels Radio-guided Surgery (RGS)

Beispiel HSmPC

„Multi-Use“-PSMA-Liganden

I M A G I N G



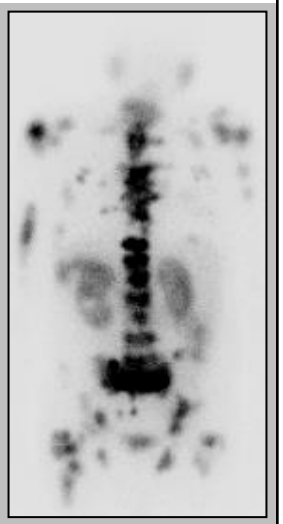
PET

- Disease localisation in biochemical recurrence
- Primary staging
- Biopsy targeting
- Patient stratification for therapy
- Therapy planning
- Response evaluation

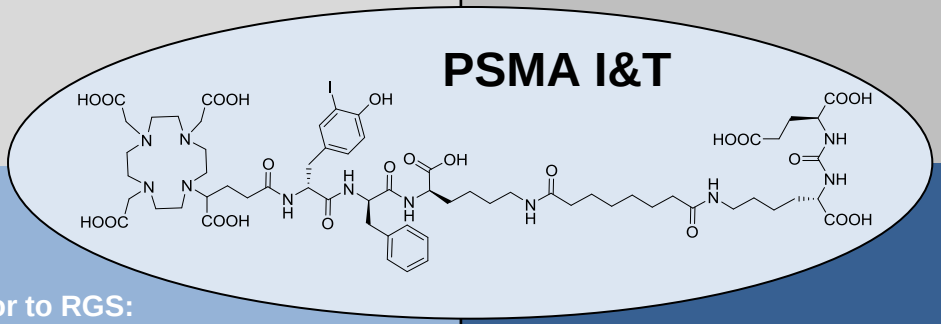
T H E R A P Y

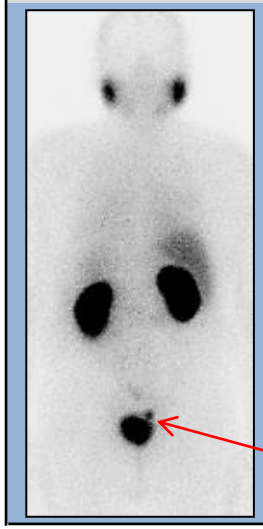
Targeted radionuclide therapy

- Currently compassionate use in meta-stastic castration resistent PCa (mCRPC)
- Potential use in earlier disease stages to be evaluated



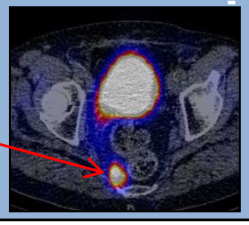
PSMA I&T





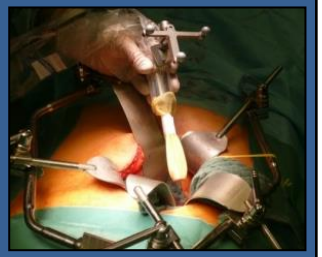
SPECT

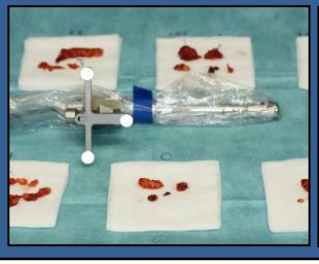
- Imaging prior to RGS: planning of surgical extent by anatomical mapping of early recurrent disease
- Potential cost-effective imaging procedure where PET is not available

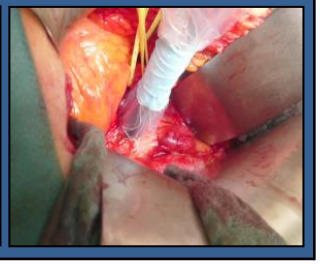


RGS

- Radioguided resection of small, atpyically localized metastases in early recurrent disease
- Use in primary PCa to be evaluated





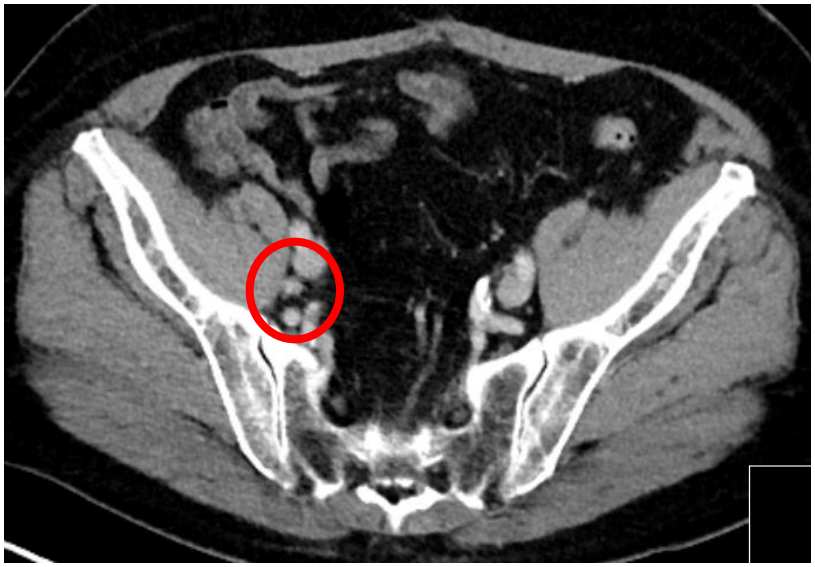


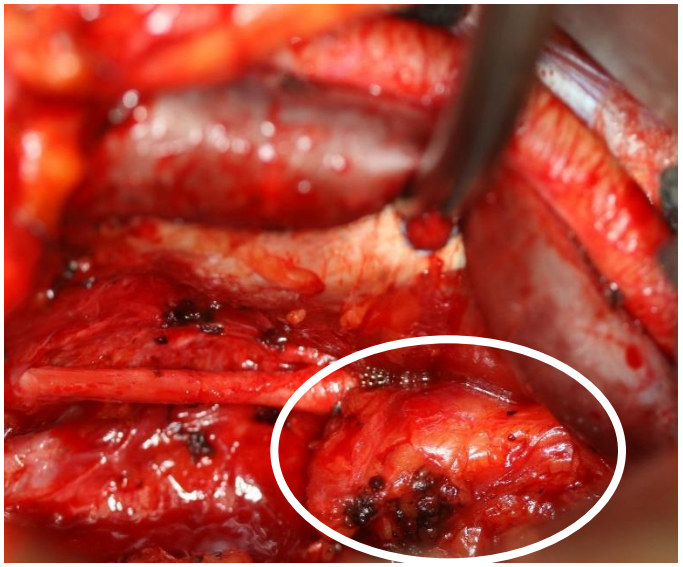
Schottelius et al., EJNMMI Res 2015

Beispiel: LK-Rezidiv im PSMA-PET nach Operation

75 Jahre, RPE 2005: pT3b pN1; Gleason 7a; 5a HTx

RTx 2014 der Loge bei PSA-Rezidiv (0,2 ng/ml); PSA 10/16: 1,1 ng/ml





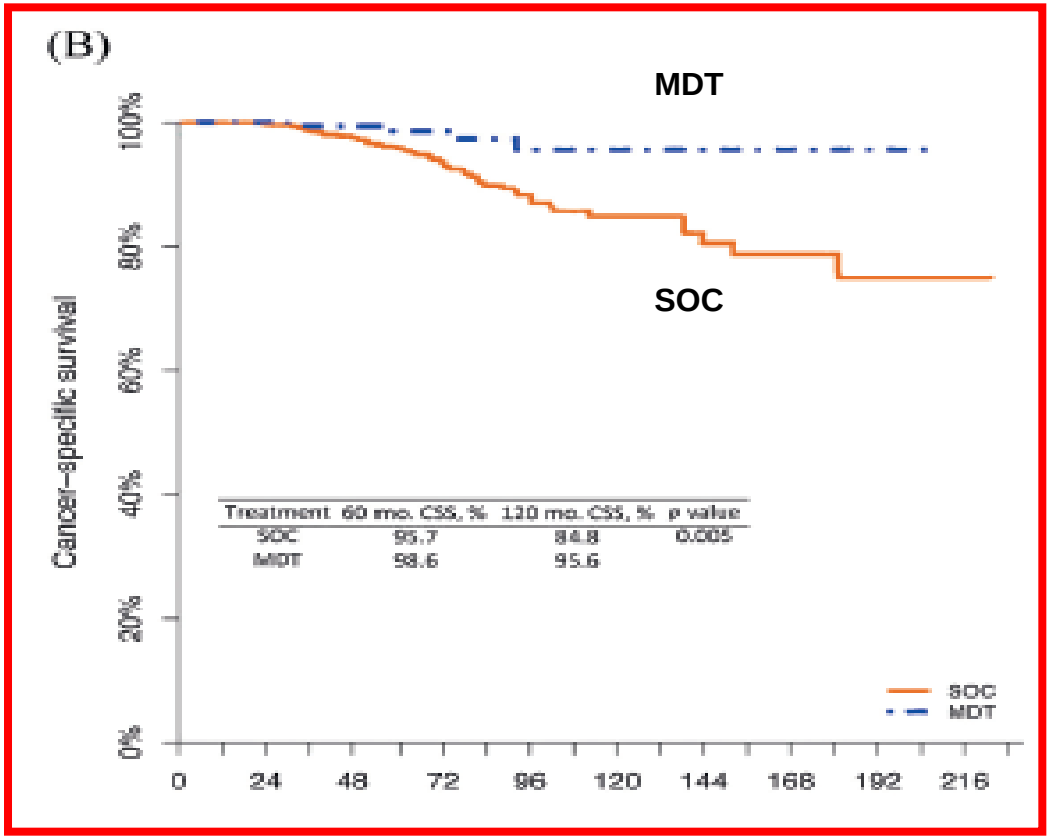
Salvage-PLA 11/16: pN1 (1/9)

Follow-up 3/17: PSA-Abfall unter Nachweisgrenze

SBRT bei Oligometastasierung N+

- Multi-Institutionell, retrospektiv
- Matched-pair-Analyse bei LK-Rezidiv
- Vergleich SOC vs. MDT
- MDT 263 (166 LND vs. 97 SBRT)
- PET in der Diagnostik, Med. NB: 70M

Krebsspez. Überleben: Propensity Matched pair-Analyse

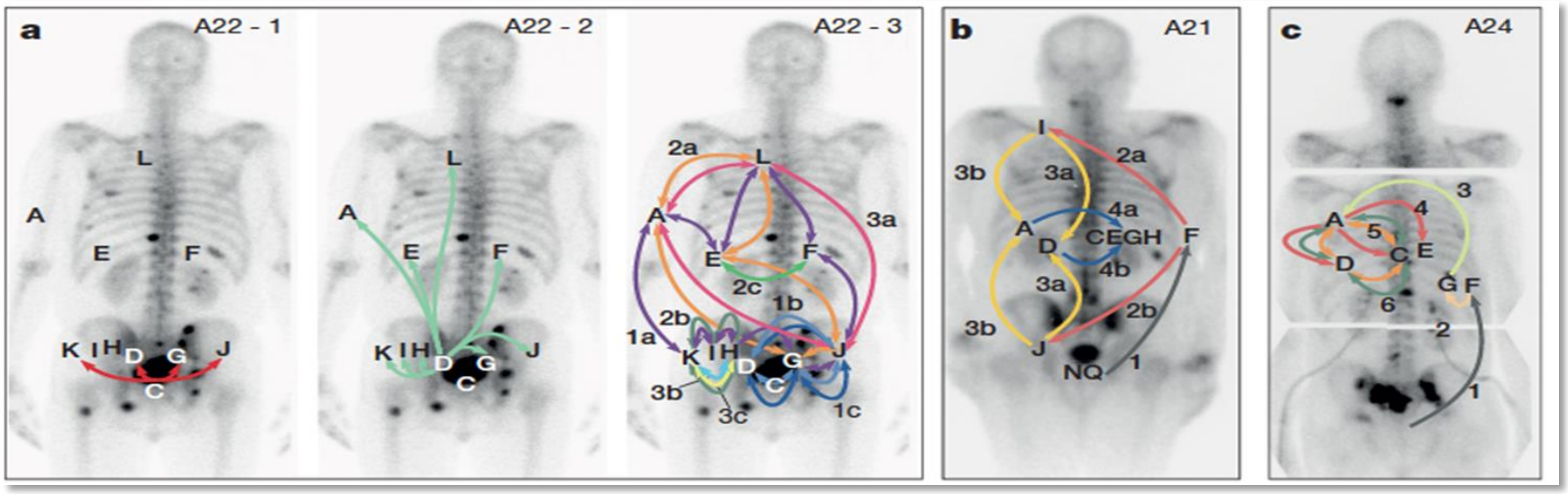


Conclusions:
MDT for nodal oligorecurrent PCa improves CSS as compared with SOC. These retrospective data from a multi-institutional pooled analysis should be considered as hypothesis-generating and inform future randomized trials in this setting.

Steuber et al., Eur. Urol. Foc. 2, 2019

Rationale zur Metastasenbehandlung beim oligometastasierten Prostatakarzinom

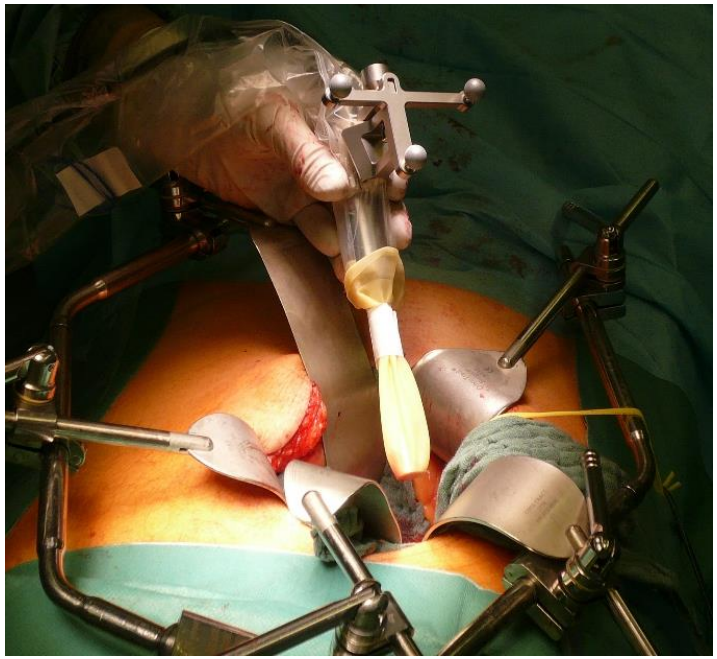
„The evolutionary history of lethal metastatic prostate cancer“

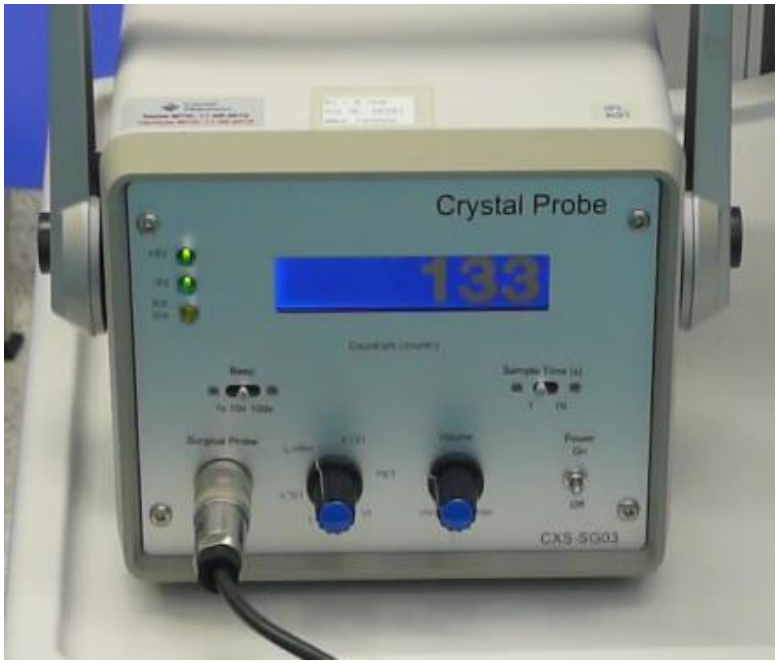


Gundem G et al. Nature 2015:353-7

Operative Therapie des PSA-Rezidivs:
^{99}TC-PSMA-basierte radio-guided surgery (RGS)

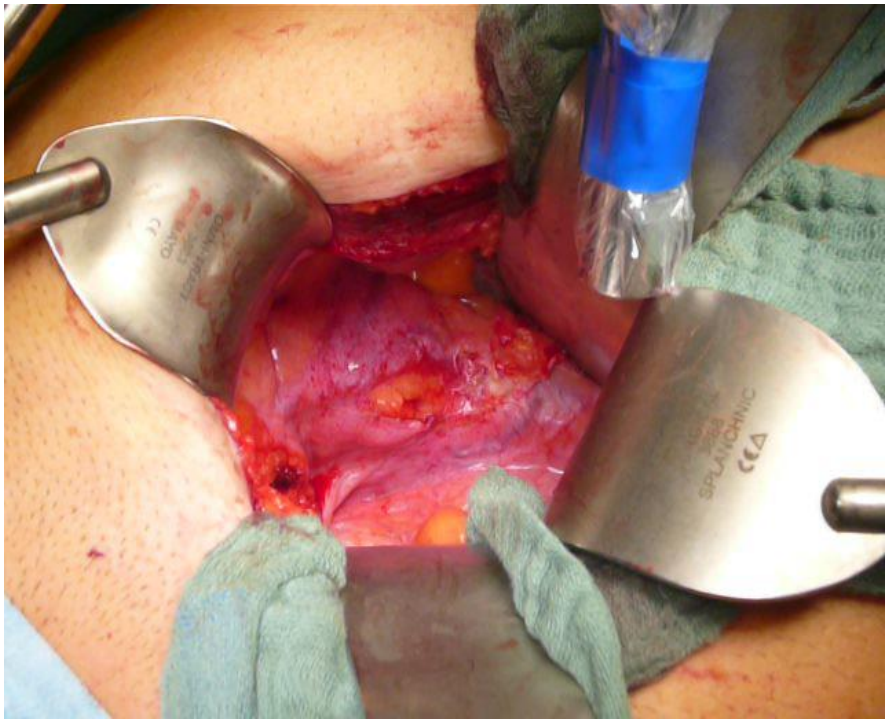
- Präoperative Injektion von ^{99}Tc-markierten PSMA-Liganden
- Intraoperative Detektion mittels Gammasonde

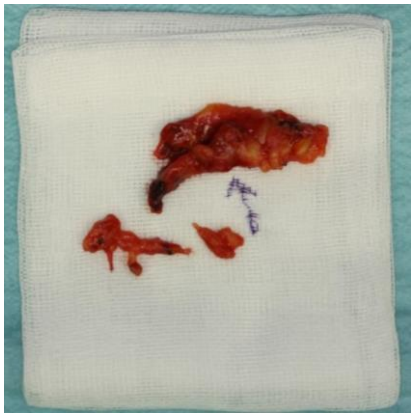


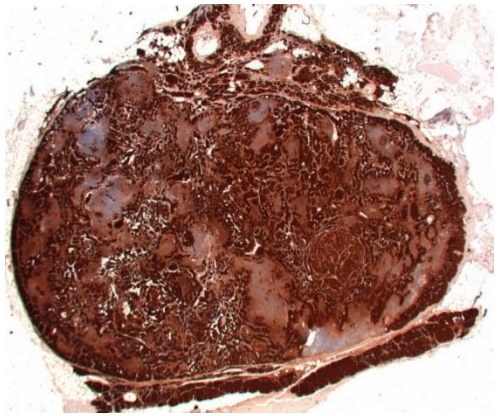


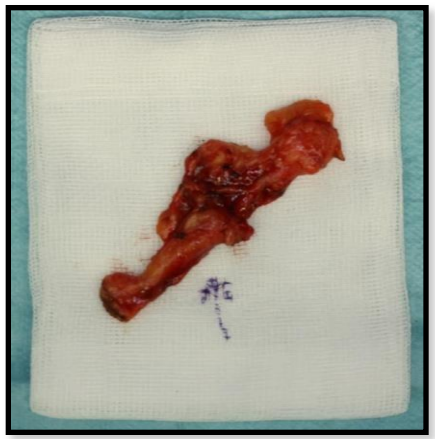
Maurer T et al., Eur Urol. 2015 Sep;68(3):530-4

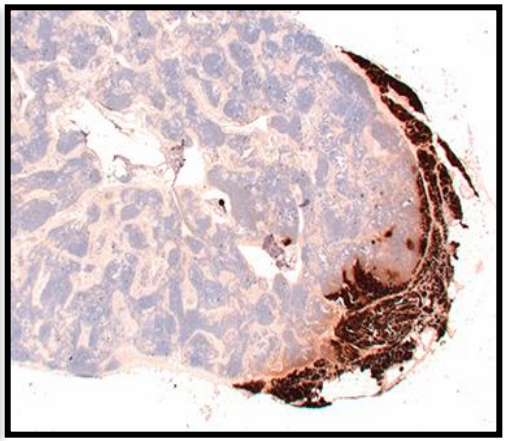
Radio-guided surgery mit ^{99}TC-markiertem PSMA

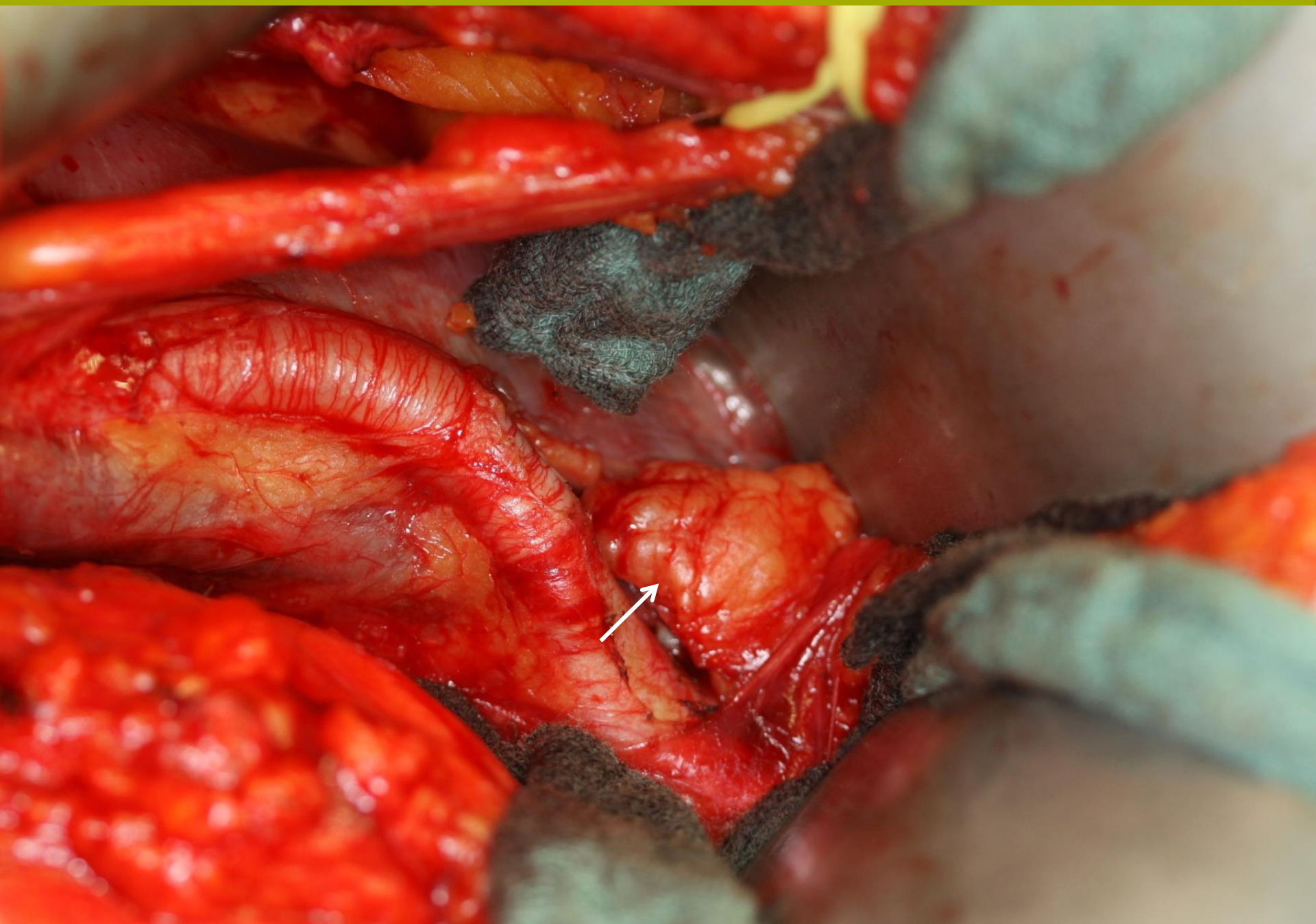












EUROPEAN UROLOGY 76 (2019) 517–523

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European Association of Urology

Prostate Cancer

Single Lesion on Prostate-specific Membrane Antigen-ligand Positron Emission Tomography and Low Prostate-specific Antigen Are Prognostic Factors for a Favorable Biochemical Response to Prostate-specific Membrane Antigen-targeted Radioguided Surgery in Recurrent Prostate Cancer

Thomas Horn[a], *Markus Krönke*[b], *Isabel Rauscher*[b], *Bernhard Haller*[c], *Stephanie Robu*[b], *Hans-Jürgen Wester*[d], *Margret Schottelius*[d], *Fijs W.B. van Leeuwen*[e], *Henk G. van der Poel*[f], *Matthias Heck*[a], *Jürgen E. Gschwend*[a], *Wolfgang Weber*[b], *Matthias Eiber*[b], *Tobias Maurer*[a,g,*]

[a] *Department of Urology, Technical University of Munich, Munich, Germany;* [b] *Department of Nuclear Medicine, Technical University of Munich, Munich, Germany;* [c] *Institute for Medical Statistics and Epidemiology, Technical University of Munich, Munich, Germany;* [d] *Institute of Pharmaceutical Radiochemistry, Technical University of Munich, Munich, Germany;* [e] *Interventional Molecular Imaging Laboratory, Department of Radiology, Leiden University Medical Centre, Leiden, The Netherlands;* [f] *Department of Urology, Antoni van Leeuwenhoek Hospital—The Netherlands Cancer Institute, Amsterdam, The Netherlands;* [g] *Martini-Klinik and Department of Urology, University Hospital Hamburg-Eppendorf, Hamburg, Germany*

Horn T, et al, Eur Urol. Apr 2019; 76: 519-523

PSMA-RGS: Postoperatives PSA-Ansprechen

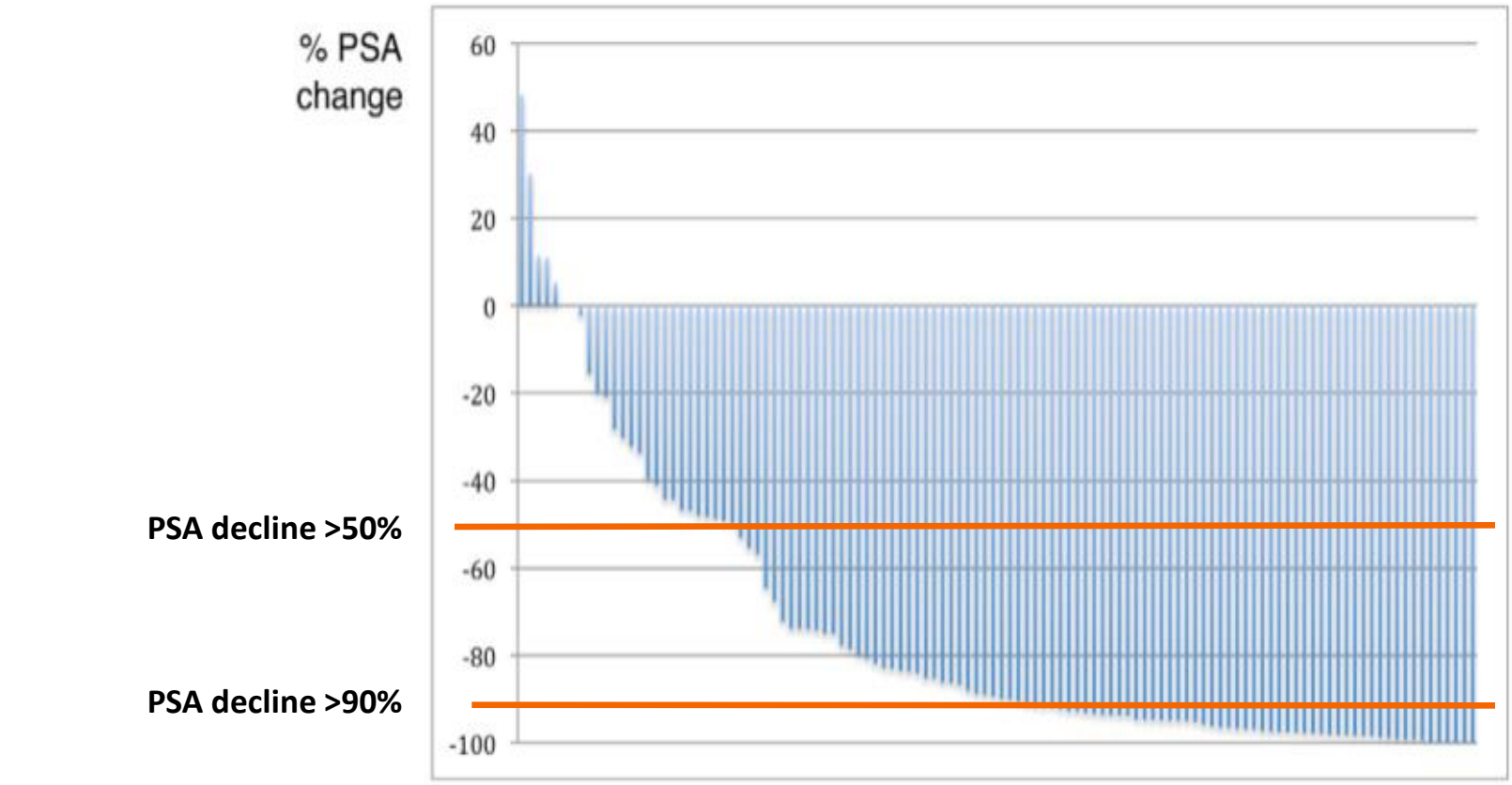
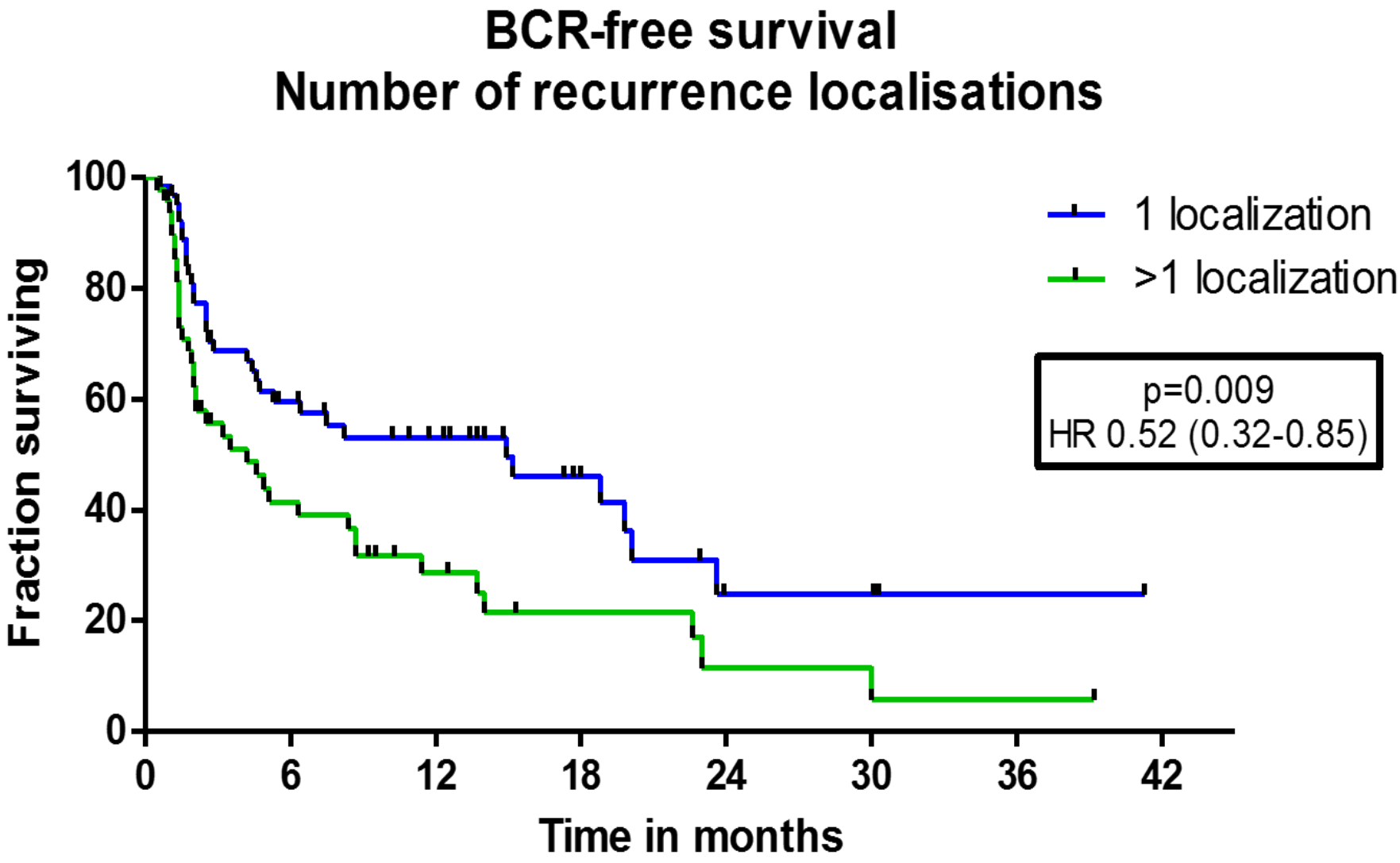
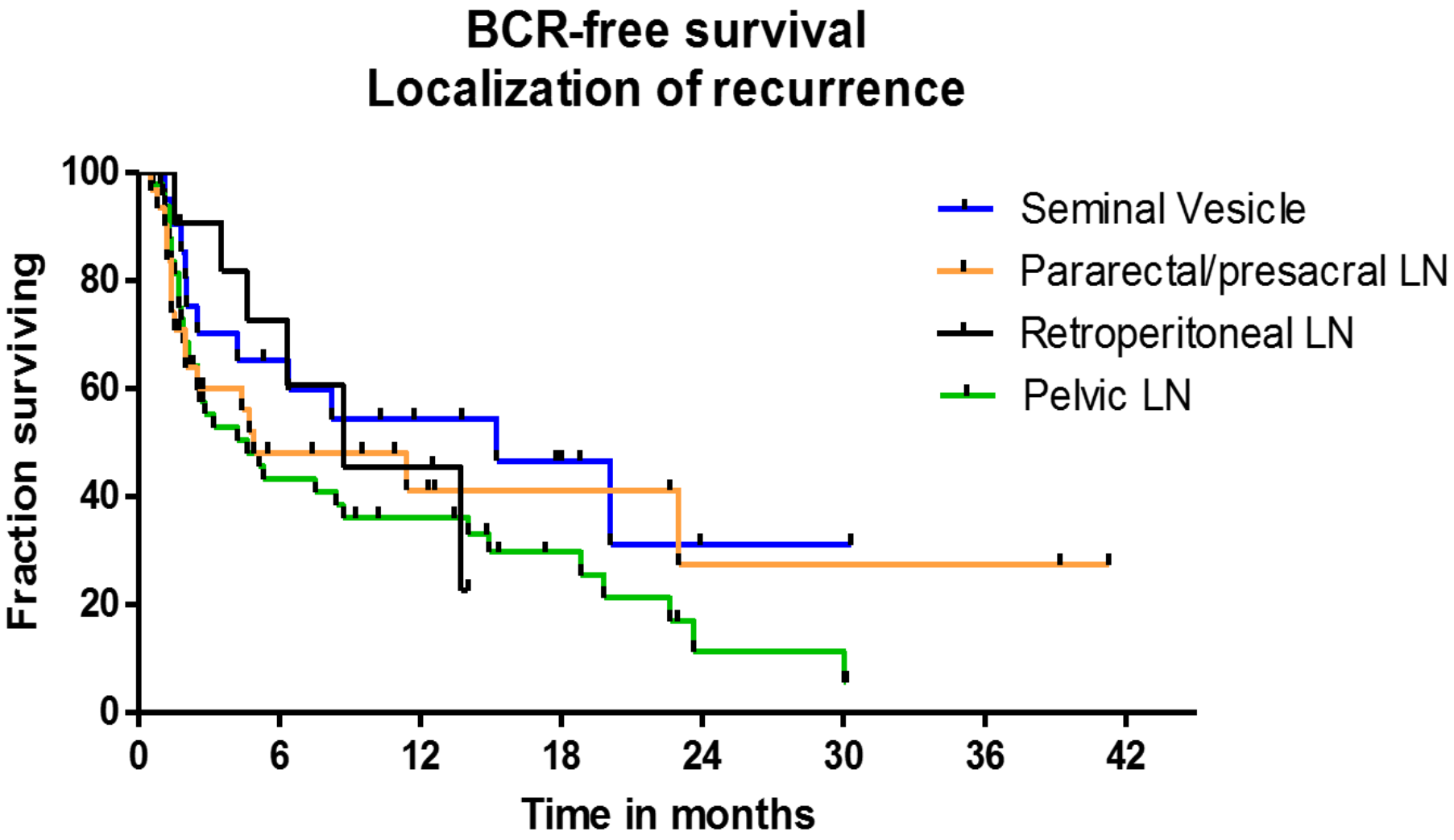


Fig. 1 – PSA responses 4–8 wk after PSMA-targeted RGS without any further treatment in 114 patients with sufficient follow-up information. PSA = prostate-specific antigen; PSMA = prostate-specific membrane antigen; RGS = radioguided surgery.

Horn T, et al, Eur Urol. Apr 2019; 76: 519-523

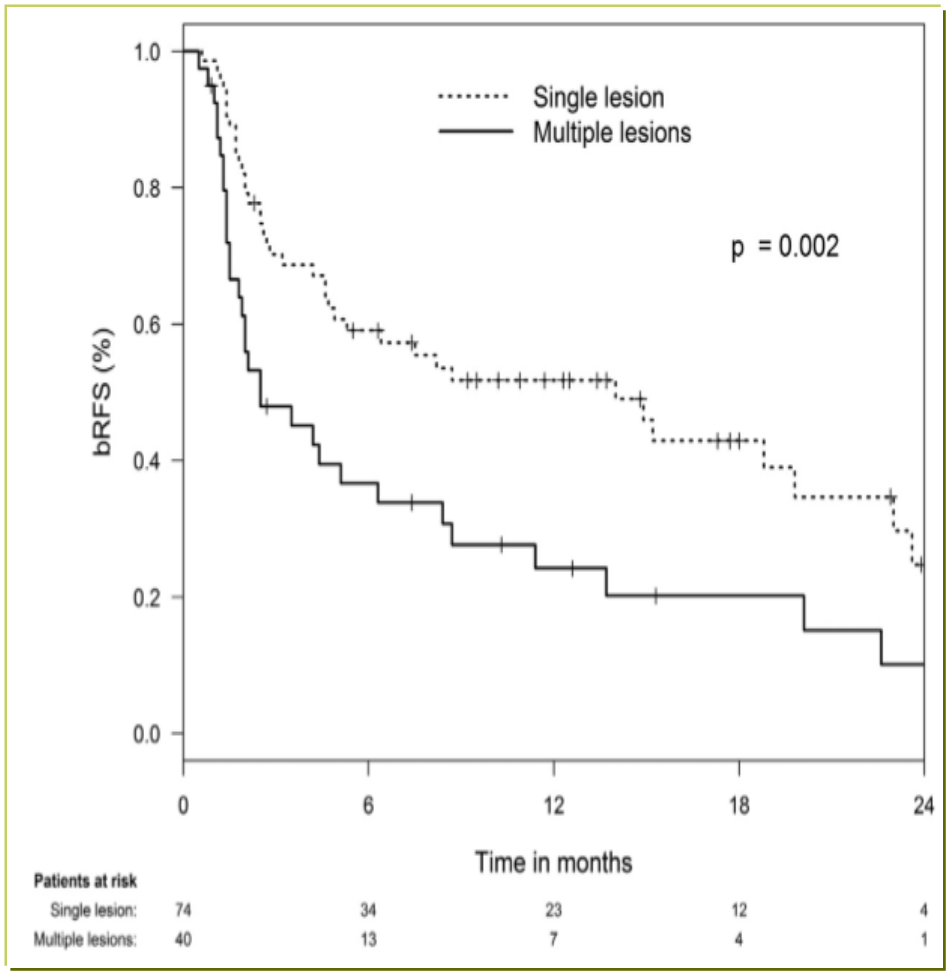


Horn T, et al, Eur Urol. Apr 2019; 76: 519-523

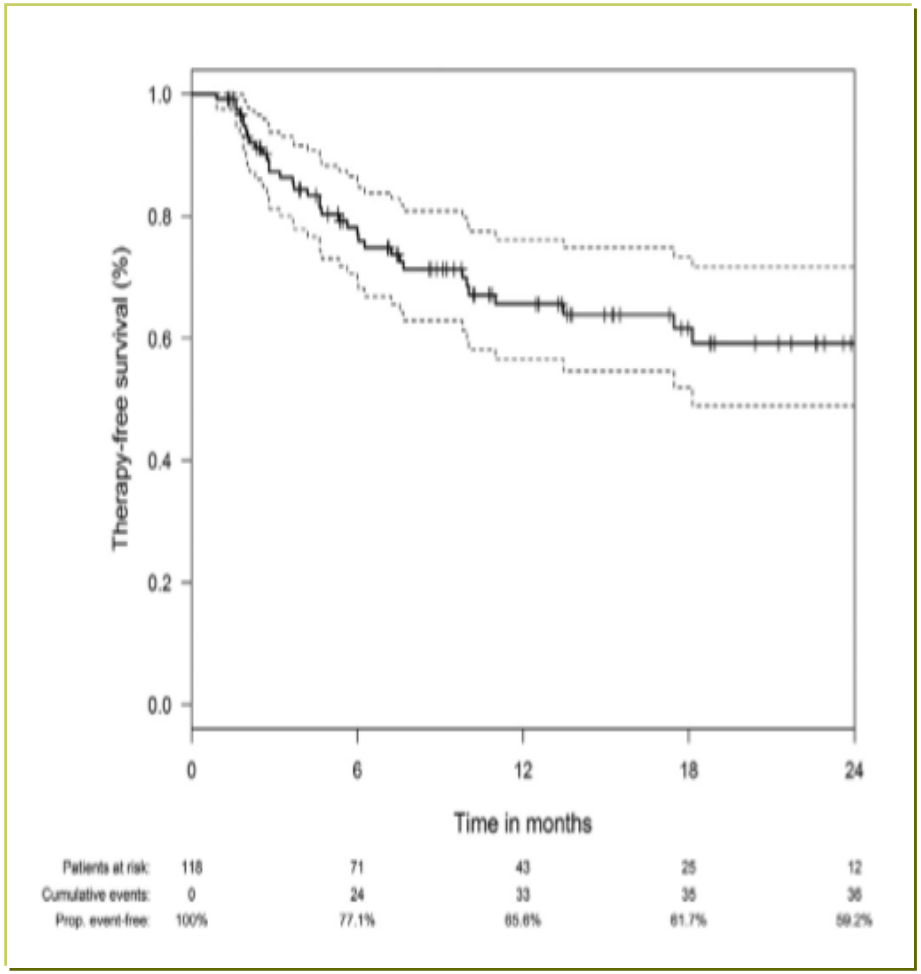


Horn T, et al, Eur Urol. Apr 2019; 76: 519-523

PSMA-RGS: bRFS und Therapie-freies Intervall



Biochemisch RFS



Therapie-freies Intervall

Horn T, et al, Eur Urol. Apr 2019; 76: 519-523

VOLUME 36 · NUMBER 5 · FEBRUARY 10, 2018

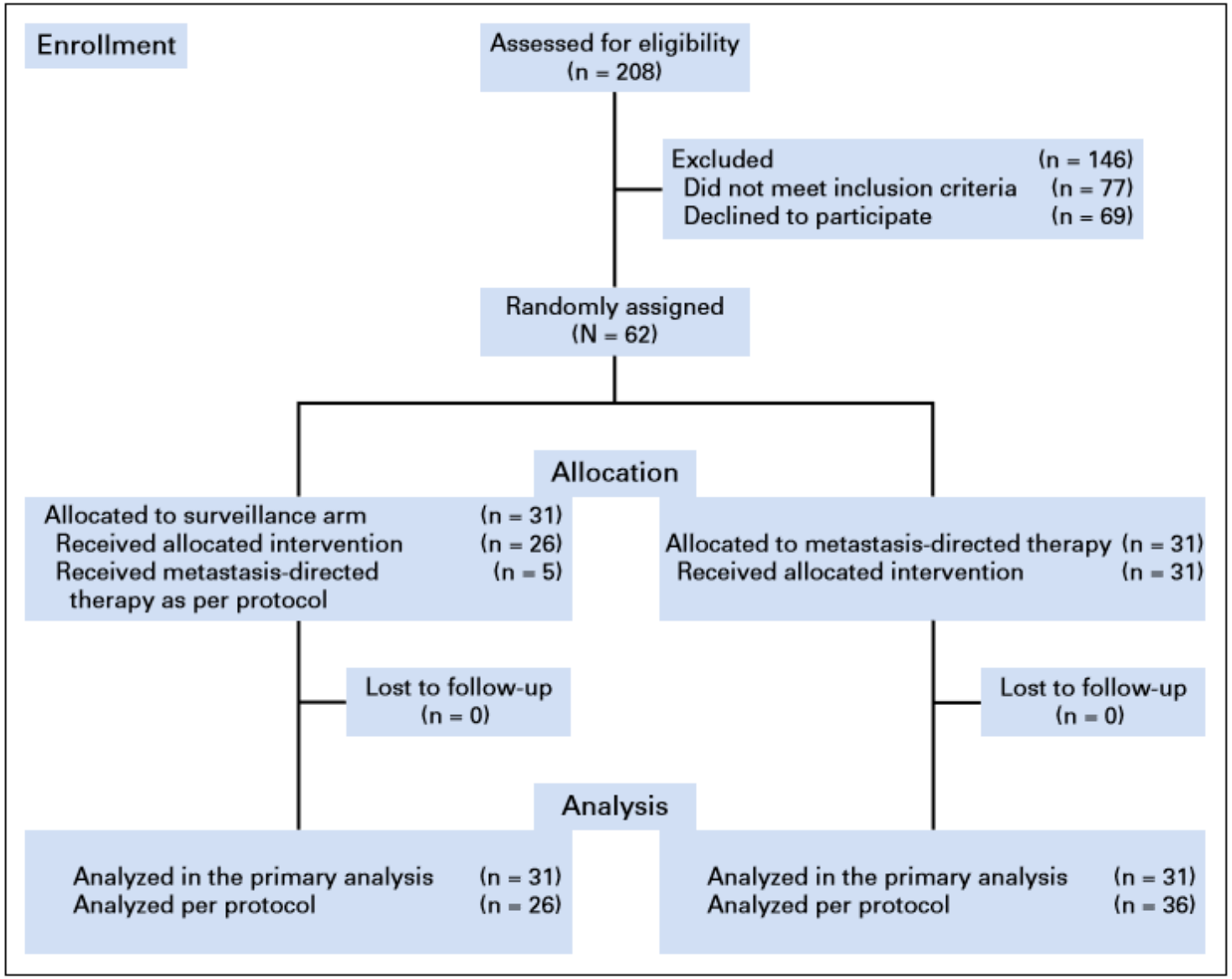
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

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

Piet Ost, Dries Reynders, Karel Decaestecker, Valérie Fonteyne, Nicolaas Lumen, Aurélie De Bruycker, Bieke Lambert, Louke Delrue, Renée Bultijnck, Tom Claeys, Els Goetghebeur, Geert Villeirs, Kathia De Man, Filip Ameye, Ignace Billiet, Steven Joniau, Friedl Vanhaverbeke, and Gert De Meerleer

Ost P et al, J Clin Oncol, VOLUME 36 • NUMBER 5 • FEBRUARY 10, 2018



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ADT-freies Überleben

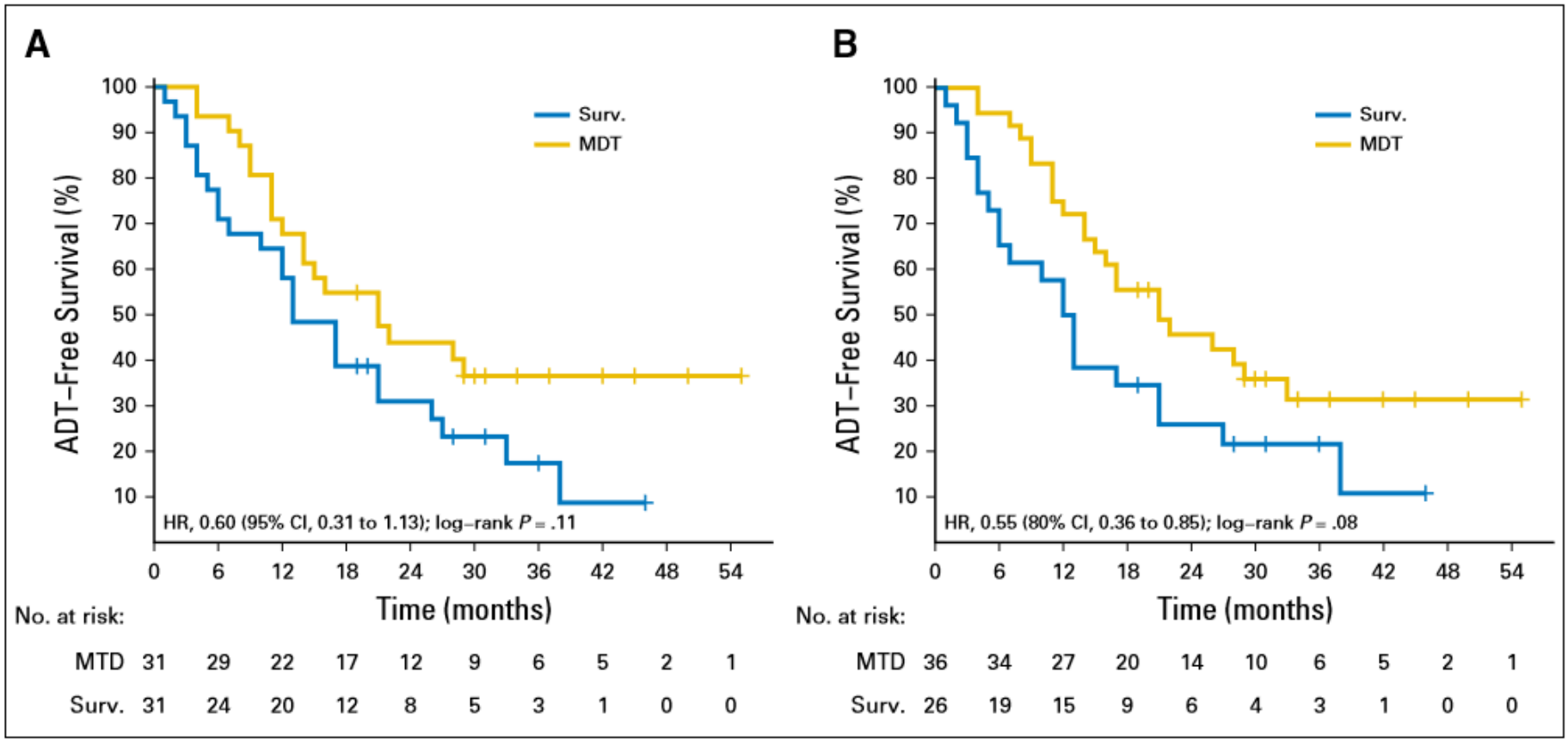
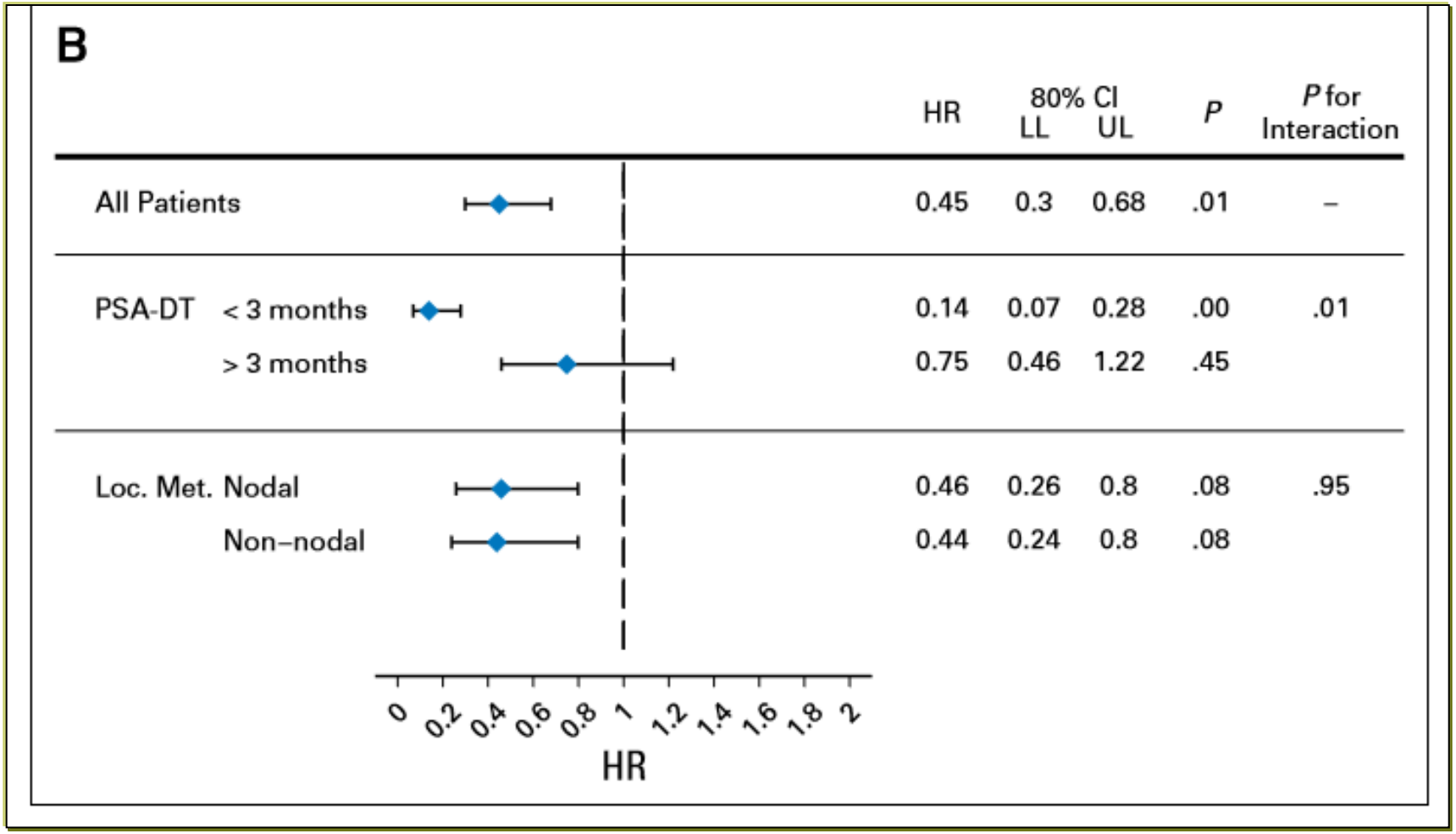


Fig 2. Kaplan-Meier plot comparing androgen deprivation therapy (ADT)–free survival of surveillance versus metastasis-directed therapy (MDT) for (A) the intention-to-treat analysis and (B) the per-protocol analysis. HR, hazard ratio; Surv., surveillance.

Ost P et al, J Clin Oncol, VOLUME 36 • NUMBER 5 • FEBRUARY 10, 2018

ADT-freies Überleben in Subgruppen (PP)



Ost P et al, J Clin Oncol, VOLUME 36 • NUMBER 5 • FEBRUARY 10, 2018

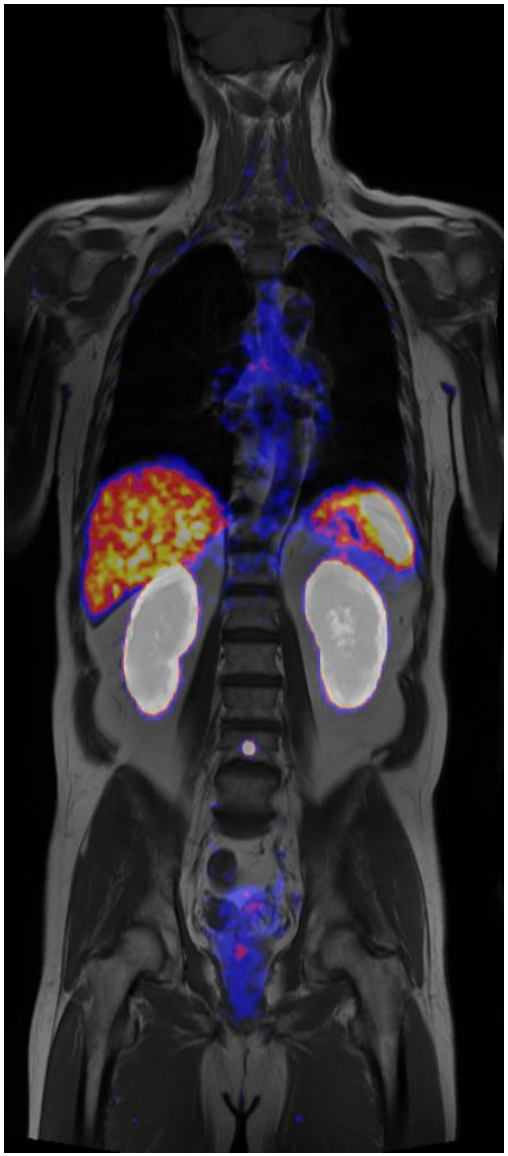
Agenda

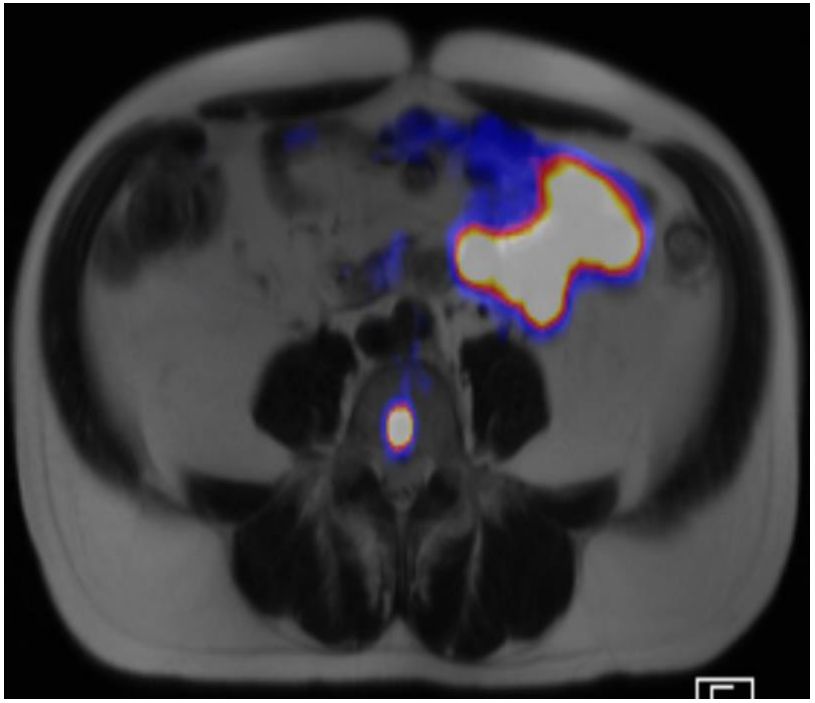
- **Bildgebung beim Prostatakarzinom**
  - Wie definieren wir „nicht-metastasiert“?
  - Wie definieren wir „oligo-metastasiert“?
- **Wie behandeln wir gestern und heute?**
  - Therapie des sekundär oligo-metastasierten PC
  - **Therapie des primär oligo-metastasierten PC**

Das oligo-metastasierte PC

- 62-jähriger Unternehmer
- 08/2015 ED: ossär und lymphogen metastasiertes Adenokarzinom der Prostata cT3b, cN1, cM1, Gleason-Score 4+4=8, iPSA 15 ng/ml
- Subjektiv ausgeprägte Miktionsymptome mit Obstruktion und LUTS

Fall (*1953): oligometastasiertes PC, Gleason 8





PSMA-PET-MRT 26.08.2015

Hypothese

Eine primär multimodal geplante Therapie ist der bessere Plan beim oligo-metastasierten Prostatakarzinom

Wir wissen, dass:

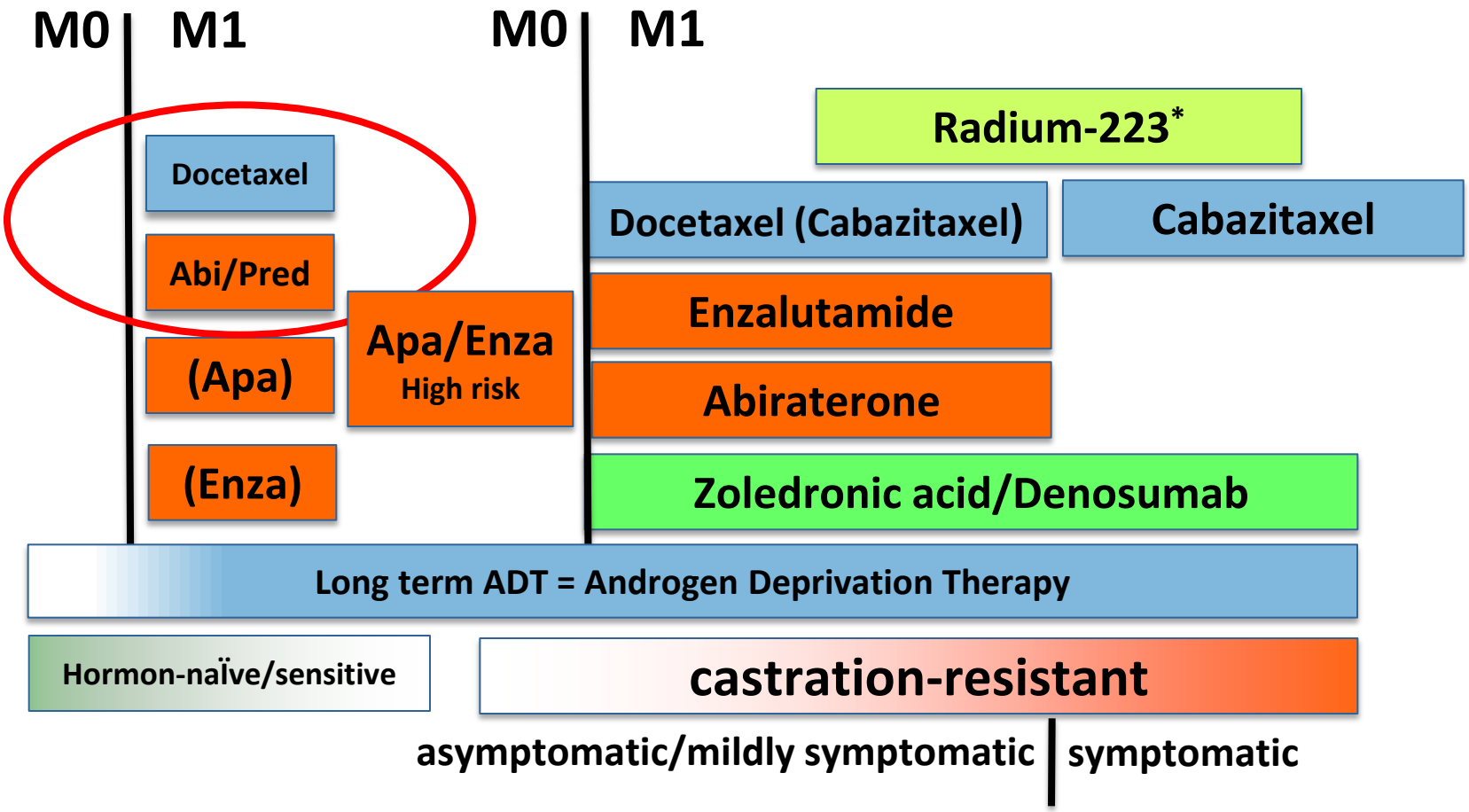
Eine frühe lokale Therapie des Primärtumors die Raten an lokaler Progression und Komplikationen reduziert

Local Prostate Treatment	Late Local Complications At CRPC
Group I: RRP (n=45)	20%
Group 2: EBRT (n=45)	47%
Group 3: No Local Therapy (n=173)	54%

RESULTS: Primary treatment of the prostate by either RRP or EBRT significantly reduces the incidence of local complications compared to no primary treatment (32.6% vs 54.6%; P = 0.001). RRP showed a significantly lower level of local complications compared to EBRT (20.0% vs 46.7%; P = 0.007). The most common local complications were bladder outlet obstruction (35.0%) and ureteric obstruction (15.2%).

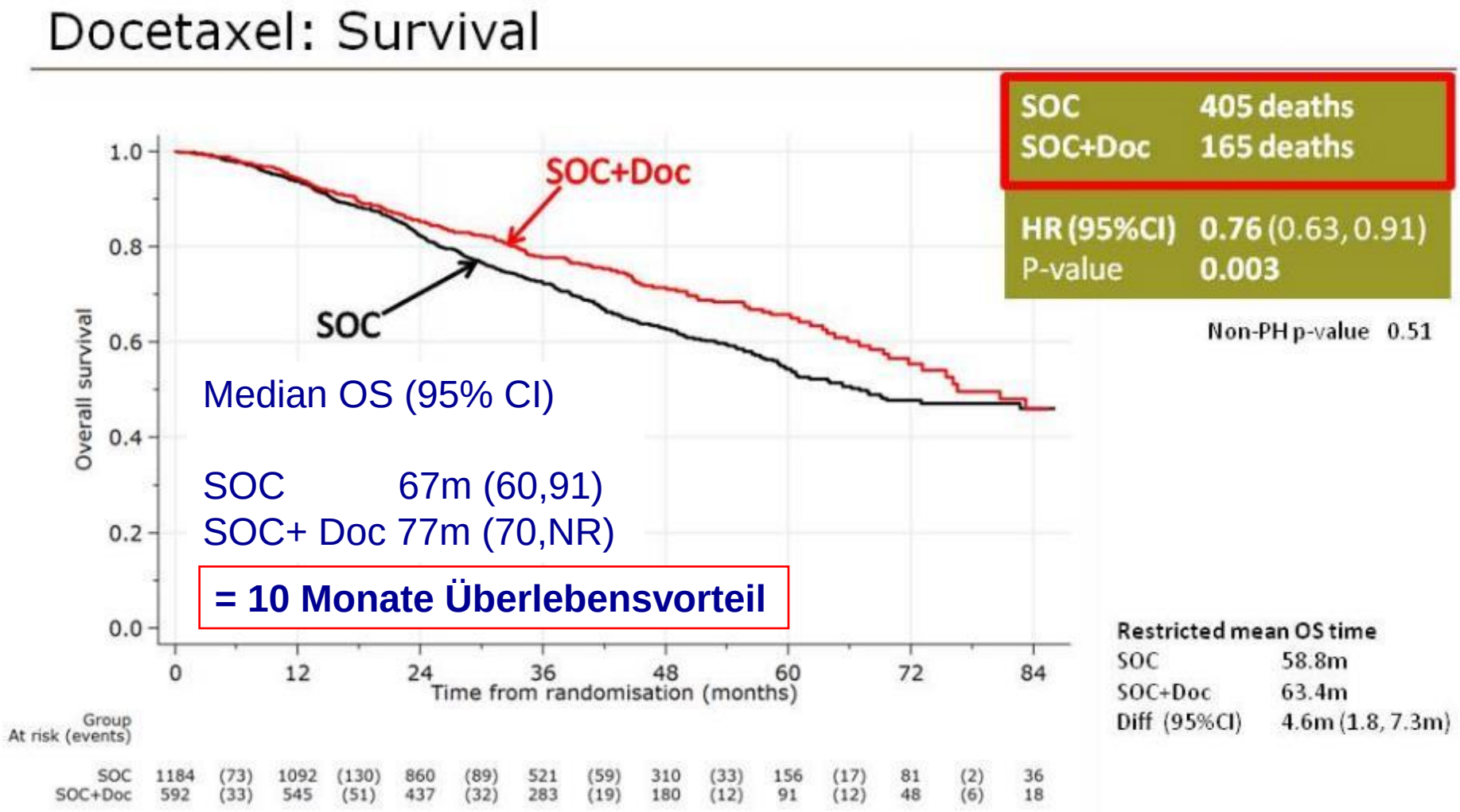
Won AC et al, BJUI (2013)

Therapie des Prostatakarzinoms 2019



*3rd-line CRPCa (EMA)

Induktive sTx vor lokaler Therapie beim mHsPC?



James et al, ASCO 2015, abstr 5001

CHAARTED: High- vs. Low-volume disease

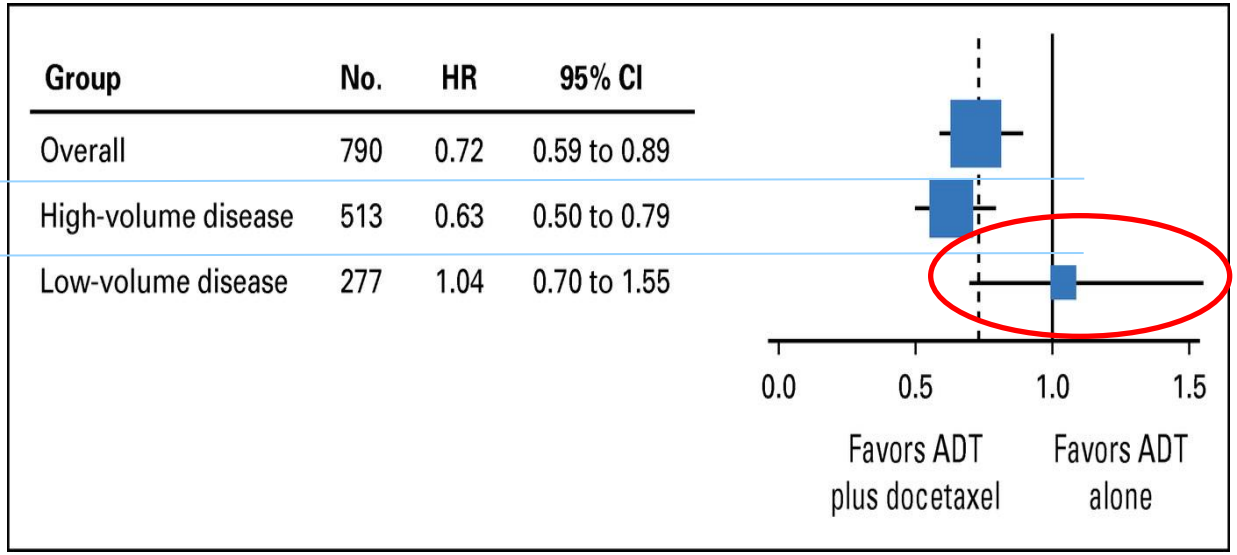


Fig 4. Test of heterogeneity between patients with high- and low-volume disease. ADT, androgen-deprivation therapy. The size of the squares is proportional to the inverse of the variance of the log hazard ratio (small squares correspond to large variances).

Published in: Christos E. Kyriakopoulos; Yu-Hui Chen; Michael A. Carducci; Glenn Liu; David F. Jarrard; Noah M. Hahn; Daniel H. Shevrin; Robert Dreicer; Maha Hussain; Mario Eisenberger; Manish Kohli; Elizabeth R. Plimack; Nicholas J. Vogelzang; Joel Picus; Matthew M. Cooney; Jorge A. Garcia; Robert S. DiPaola; Christopher J. Sweeney; *JCO* Ahead of Print
DOI: 10.1200/JCO.2017.75.3657

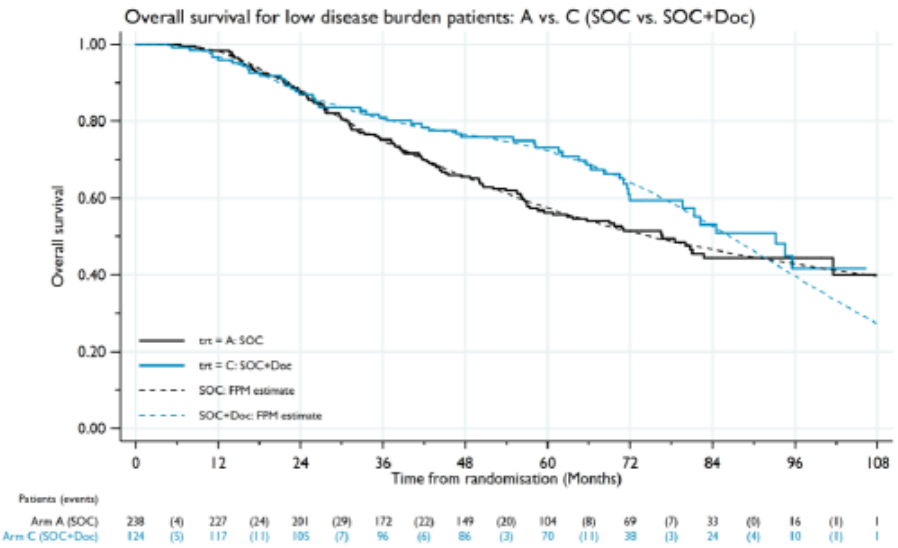
ADDITION OF DOCETAXEL TO HORMONAL THERAPY IN LOW AND HIGH BURDEN METASTATIC HORMONE SENSITIVE PATIENTS: LONG TERM SURVIVAL RESULTS FROM THE STAMPEDE TRIAL

Presenter: Professor Nick James

Noel W. Clarke, Adnan Ali, Fiona Ingleby, Alex Hoyle, Claire Amos, Gerhardt Attard, Simon Chowdhury, David Dearnaley, Hassan Douis, Silke Gillessen, Rob Jones, Zafar Malik, Malcolm Mason, Robin Millman, Chris Parker, Hannah Rush, Aurelius Omlin, Matthew Sydes, Mahesh Parmar, Nick James
on *behalf of the STAMPEDE trial*

Overall Survival: All Patients

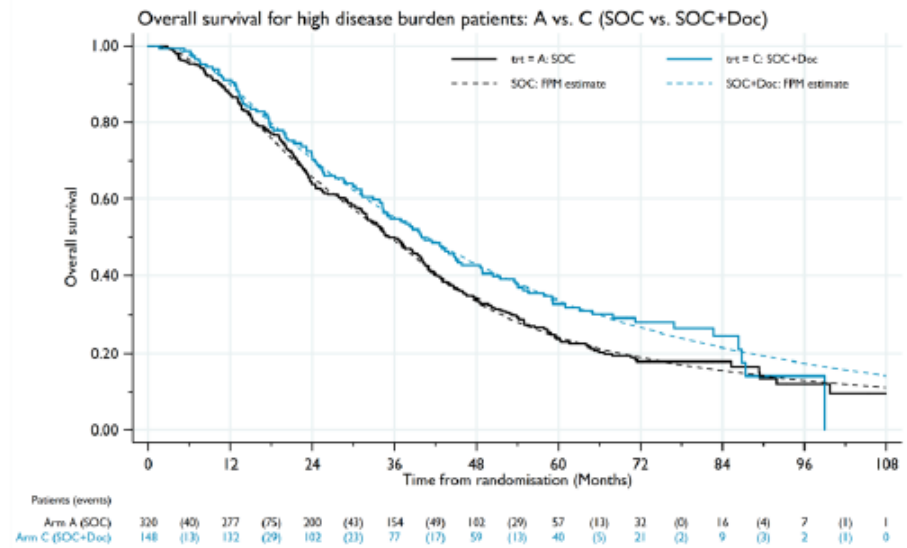
Low Burden



HR 0.76
95% CI 0.54 – 1.07
P = 0.107
Non-PH 0.809

5-yr survival:
A 57%
C 72%

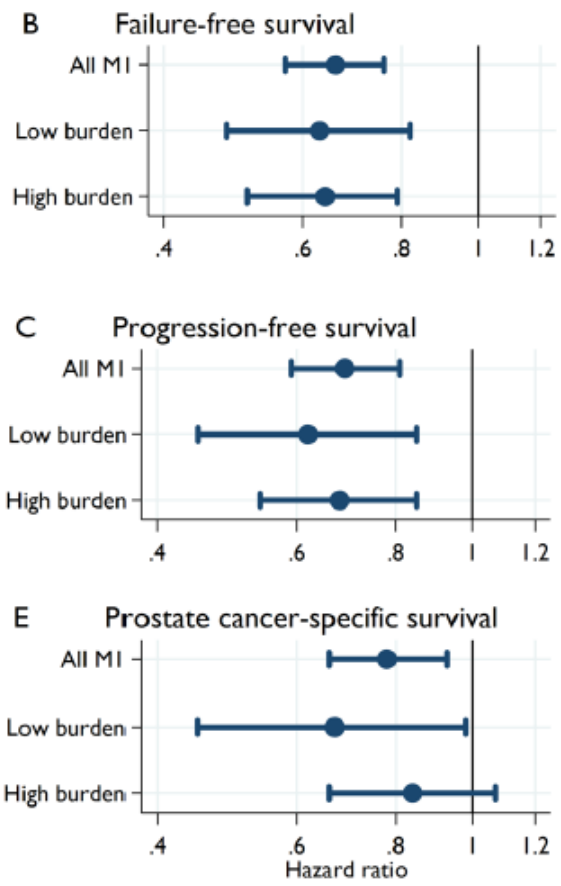
High Burden



HR 0.81
95% CI 0.64 – 1.02
P = 0.064
Non-PH 0.251

5-yr survival:
A 24%
C 34%

Other Outcomes: Subgroup Analysis by Metastatic Burden



Treatement * metastasis burden interaction:

P=0.792

P=0.855

P=0. 413

BARCELONA 2019 ESMO congress

Role of Abiraterone Acetate + Prednisolone + ADT in High and Low Risk Metastatic Hormone Naïve Prostate Cancer

Mr Alex Hoyle MBChB MRCS

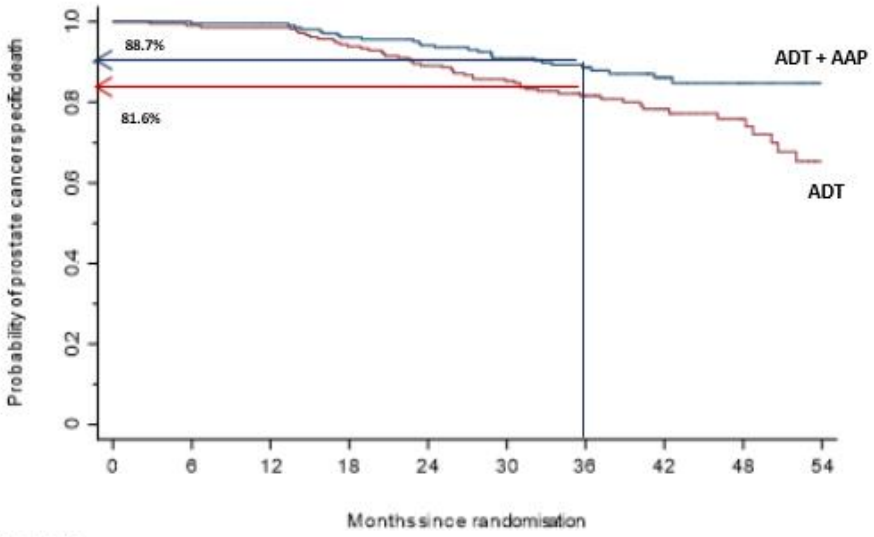
(Christie GenitoUrinary Research Group Fellow, UK)

Adnan Ali, Nick James, Chris Parker, Adrian Cook, Gert Attard, Simon Chowdhury, Bill Cross, David Dearnaley, Johann de Bono, Clare Gilson, Silke Gillessen, Rob Jones, David Matheson, Malcolm Mason, Alastair Ritchie, Martin Russell, Max Parmar, Matt Sydes, Noel Clarke;

for the STAMPEDE trial

RESULTS: PROSTATE CANCER SPECIFIC SURVIVAL

Low Risk

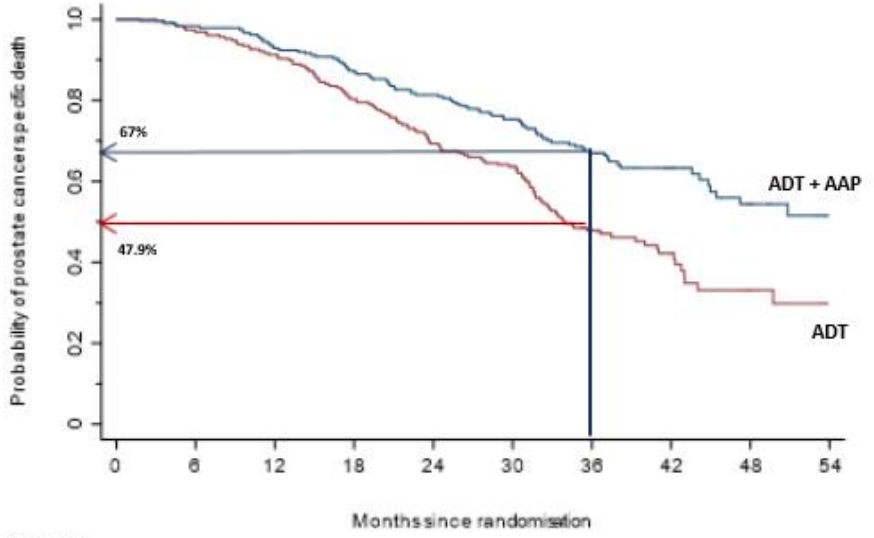


No. of patients (Events)

AAP	208	(1)	205	(11)	186	(10)	131	(4)	45
ADT alone	220	(3)	210	(20)	186	(15)	125	(6)	43

PCSS – 7.1%
HR 0.51 (0.31-0.84)
p=0.008

High Risk



No. of patients (Events)

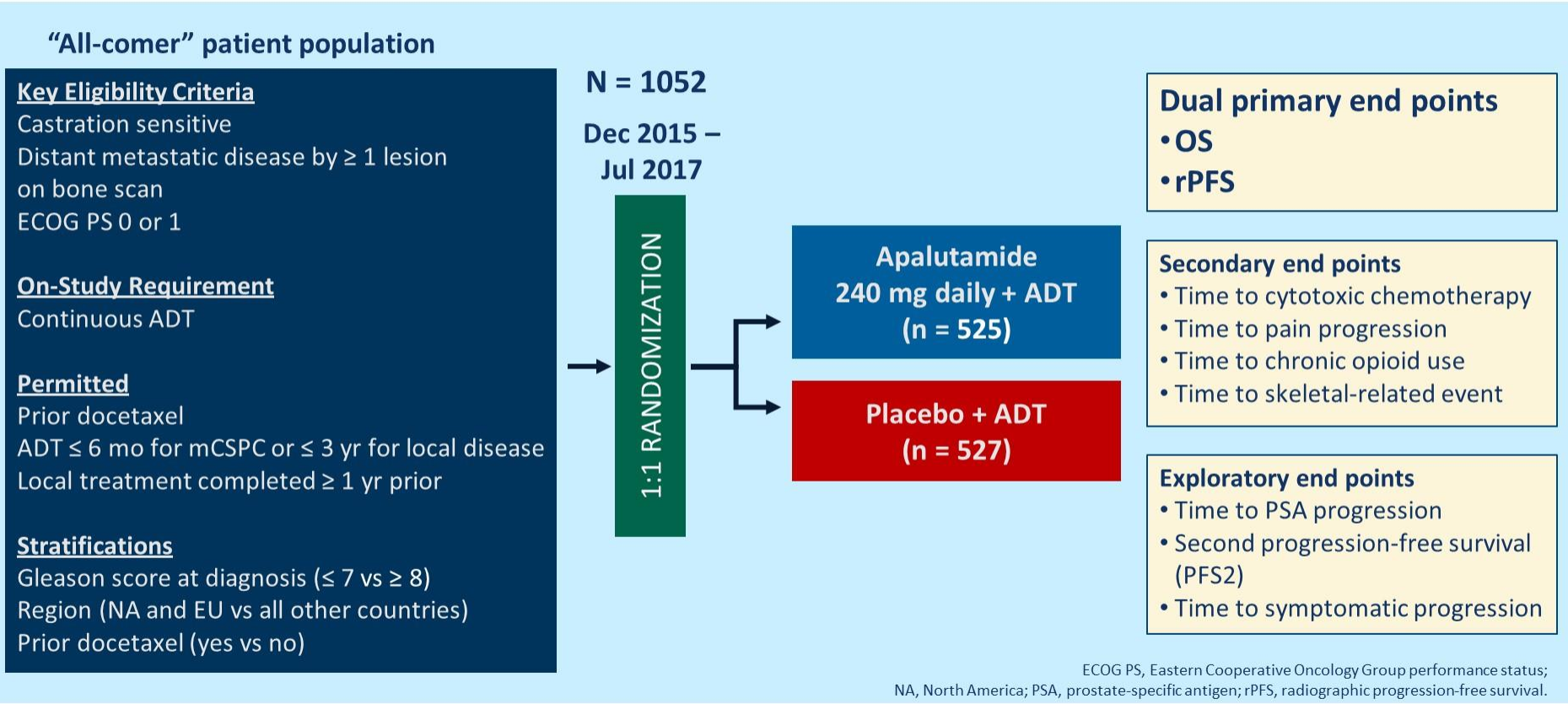
AAP	241	(17)	220	(27)	190	(31)	106	(11)	28
ADT alone	232	(20)	204	(48)	148	(42)	71	(12)	13

PCSS – 19.1%
HR 0.57 (0.43-0.75),
p<0.001

MUNICH 2018 ESMO congress

Hoyle, ESMO 2018

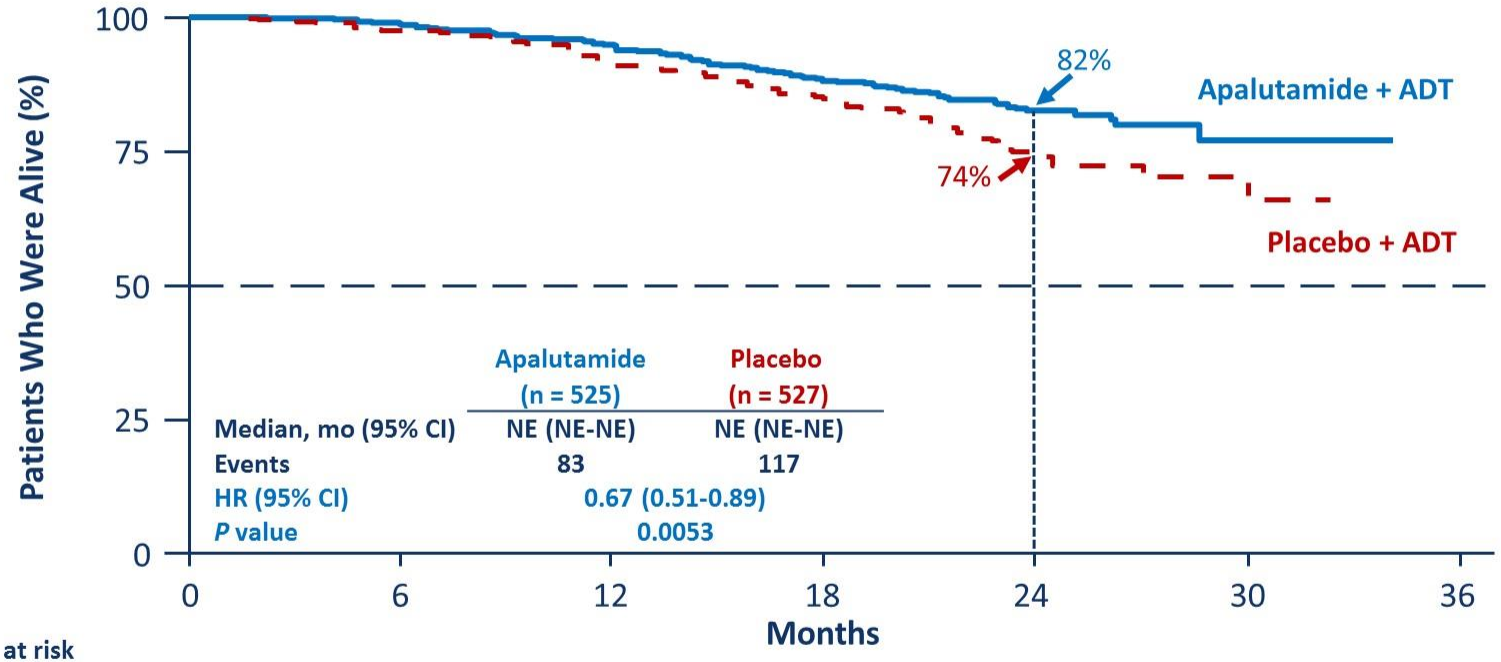
TITAN Study Design



ECOG PS, Eastern Cooperative Oncology Group performance status; NA, North America; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival.

Presented By Kim Chi at 2019 ASCO Annual Meeting

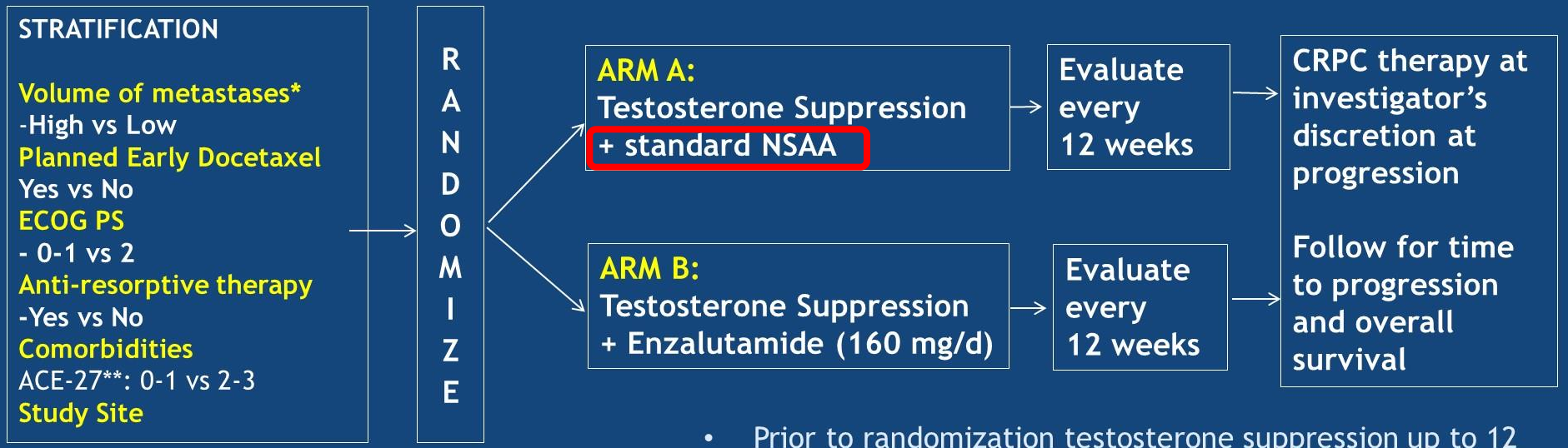
TITAN OS: Apalutamide Significantly Reduced the Risk of Death by 33%



No. at risk							
Apalutamide	525	513	490	410	165	14	0
Placebo	527	509	473	387	142	16	0

Presented By Kim Chi at 2019 ASCO Annual Meeting

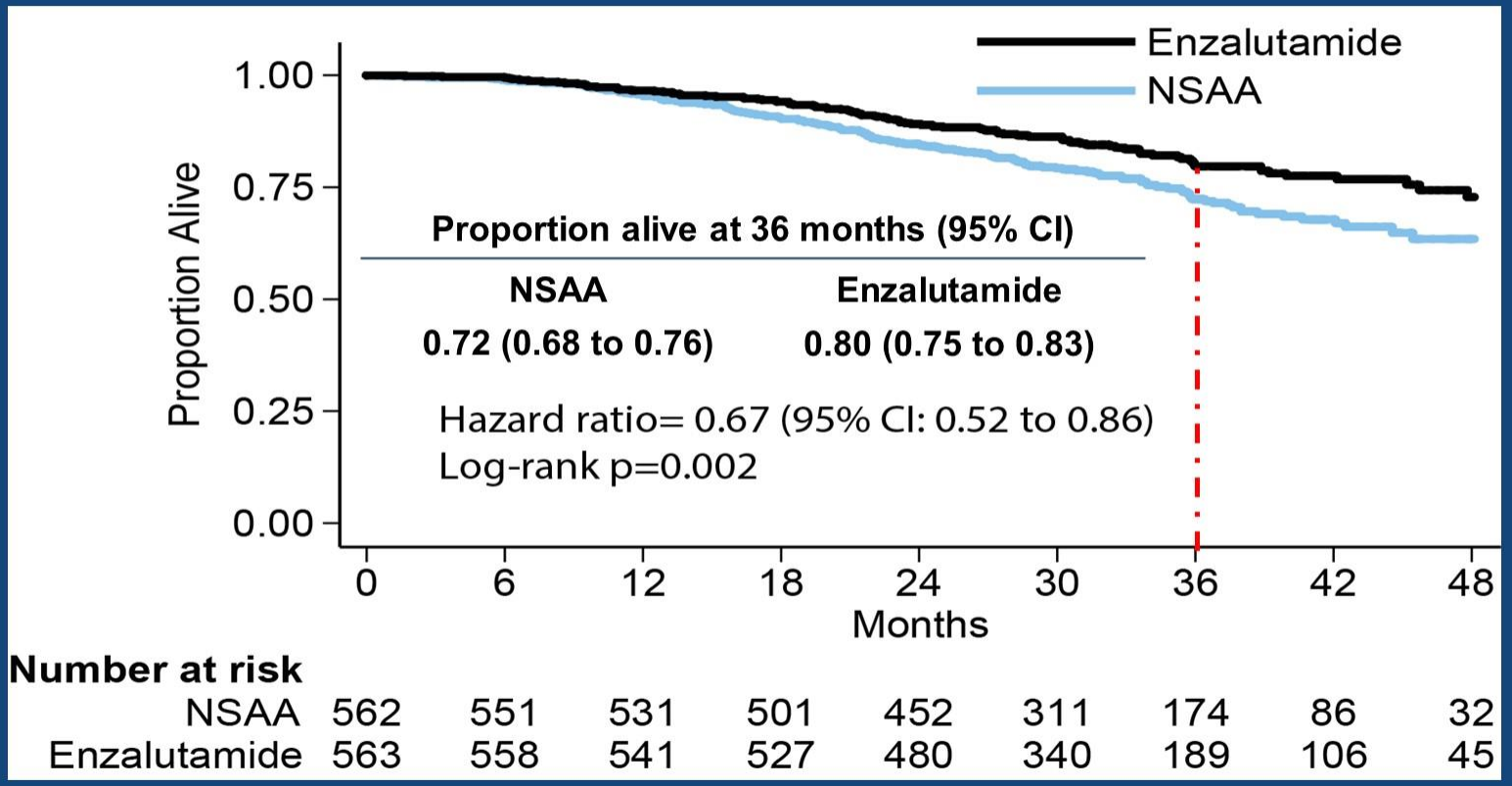
ENZAMET Treatment



- Prior to randomization testosterone suppression up to 12 weeks and 2 cycles of docetaxel was allowed.
- Intermittent ADT and cyproterone were not allowed
- NSAA: bicalutamide; nilutamide; flutamide
- *High volume: visceral metastases and/or 4 or more bone metastases (at least 1 beyond pelvis and vertebral column)
- **Adult Co-morbidity Evaluation-27

Presented By Christopher Sweeney at 2019 ASCO Annual Meeting

Primary endpoint: Overall survival



Presented By Christopher Sweeney at 2019 ASCO Annual Meeting

Offene Fragen:

Lokale Therapie beim mHSPC ?

Niedrige versus hohe Metastasenlast ?

Operation versus Strahlentherapie ?

Studien zur ADT ± lokale Therapie beim mHsPC?

Studientitel	Institution und Details	Intervention	Studienendpunkte
Best Systemic Therapy or Best Systemic Therapy (BST) Plus Definitive Treatment (Radiation or Surgery) [22]	M. D. Anderson, USA Phase II N = 120 NCT01751438	Rad. Prostatektomie oder Radiatio plus Systemtherapie vs. Systemtherapie	Progressionsfreies Überleben Lebensqualität
Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy. STAMPEDE Trial, Arm H [23]	Multiinstitutional, England und Schweiz 2005–2017 PhaseIII NCT00268476	Standard of care (ADT) vs. Standard of care plus Radiatio	Gesamtüberleben Progressionsfreies Überleben
A randomised study about the effect on survival of hormonal therapy plus local external radiation therapy in patients with primary diagnosed metastasized (M+) prostate cancer. HORRAD Study [24]	Multiinstitutional, Niederlande N = 446, 2004–2011 Rekrutierung komplettiert ISRCTN06890529	ADT vs. ADT und Radiatio	Gesamtüberleben Progressionsfreies Überleben Lebensqualität
EORTC-1201-GUCG-ROG. A prospective randomised phase III study of androgen deprivation therapy (± docetaxel) with or without local radiotherapy with or without abiraterone acetate and prednisone in patient with metastatic hormone-naïve prostate cancer [25]	Multiinstitutional, Europa N = 15501, 2004–2012 NCT01957436	Arm A: ADT (± Doc) vs. Arm B: ADT (± Doc) plus Abirateron vs. Arm C: Arm A plus Radiatio vs. Arm D: Arm B plus Radiatio	Gesamtüberleben Progressionsfreies Überleben Lebensqualität
AP 75/13G-RAMPP - Multizentrische prospektive randomisierte Studie zur Evaluierung des Effektes der medikamentösen Standardtherapie mit oder ohne radikale Prostatektomie bei Patienten mit einem begrenzt ossär metastasierten Prostatakarzinom [26]	Multiisntitutional, Deutschland N = 452, 2015–2025 NCT02454543	Systemtherapie (ADT ± Doc) vs. Systemtherapie (ADT ± Doc) plus rad. Prostatektomie	Gesamtüberleben Progressionsfreies Überleben Lebensqualität

Aus Steuber et al. Aktuelle Urologie 2016

MRC Clinical Trials Unit

Smarter Studies
Global Impact
Better Health

STAMPEDE

UCL

Radiotherapy to the primary tumour for men with newly-diagnosed metastatic prostate cancer: Survival results from STAMPEDE

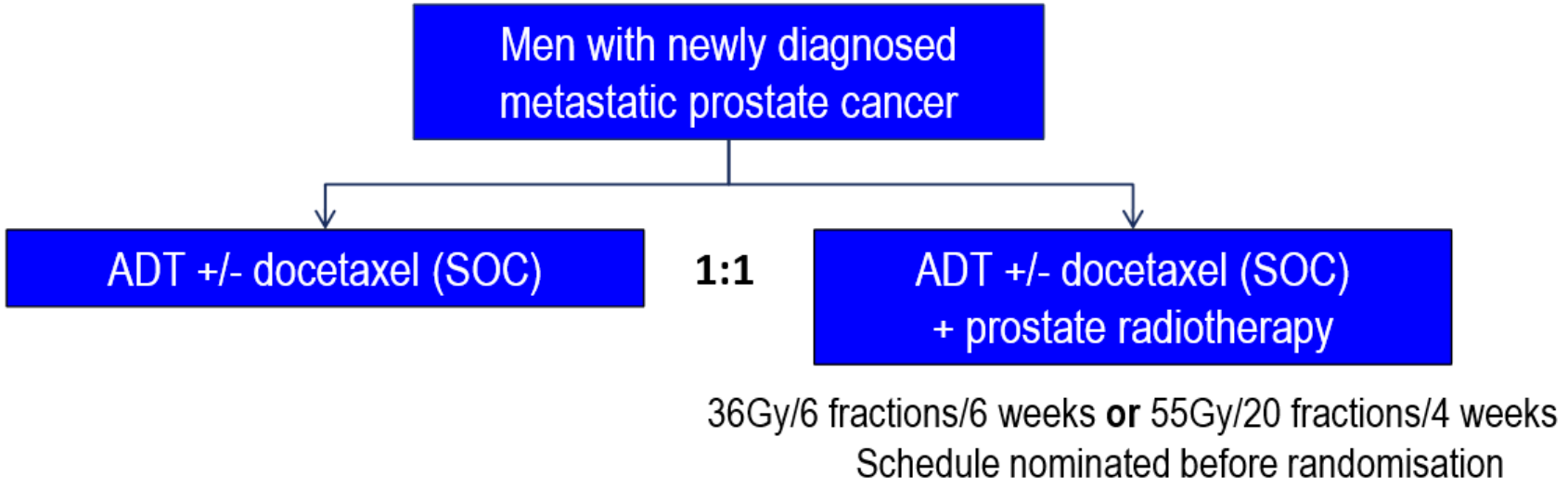
CC Parker, ND James, CD Brawley, NW Clarke, G Attard, S Chowdhury, W Cross, DP Dearnaley, S Gillessen, C Gilson, RJ Jones, MD Mason, R Millman, C Eswar, J Gale, JF Lester, DJ Sheehan, AT Tran, MKB Parmar, MR Sydes.

MUNICH 2018 ESMO congress

The ROYAL MARSDEN NHS Foundation Trust

CANCER RESEARCH UK

Study design

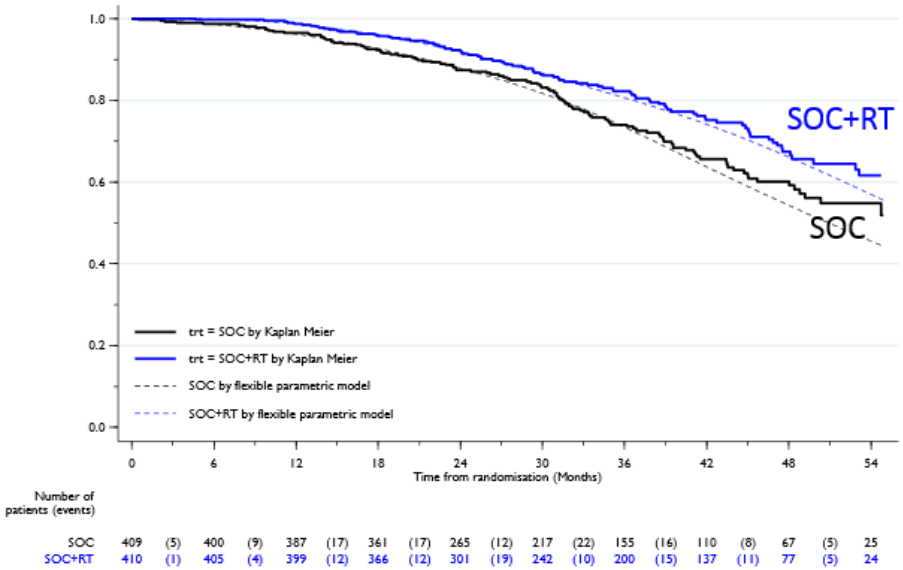


Stratification variables

Age (<70 vs ≥70 years), nodal involvement (N0 vs N1 vs Nx), randomising site, WHO performance status (0 vs 1 or 2), type of ADT, aspirin or NSAID use, docetaxel use

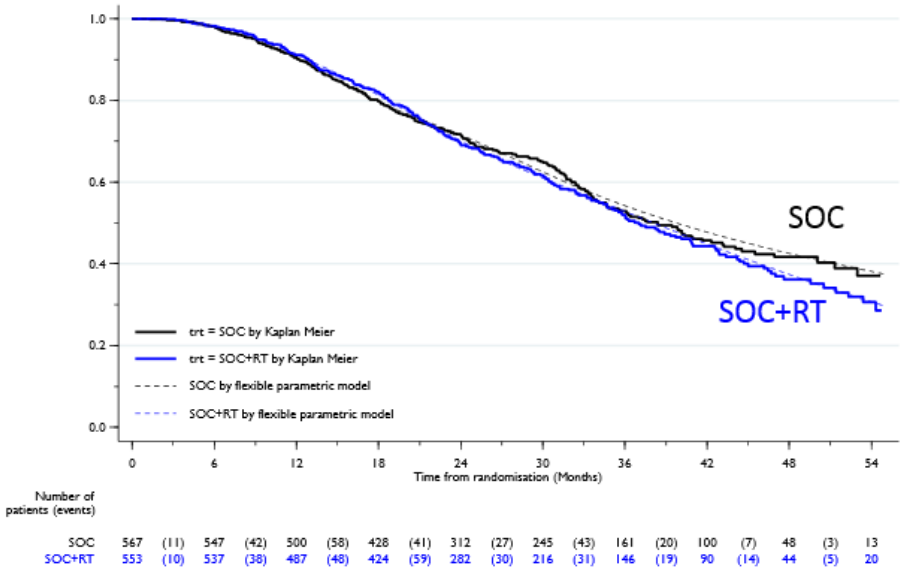
Overall survival: metastatic burden subgroup analysis

Low burden



HR: 0.68 (95% CI 0.52-0.90); p=0.007
3 year OS (%): SOC = 73%
SOC+RT = 81%

High burden



HR: 1.07 (95% CI 0.90-1.28); p=0.420
3 year OS (%): SOC = 54%
SOC+RT = 53%

MUNICH 2018 ESMO congress

MRC CTU at UCL

Parker, ESMO 2018

Zytoreduktive Prostatektomie beim mHsPC

EUROPEAN UROLOGY FOCUS XXX (2017) XXX–XXX

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

Brief Correspondence

Does Cytoreductive Prostatectomy Really Have an Impact on Prognosis in Prostate Cancer Patients with Low-volume Bone Metastasis? Results from a Prospective Case-Control Study

Thomas Steuber [a,1,], Kasper D. Berg [b,1], Martin A. Røder [b], Klaus Brasso [b], Peter Iversen [b], Hartwig Huland [a], Anne Tiebel [a], Thorsten Schlomm [a], Alexander Haese [a], Georg Salomon [a], Lars Budäus [a], Derya Tilki [a], Hans Heinzer [a], Markus Graefen [a], Philipp Mandel [a]*

[a] Martini-Klinik Prostate Cancer Center, University Hospital Hamburg-Eppendorf, Hamburg, Germany; [b] Copenhagen Prostate Cancer Center, Department of Urology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

Article info

Article history:
Accepted June 27, 2017

Associate Editor:
James Catto

Keywords:
Cytoreductive radical prostatectomy
Bone metastases
Castration-resistant prostate cancer
Oncological outcome

Abstract

The impact of cytoreductive radical prostatectomy (CRP) on oncological outcomes in patients with prostate cancer (PCa) and distant metastases has been demonstrated by retrospective data with their potential selection bias. Using prospective institutional data, we compared the outcomes between 43 PCa patients with low-volume bone metastases (1–3 lesions) undergoing CRP (median follow-up 32.7 mo) and 40 patients receiving best systemic therapy (BST; median follow-up 82.2 mo). The inclusion criteria for both cohorts were identical. So far, no significant difference in castration resistant-free survival ($p = 0.92$) or overall survival ($p = 0.25$) has been detected. Compared to recent reports, the outcomes for our control group are more favorable, indicating a potential selection bias in the previous retrospective studies. Therefore, the unclear oncological effect has to be weighed against the potential risks of CRP. However, patients benefit from a significant reduction in locoregional complications (7.0% vs 35%; $p < 0.01$) when undergoing CRP.

Patient summary: In this study we analyzed the impact of surgery in patients with prostate cancer and bone metastases. Using prospective data, we could not show a significant benefit of surgery on survival, but the rate of locoregional complications was lower. Therefore, patients should be treated within prospective trials evaluating the role of cytoreductive prostatectomy in low-volume, bone metastatic prostate cancer.

† These authors contributed equally to this work.
* Corresponding author. Martini-Klinik Prostate Cancer Center, University Hospital Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany. Tel./Fax: +49 40 74100.
E-mail address: steuber@uke.de (T. Steuber).

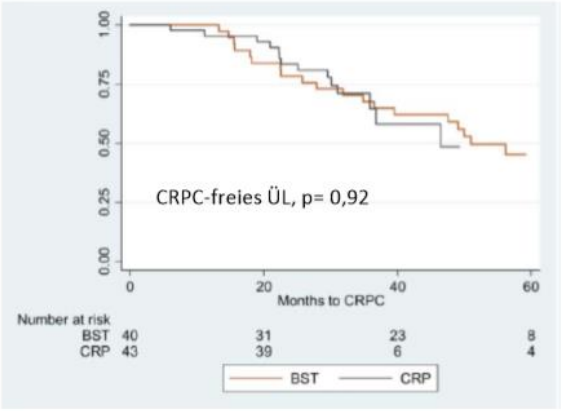
The rationale for performing cytoreductive radical prostatectomy (CRP) in newly diagnosed metastatic prostate cancer (PCa) might be to prevent locoregional symptoms, observed in up to 56% of men with progressing PCa, and to prolong survival [1]. The feasibility of CRP in patients with distant metastases has already been proven [2].

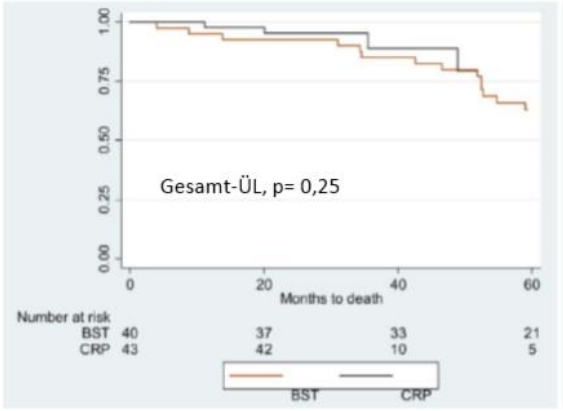
As prospective randomized trials investigating the impact of CRP in men with metastatic disease are still currently recruiting (NCT01751438, NCT02454543), evidence is drawn from regional cancer registries [3], multi-institutional databases [4,5], and single-institution case-(control) studies [6,7]. Most of these studies suggest a survival benefit for CRP compared to best systemic therapy (BST) alone. Nevertheless, besides the retrospective nature of the data, these results might be limited by potential selection bias, as healthier asymptomatic patients with a

http://dx.doi.org/10.1016/j.euf.2017.04.016
2405-4569/

Prospektive Fall-Kontrol Studie, cytoreduktive RP vs. ADT, gleiche Einschlußkriterien

- PSA <150 ng/ml
- max 3 Metastasen (low volume, max cT3b)
- ECOG-0/1, keine Schmerzen
- Martini-Klinik (PROMPT-Studie,n=43) vs. Kopenhagen PCa-Register (n= 40)





Steuber et al, Eur Urol Focus 2017

Aktuelle, rekrutierende klinische Studien: Zytoreduktive Prostatektomie

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Recruiting	**Cytoreductive Prostatectomy** Versus **Cytoreductive Prostate** Irradiation as a Local Treatment Option for Metastatic **Prostate Cancer**: a Multicentric Feasibility Trial	• **Prostate Cancer** Metastatic	• Procedure: radical **prostatectomy** • Radiation: Whole pelvis radiotherapy	• University Hospital Ghent Ghent, Belgium
2	☐	Recruiting	Safety and Early Efficacy of Radical **Prostatectomy** for Newly Diagnosed Very High Risk Locally Advanced and Oligometastatic **Prostate Cancer**	• Locally Advanced and Metastatic **Prostate Cancer**	• Procedure: Radical **prostatectomy**	• Medical University of Vienna Vienna, Austria
3	☐	Recruiting	Therapeutic Effect of **Cytoreductive** Radical **Prostatectomy** in Men With Newly Diagnosed Metastatic **Prostate Cancer**	• Stage IV **Prostate** Adenocarcinoma AJCC v7	• Drug: Antiandrogen Therapy • Drug: Docetaxel • Other: Laboratory Biomarker Analysis • (and 3 more...)	• City of Hope Duarte, California, United States • University of California Irvine, California, United States • University of Southern California Los Angeles, California, United States • (and 7 more...)
4	☐	Recruiting	Adjuvant Treatments to the Local **Tumour** for Metastatic **Prostate Cancer**: Assessment of Novel Treatment Algorithms	• **Prostate Cancer** • Metastatic **Prostate Cancer**	• Combination Product: Standard of Care • Procedure: Minimally Invasive Ablative Therapy (MIAT) • Procedure: Radical Therapy (**Prostatectomy** or Radiotherapy)	• Wexham Park Hospital, Frimley Health NHS Foundation Trust Frimley, Surrey, United Kingdom • The Royal United Hospital, Royal United Hospitals Bath NHS Foundation Trust Bath, United Kingdom • Wirral University Teaching Hospital, Wirral University Teaching Hospital NHS

17.11.2019: https://clinicaltrials.gov/ct2/results?cond=Prostate+Cancer&term=cytoreductive+prostatectomy

Cytoreductive radical prostatectomy after chemohormonal therapy in patients with primary metastatic prostate cancer

- **38 patients with mHSPC**, cRP was performed after primary chemohormonal therapy (3-monthly LHRH-analogue + 6 cycles 3-weekly docetaxel 75mg/m^2) at two centers between September 2015 and December 2018.
- Overall, **10 (26%) patients had high volume and 28 (74%) patients had low volume disease** at diagnosis, according to CHAARTED definition.
- Median PSA decreased **from 65ng/ml (IQR 35-124.5) pre-chemo to 1ng/ml** (IQR 0.3-1.7) post-chemo.
- Within 30 days postoperatively Clavien-Dindo grade 3 complications were observed in 4 (11%) patients (3x lymphocele and 1x hydronephrosis).
- **Continence was reached in 92% of patients after six months.**
- Cytoreductive RP after chemohormonal therapy in selected patients is feasible with no major complications and good postoperative continence rates.

Under submission: Christa Babst[*,1], Thomas Amiel[*,1], Tobias Maurer[2,3], Sophie Knipper[2], Lukas Lunger[1], Robert Tauber[1], Margitta Retz[1], Kathleen Herkommer[1], Matthias Eiber[4], Gunhild v. Amsberg[2,5], Markus Graefen[2], Jürgen E. Gschwend[1], Thomas Steuber[#,2,3], Matthias M. Heck[#,1]

Cytoreductive radical prostatectomy after chemohormonal therapy in patients with primary metastatic prostate cancer

Table 2 - Continence and pad use		
Continence, n (%)	First month after surgery, n=31	After 6 months, n=25
0 pad	2 (6%)	15 (60%)
1 pad (for security)	25 (81%)	8 (32%)
1 wet pad (mild incontinence)	1 (3 %)	1 (4%)
2 wet pads (moderate incontinence)	3 (10 %)	1 (4%)
≥ 3 pads (severe incontinence)	0 (0%)	0 (0%)
	7 unknown	13 unknown

Under submission: Christa Babst[*,1], Thomas Amiel[*,1], Tobias Maurer[2,3], Sophie Knipper[2], Lukas Lunger[1], Robert Tauber[1], Margitta Retz[1], Kathleen Herkommer[1], Matthias Eiber[4], Gunhild v. Amsberg[2,5], Markus Graefen[2], Jürgen E. Gschwend[1], Thomas Steuber[#,2,3], Matthias M. Heck[#,1]

Fall (*1953): oligometastasiertes PC, Gleason 8

- 62-jähriger Unternehmer
- 08/2015 ED: ossär und lymphogen metastasiertes Adenokarzinom der Prostata cT3b, cN1, cM1, Gleason-Score 4+4=8, iPSA 15 ng/ml
- Subjektiv ausgeprägte Miktionsymptome mit Obstruktion und LUTS

Fall (*1953): oligometastasiertes PC, Gleason 8

Therapieverlauf:

- 10/15 - 02/16 Einleitung einer kombinierten Hormonchemotherapie mit 6 Zyklen Docetaxel (75 mg/m² KOF im 3-Wochenintervall) in Kombination mit LHRH-Analogon

Fall (*1953): oligometastasiertes PC, Gleason 8

Weiterer Therapieverlauf:

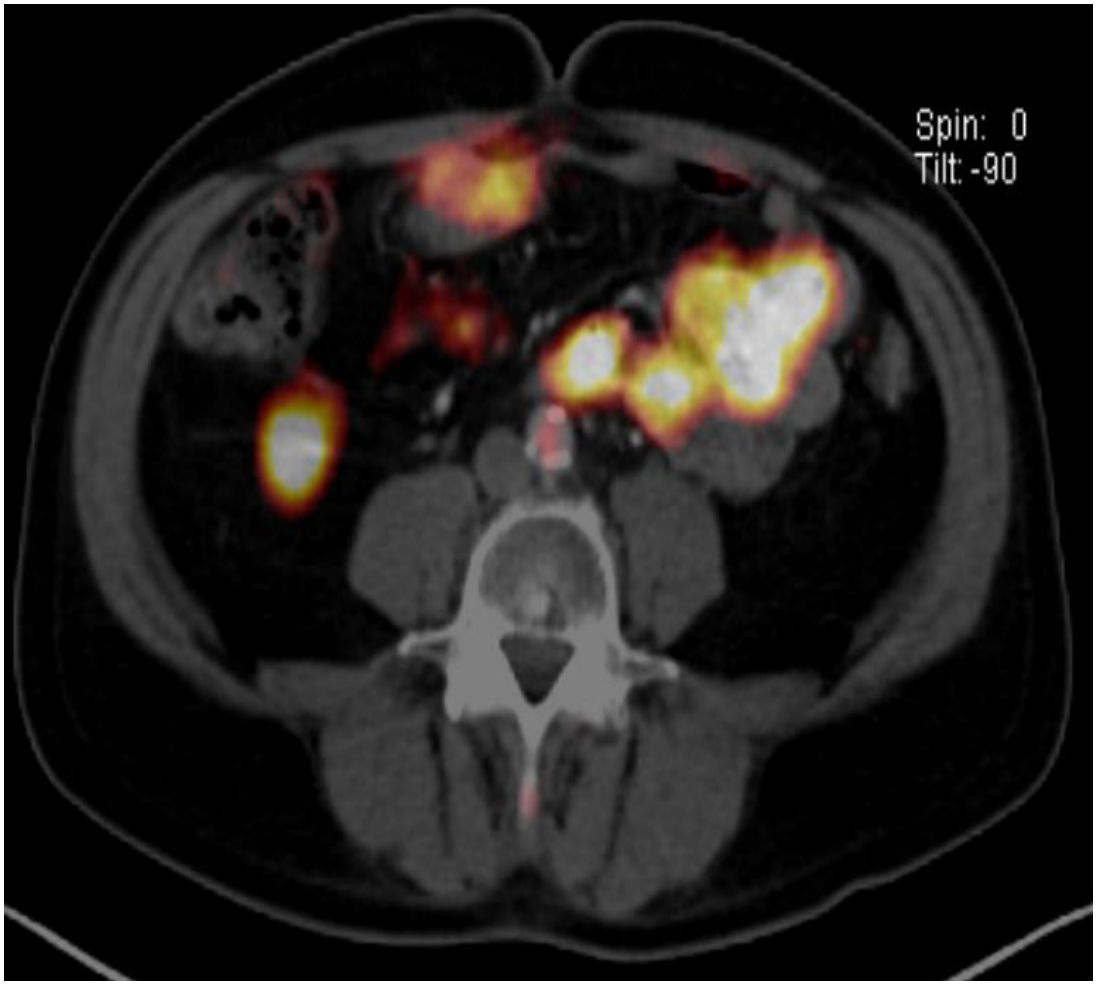
- 04/16 lokale Bestrahlung LWK 4 (35 Gy) in domo

- 05/16 radikale Prostatektomie & PLND:
  pT3b, pN1 (1/20), cM1 (ossär), Gleason-Score 4+4=8, R1

- Postoperativ keine lokalen Symptome, volle Kontinenz ohne jeglichen Bedarf für Pads

Fall (*1953): oligometastasiertes PC, Gleason 8

PSMA-PET-CT 16.11.2016

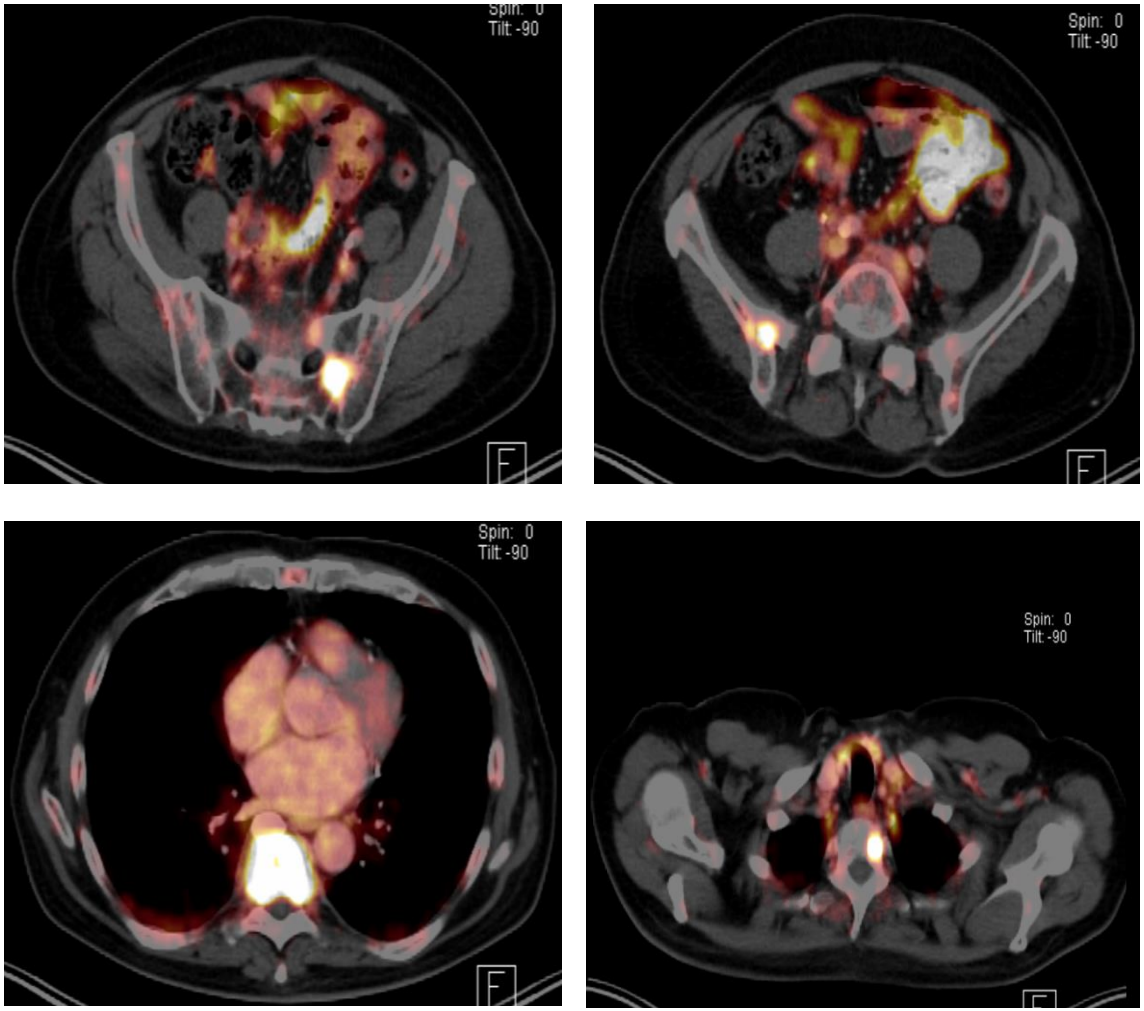


Fall (*1953): oligometastasiertes PC, Gleason 8

- 09/16 akutes Koronarsyndrom → 5-fach ACVB-Operation
- 04/17 Progression der lymphogen und ossären Metastasen unter intermittierender Hormontherapie mit LHRH-Analogon (nach Therapiepause seit 6/16 nach OP)
- 06/17 - 11/17 ADT-Re-Induktion mit 2 Injektionen
- 11/17 - 04/18 erneute Pause der ADT

Fall (*1953): oligometastasiertes PC, Gleason 8

PSMA-PET-CT 05.09.2018



Fall (*1953): oligometastasiertes PC, Gleason 8

- 08/18 unter ADT PSA-Anstieg auf 9,7 ng/ml
- 09/18 weitere Progression der lymphogenen und ossären Metastasen, Tumorinfiltration von BWK 8 im PET-CT
- Bei Schmerzsymptomatik: Schmerzmedikation und Strahlentherapie BWK 8 sowie Zugabe Abirateron/Prednison (ARV-7-Status negativ), weiterhin keine lokalen Probleme
- Aktuell: ECOG 0, schmerzfrei, PSA 2 ng/ml

Take home message: oligo-metastasiertes mHSPC

- Diagnostik der Wahl beim PSA-Rezidiv ist PSMA-PET-basiert
- Eine Salvage-Chirurgie (RGS) oder Radiochirurgie scheint im kurzfristigen Verlauf zumindest bei hormon-naiven Patienten effektiv zu sein
- Eine ADT ist in palliativer Intention dann immer noch möglich
- Eine lokale Tx-Strategie scheint auch beim primär oligo-metastasierten mHsPC effektiv zu sein
- Multimodale Konzepte (OP, ADT + X, Strahlentherapie) scheinen optimaler zu sein als alleinige Systemtherapie