

# **Local treatment of the primary tumour (surgery) in the metastatic situation**

29 – 31 August 2019, Basel / Switzerland

Disclosure:

Advisor/Speaker for Astellas, Amgen, Bayer, ProteoMedix, Sanofi

AND

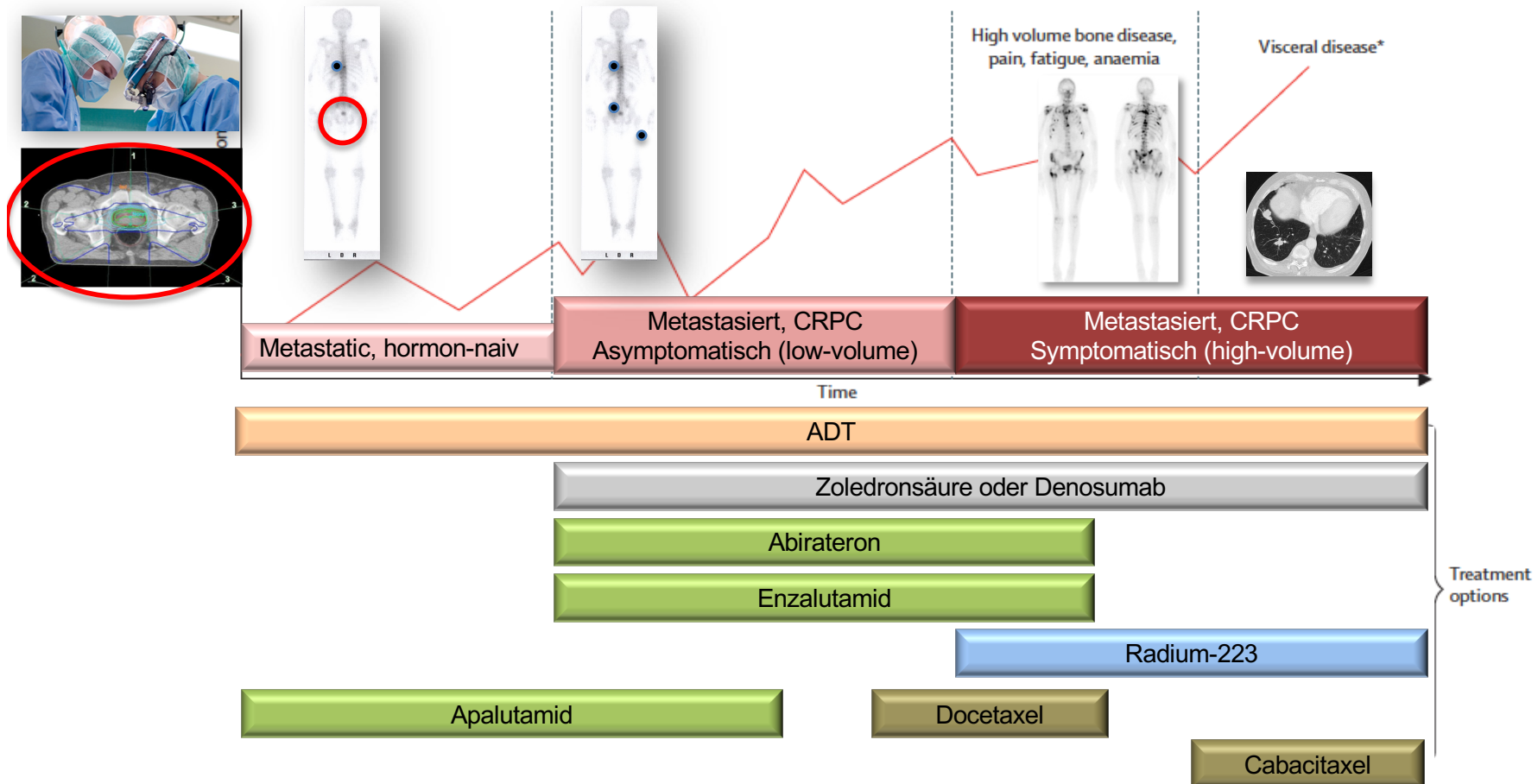
I am a Prostate Cancer Surgeon

### Treatment of the Primary...

- ...is considered standard of care in other malignancies (colo-rectal, Ovarial-Ca)
- ...may prevent local complications (Obstruction, Hematuria, Rectal stenosis...)
- ...may prevent further seeding from uncontrolled primary!?
- ...may destroy cells with potential genetic instability?

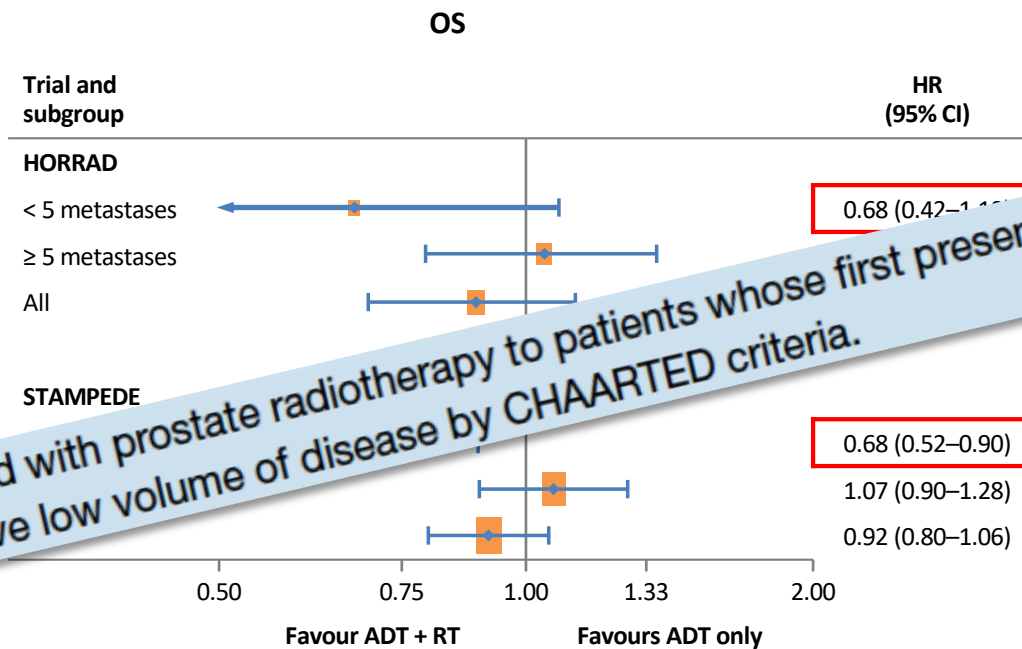
**Improves prognosis of  
men with HSMPC**

# Treatment landscape, metastatic prostate cancer





## OS benefits similar in similar patient subgroups in both the HORRAD and STAMPEDE trials



Benefit was observed in patients with low-volume disease, so ADT alone is no longer adequate

„It is possible that other forms of local treatment – such as radical prostatectomy- might also be effective.

However, radiotherapy might be effective via other mechanisms (eg, immune modulation), so the role of surgery remains unproven and needs to be tested in g-RAMPP trial and TomBone trial.“



Parker CC, et al. Lancet. 2018;392:2353-66.



„PS“ & Markus Graefen

**„Is cytoreductive Prostatectomy feasible?“**

### Platinum Priority – Prostate Cancer

Editorials on pp. 795–796 and on pp. 797–799 of this issue

### A Multi-institutional Analysis of Perioperative Outcomes in 106 Men Who Underwent Radical Prostatectomy for Distant Metastatic Prostate Cancer

Prasanna S...  
 Francesco M...  
 Christian G...  
 Tommy Nyb...

as Manka

- CRP is feasible, comparable to high risk PCa
- Clavien?
- QoL?

| Postoperative                          | n (%)     |
|--|-----------|
| 0–1 pads (mild incontinence)           | 38 (64.4) |
| 1–2 pads (moderate incontinence)       | 10 (17.0) |
| ≥3 pads (moderate/severe incontinence) | 11 (18.6) |

|                          | n (%)     |
|--------------------------|-----------|
| Reoperation              | 2 (1.9)   |
|                          | 4 (3.8)   |
|                          | 15 (14.2) |
|                          | 0 (0)     |
|                          | 0 (0)     |
|                          | 1 (0.9)   |
|                          | 0 (0)     |
|                          | 0 (0)     |
|                          | 0 (0)     |
|                          | 0 (0)     |
|                          | 1 (0.9)   |
|                          | 1 (0.9)   |
|                          | 0 (0)     |
|                          | 0 (0)     |
|                          | 0 (0)     |
|                          | 2 (1.9)   |
| Postoperative lymphocele | 9 (8.5)   |
| Anastomotic leak         | 7 (6.6)   |
| Anastomotic stricture    | 1 (0.9)   |
| Sepsis                   | 1 (0.9)   |
| Wound infection          | 5 (4.7)   |
| Wound dehiscence         | 0 (0)     |

- TromBone: 8% Clavien 3-4 (major) complication rate; similar to BAUS Averages for high-risk prostate cancer
- QoL better for surgery than for ADT alone

**„Does cytoreductive Prostatectomy prevent local complications?“**

## Rationale for cytoreductive Prostatectomy, local control



Local complications (up to 55%):

- bleeding
- obstruction
- retention
- hydronephrosis
- rectal stenosis
- pain

## Rationale for cytoreductive Prostatectomy, local control

### Primary treatment of the prostate improves local palliation in men who ultimately develop castrate-resistant prostate cancer

Andy C.M. Won, Howard Gurney\*, Gavin Marx†, Paul De Souza‡ and Manish I. Patel

Urological Cancer Outcomes Centre, Sydney Medical School, \*Department of Medical Oncology, Westmead Hospital, †Sydney Haematology & Oncology Clinic's Clinical Trials Unit, Sydney Adventist Hospital, University of Sydney, and ‡Department of Medical Oncology, Liverpool Hospital, University of Western Sydney, Sydney, NSW, Australia

- n= 263, 5 hospitals
- mCRPC, RRP (n= 45) vs. RT (n= 45) vs. Nil (n=173)
- local complication (20% vs. 47% vs. 55%; p = 0.001)
- obstruction (35%) and hydronephrosis (15%)

### RP+ADT vs. ADT in oligometastatic PCa

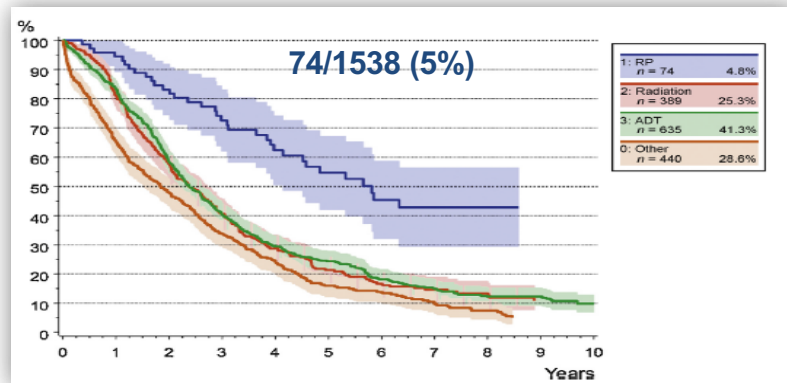
- 20% vs. 29% (p= 0.02)  
*Heidenreich A et al., J Urol 2015*
- 7% vs. 35% (p<0.05)  
*Steuber et al. Eur Urol Focus 2017*

**„Does cytoreductive Prostatectomy have an impact on OS?“**



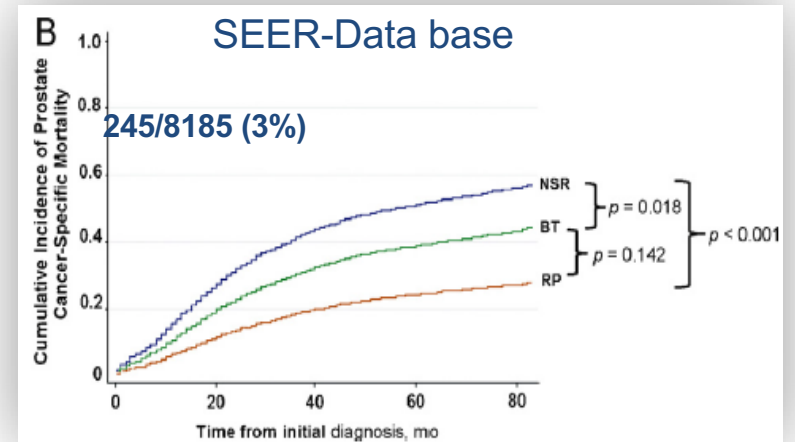
## Rationale for Prostatectomy in metastatic PCa, improved OS?

### Munich Tumor registry



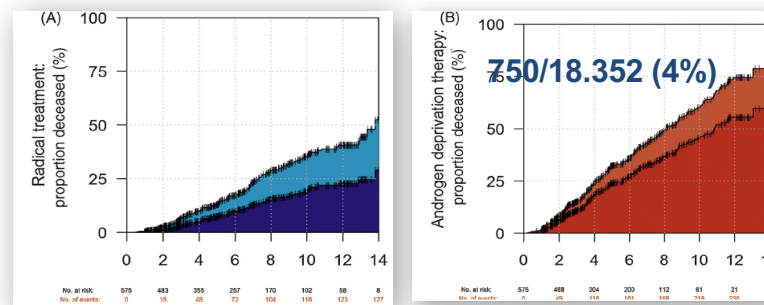
Gratzke et al., Eur Urol 2014

### SEER-Data base



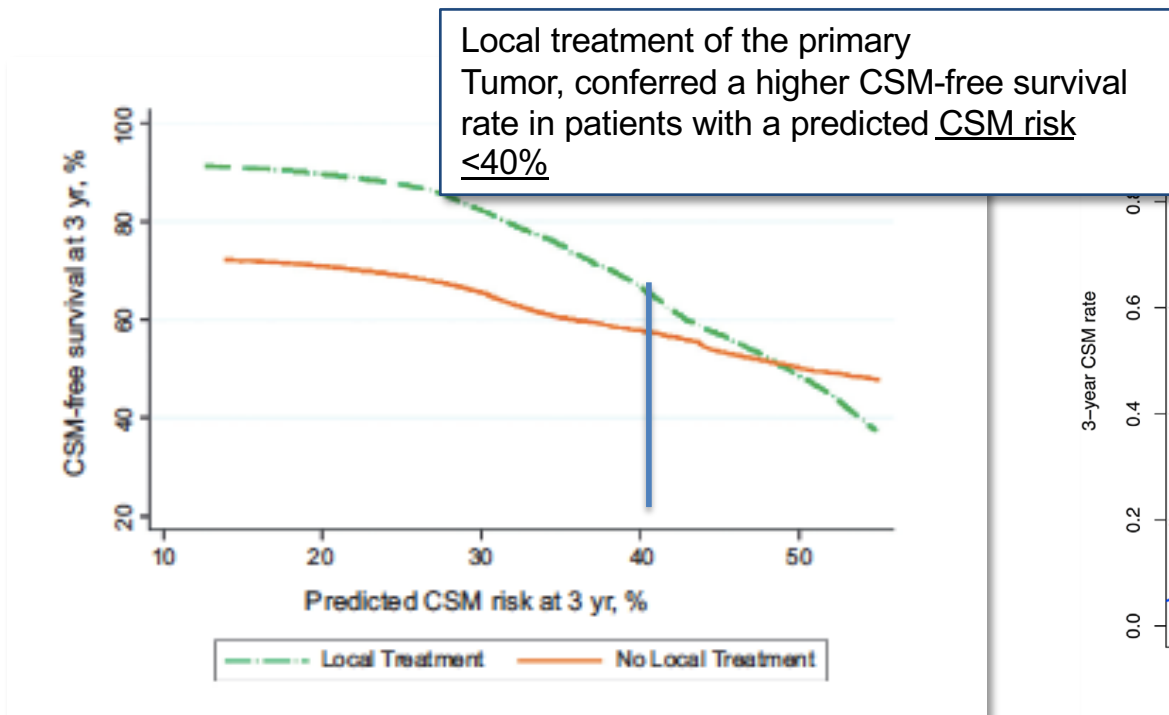
Culp et al., Eur Urol 2014

### Prostate Cancer Register Sweden (RP)

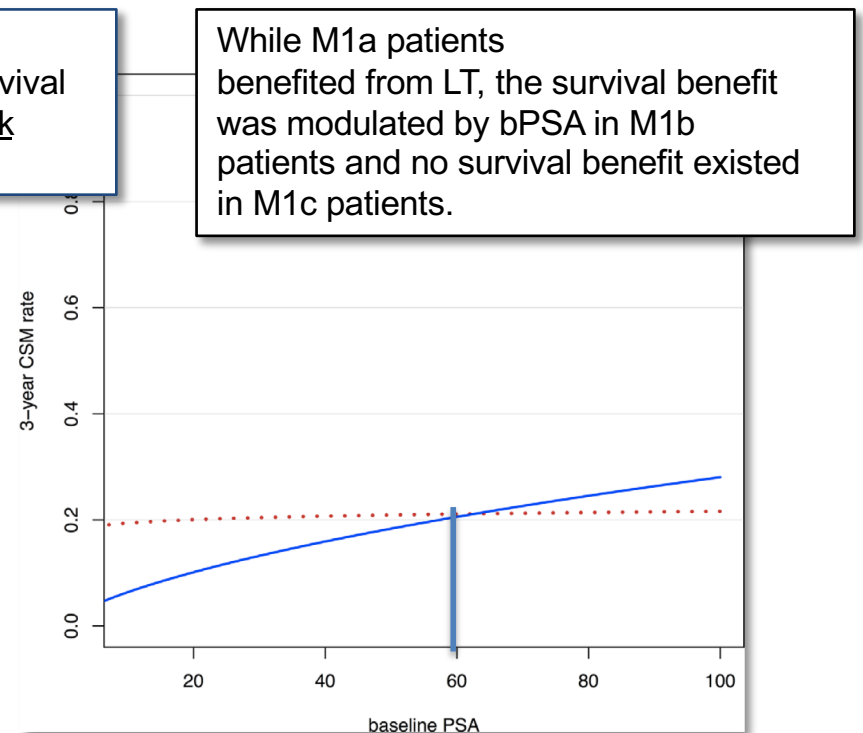


Sooriakumaran et al., Eur Urol 2017

## Radical prostatectomy in HSMPC...only for selected men?



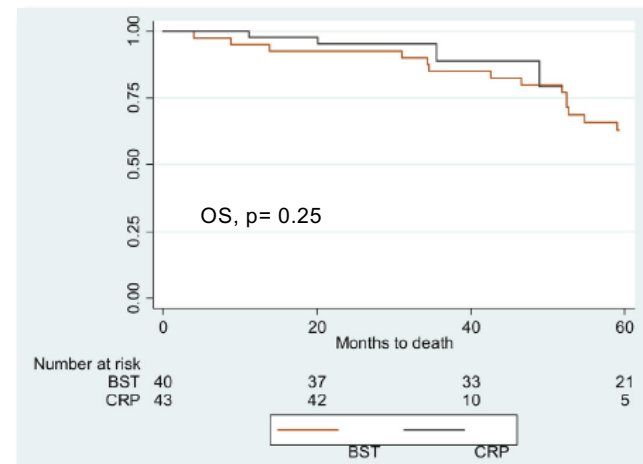
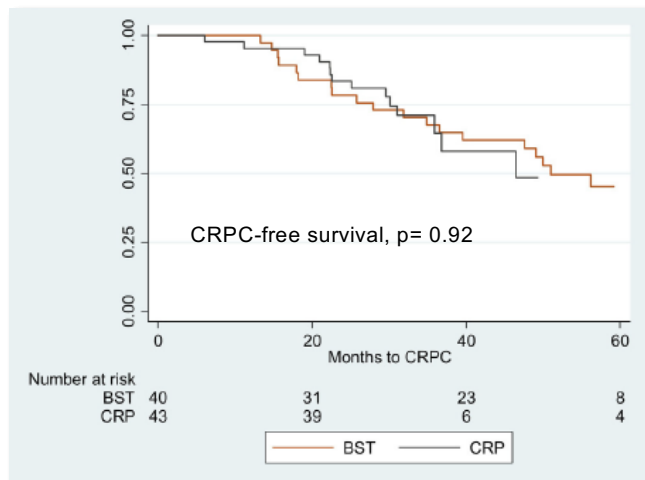
Fossati N. Eur Urol 2015



Pompe R. et al: Prostate 2018

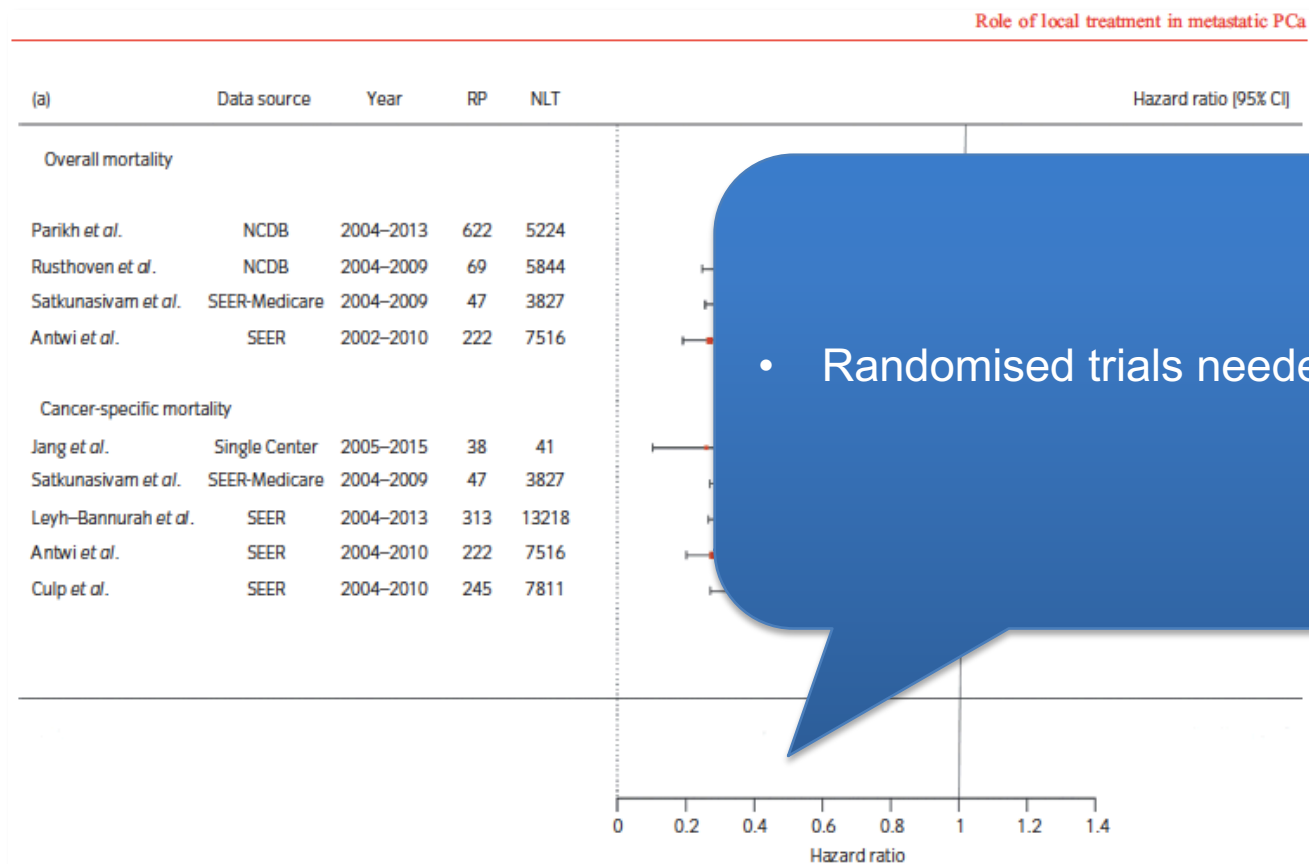
### Case control study, cytoreduktive RP/ADT vs. ADT,

- PSA <150 ng/ml
- M1b, low volume (CHAARTED), max cT3b
- ECOG-0/1 asymptomatic
- Martini-Klinik (n=43) vs. Copenhagen PCa-Register (n= 40)



Steuber et al, Eur Urol Focus 2017

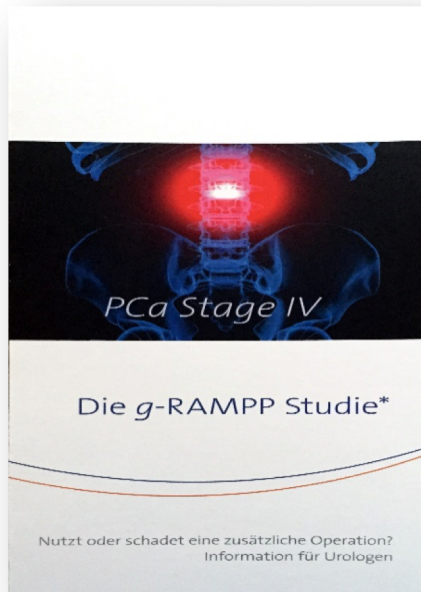
## OS-Benefit for radical Prostatectomy in retrospective studies



| Study                               | N    | Population                     | Treatment          | Endpoint         |
|-------------------------------------|------|--------------------------------|--------------------|------------------|
| M.D. Anderson Phase II, NCT01751438 | 120  | Any M1 on conventional imaging | BST+/- RP or EBRT  | PFS, QoL         |
| SWOG 1802 NCT03678025               | 1273 | De novo, all comers            | BST +/- RP or EBRT | OS               |
| TromBone ISRCTN1570486              | 50   | M1b, low volume                | BST +/- RP         | Feasibility, QoL |
| G-RAMPP NCT02454543                 | 452  | M1b, 1-5 mets                  | BST +/-            | CSS, OS, QoL     |

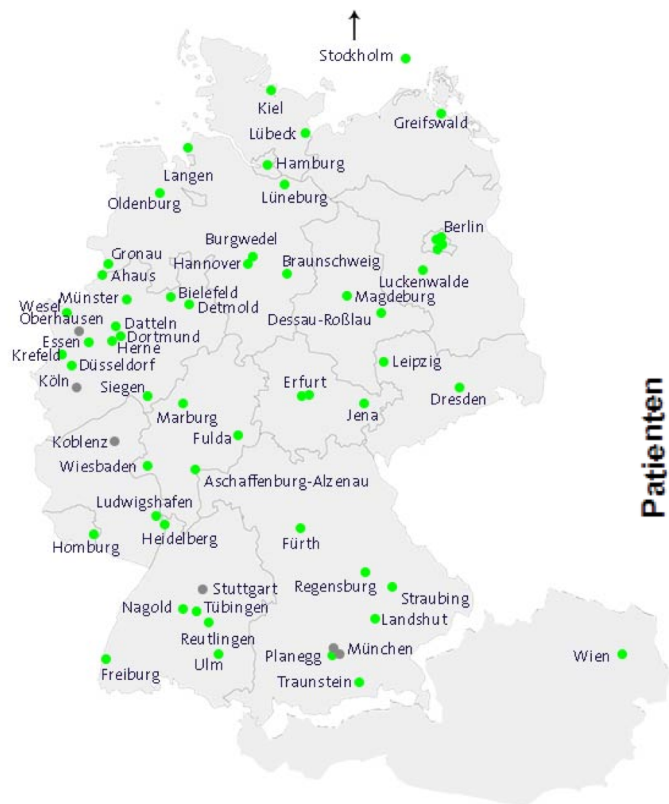
## g-RAMPP-Study

***Multicentric prospective randomised Study to evaluate the effect of best systemic treatment **with or without radical prostatectomy** in men with limited bone metastatic disease.***

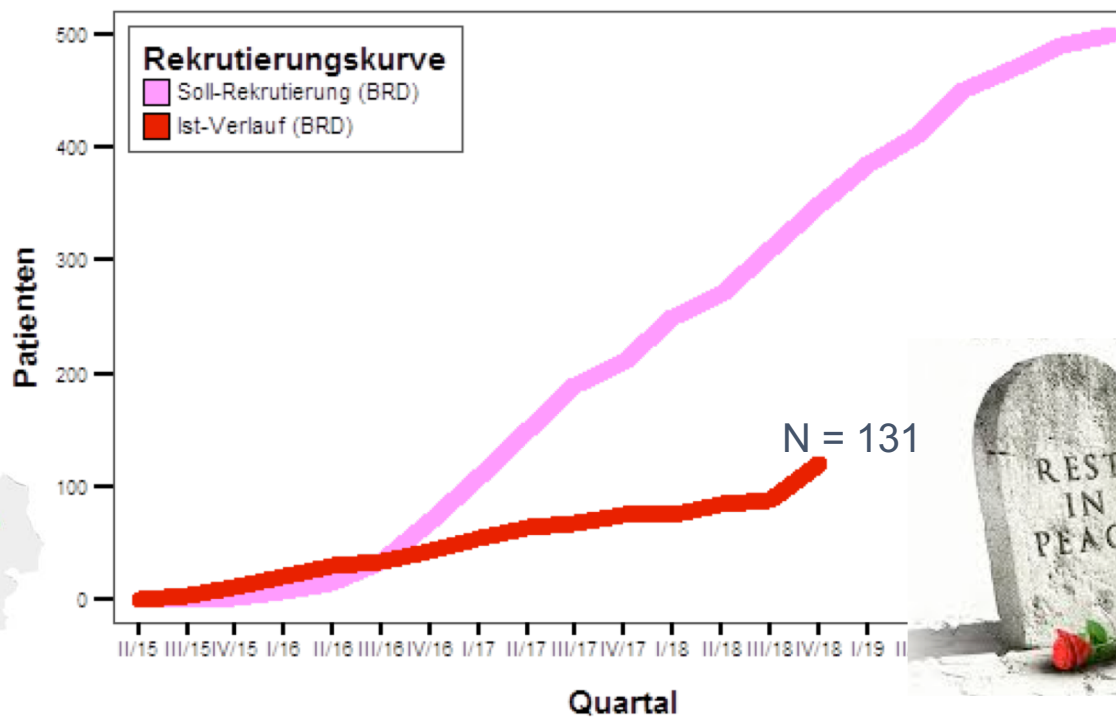


- M1b max 5 bone metastasis (Bone scan, CT/MRI)
- PSA at diagnosis < 200 ng/ml
- Asymptomatic
- Locally resectable (  $\leq$ cT3)
- ECOG Performance Status 0-1
- Age  $\geq$  18 to  $\leq$  75 years

# g-RAMPP recruitment



Verlauf AP 75/13 - G-RAMPP



- Cytoreductive Prostatectomy...
- ...is feasible, similar side effects compared to localized, high risk PCa, should be restricted to high volume surgeons
- ...prevents local control, may lead to improved QoL
- ...OS benefit visible in retrospective trials, mainly from large public health registries
- ...should be offered to men not suitable for EBRT (LUTS, irritative voiding symptoms etc. )
- ...look at data from gRAMPP and TromBone (131 + 51= 182)
- ...results from prospective trials awaited (SWOG, M.D. Anderson)



Treatment of the primary in HSMPC (low volume):

- Cytoreductive RP or EBRT better ?
- Does local treatment also works in the context of combined systemic treatment (ADT+Abi/Apa/Doce/Enza) (PEACE1 awaited)

# Radiotherapy as a Standard of Care

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## **ASCO 2019:**

*“A multimodal approach to patients with oligometastatic disease is needed, with evidence for surgery, radiotherapy, and systemic therapy, alone or in combination, improving patient outcomes”*



## Hamburg new concert hall, „Elbphilharmonie“



Thank you!!