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# **Treatment of Oligometastases in Genitourinary Malignancies**

11.12.2015| Univ.-Prof. Dr. med. Axel Heidenreich



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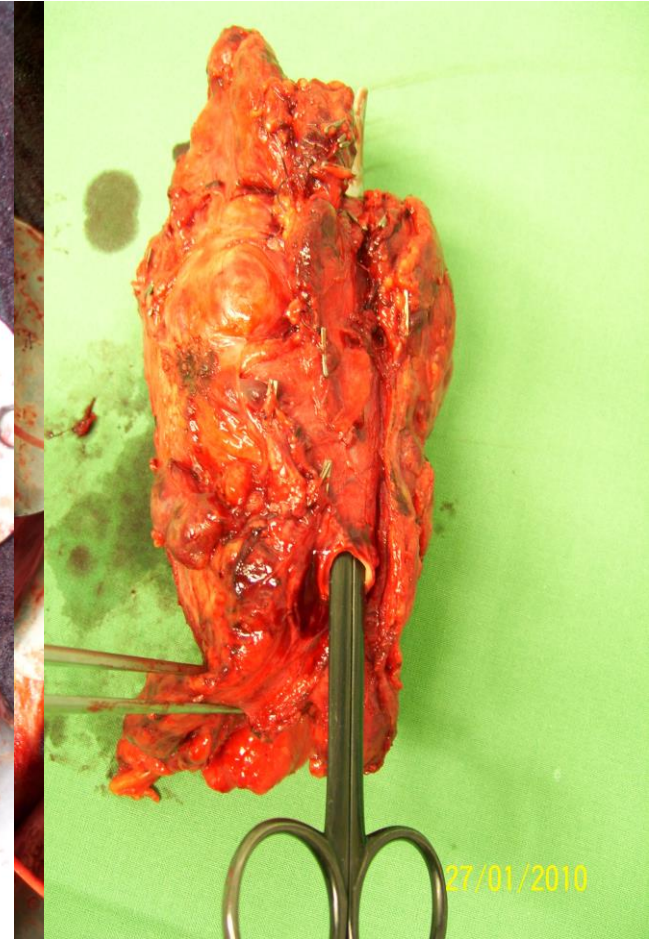
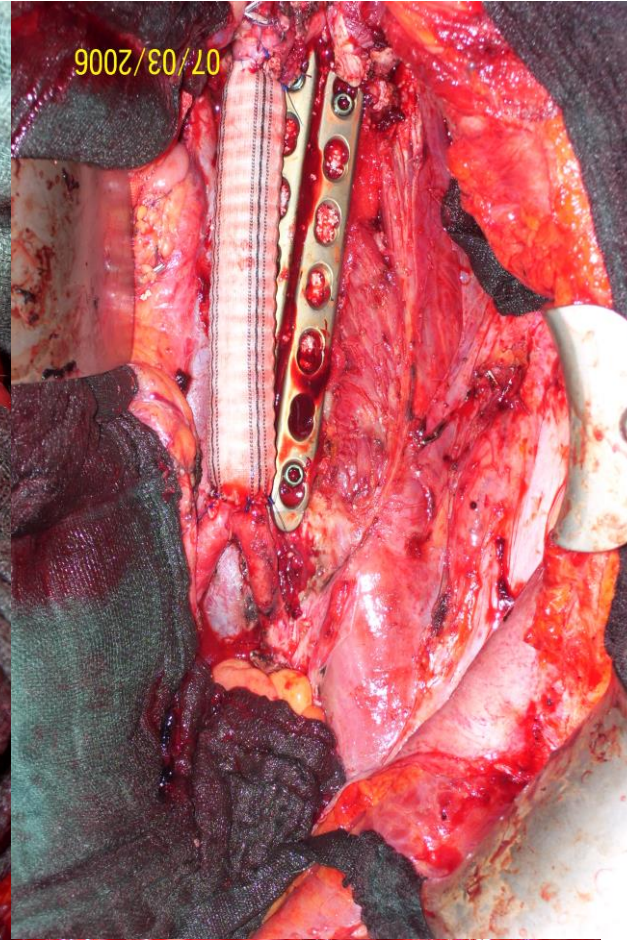
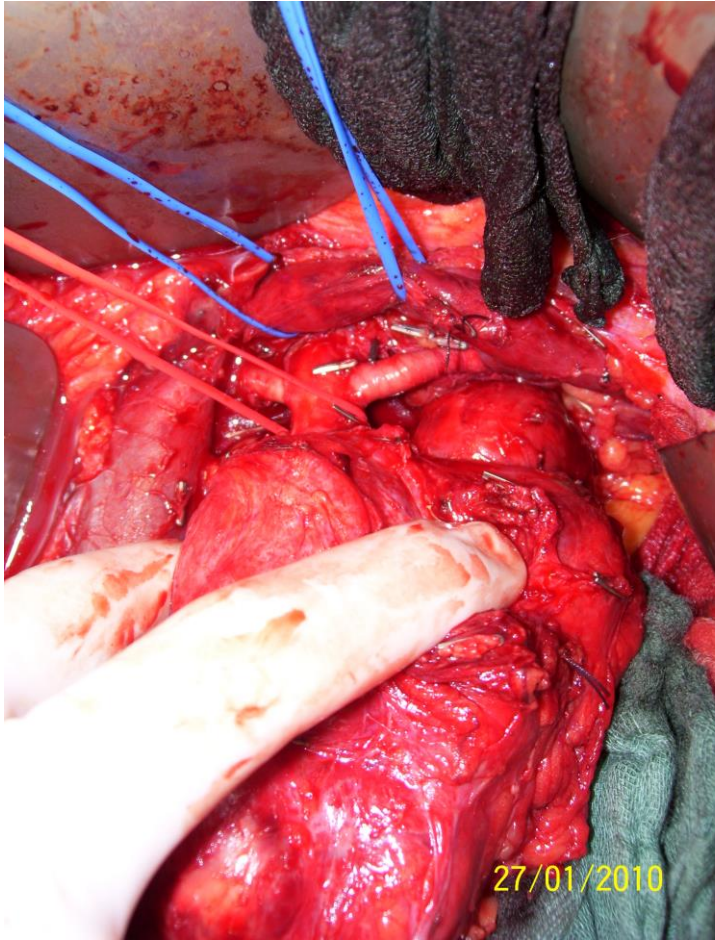
# Greetings from Cologne





# Local management of oligometastases









- definition of oligometastases
- goals of treatment
- treatment options in
  - renal cell cancer
  - bladder cancer
  - prostate cancer



# Oligometastases - Definition

- introduced by Hellmann & Weichselbaum in 1995
- oligometastatic state as an intermediate state of tumour spread with limited metastatic capacity
  - locoregional spread with better prognosis than systemic spread
  - low volume metastatic disease with better prognosis
  - metastasis-directed therapy might be effective



## Prerequisites for successful local treatment

1. accurate imaging to detect early metastases
2. complete eradication of all oligometastatic sites
3. acceptable toxicity



## Goals of Treatment

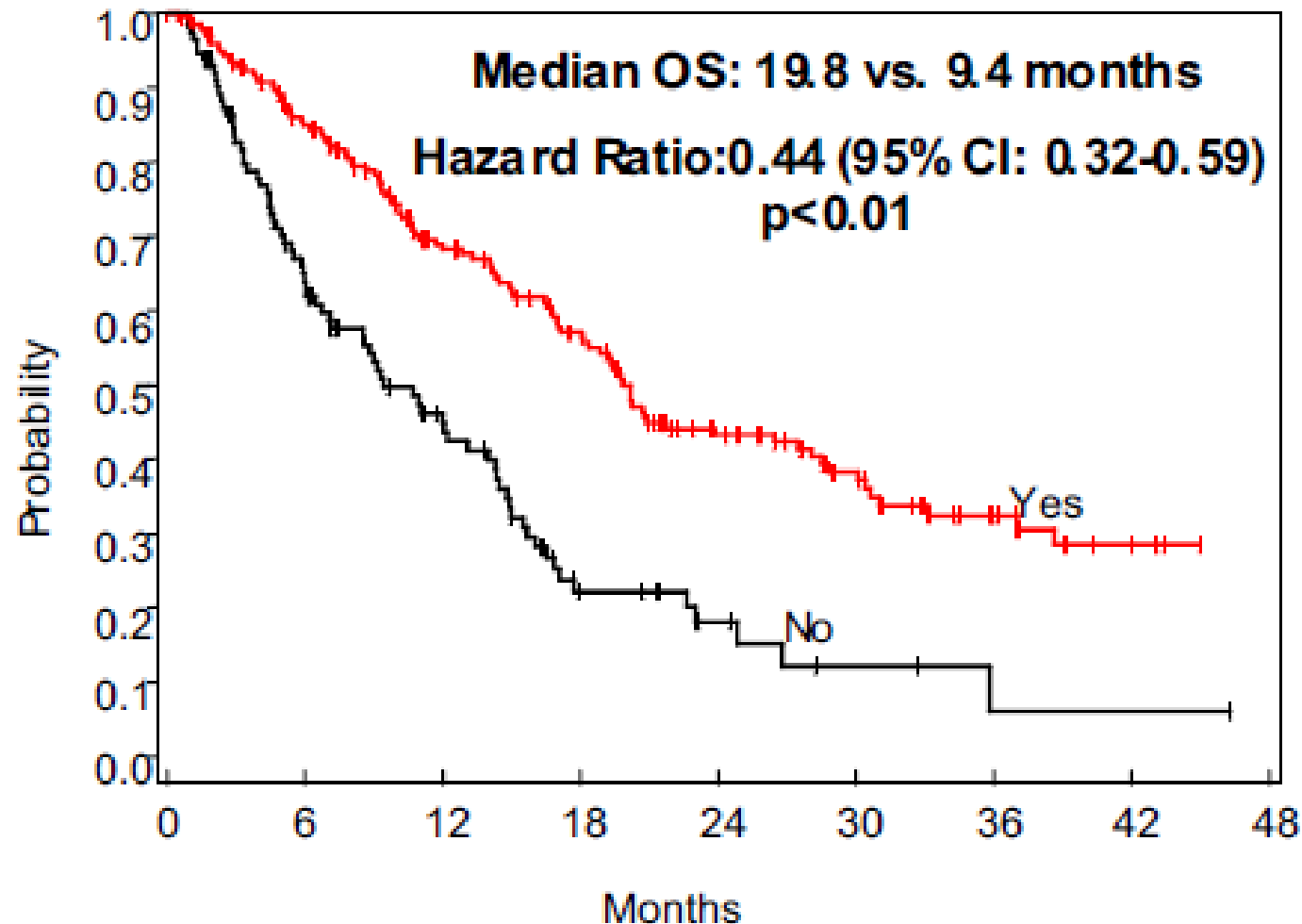
1. improvement of cancer-specific survival
2. improvement of symptom-free survival
3. prolongation until time for systemic treatment





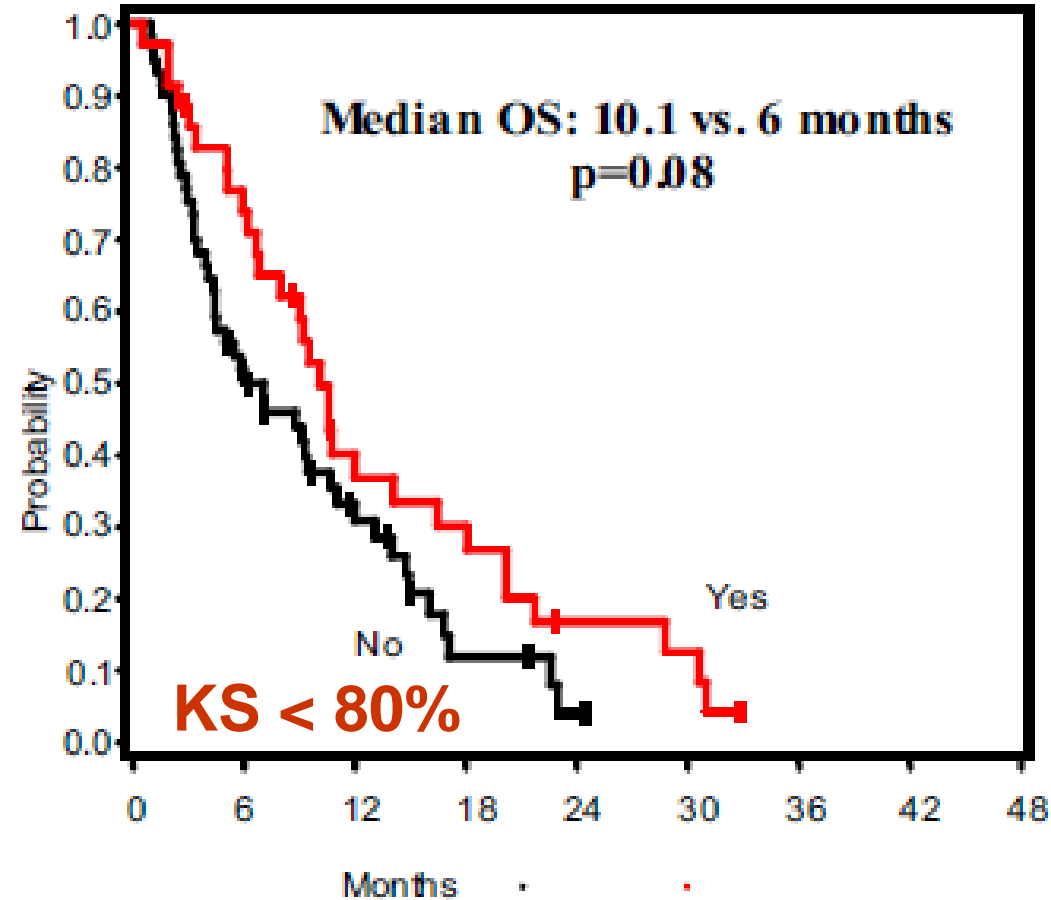
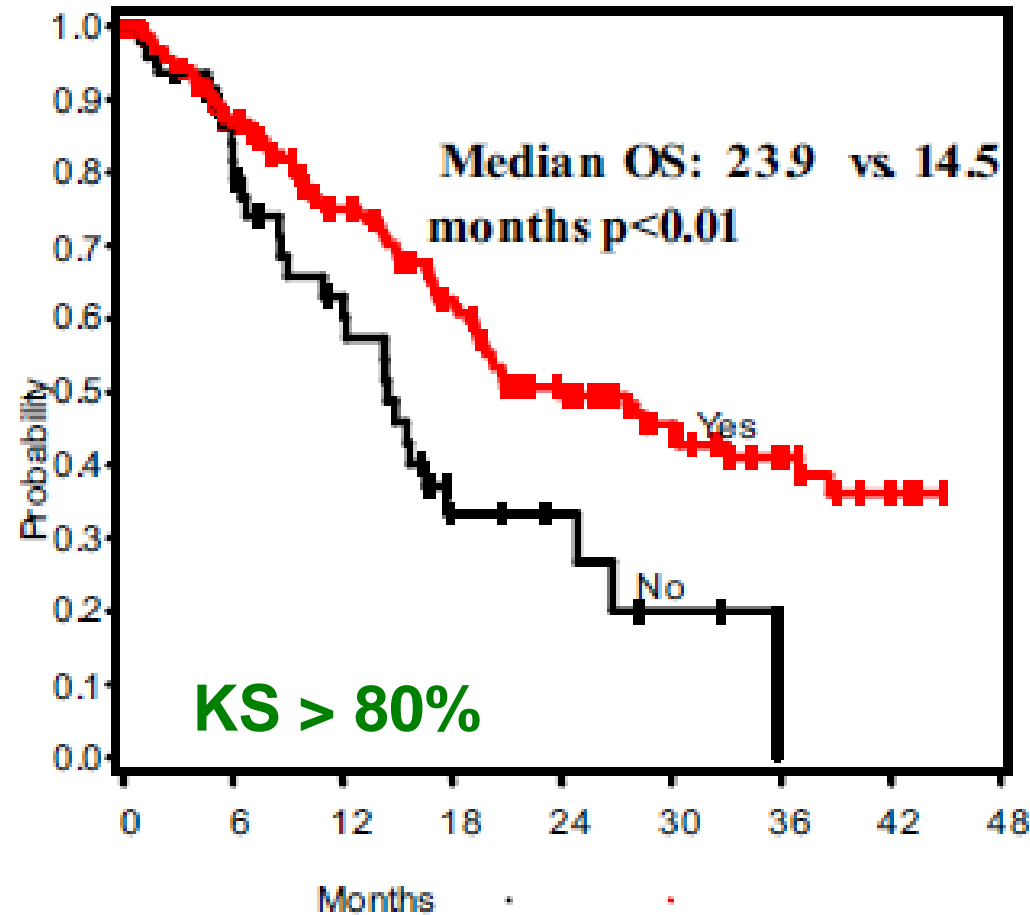
- definition of oligometastases
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- **treatment options in**
  - **renal cell cancer**
  - bladder cancer
  - prostate cancer

# Oligometastases – renal cell cancer: what about the primary?





# Oligometastases – renal cell cancer: what about the primary?





# Oligometastases – renal cell cancer

- surgical resection of the primary and metastatic deposits is the only intervention with long-term cure

	curative resection	non-curative resection	nonsurgical therapy
n	148	70	67
5-year OS	44%	14%	11%

pts with lung metastases have the best outcome



- surgical resection of the primary and metastatic deposits is the only intervention with long-term cure
- **Lung studies<sup>1</sup>:** n = 152  
36.3 vs 30.4 vs 18.0 months ( $p < 0.05$ )
- **Liver studies<sup>2</sup>:** n = 88 142  
vs 27 months ( $p = 0.003$ )
- **Pancreas studies<sup>3</sup>:** n = 36  
88% vs 47% 5-year OS

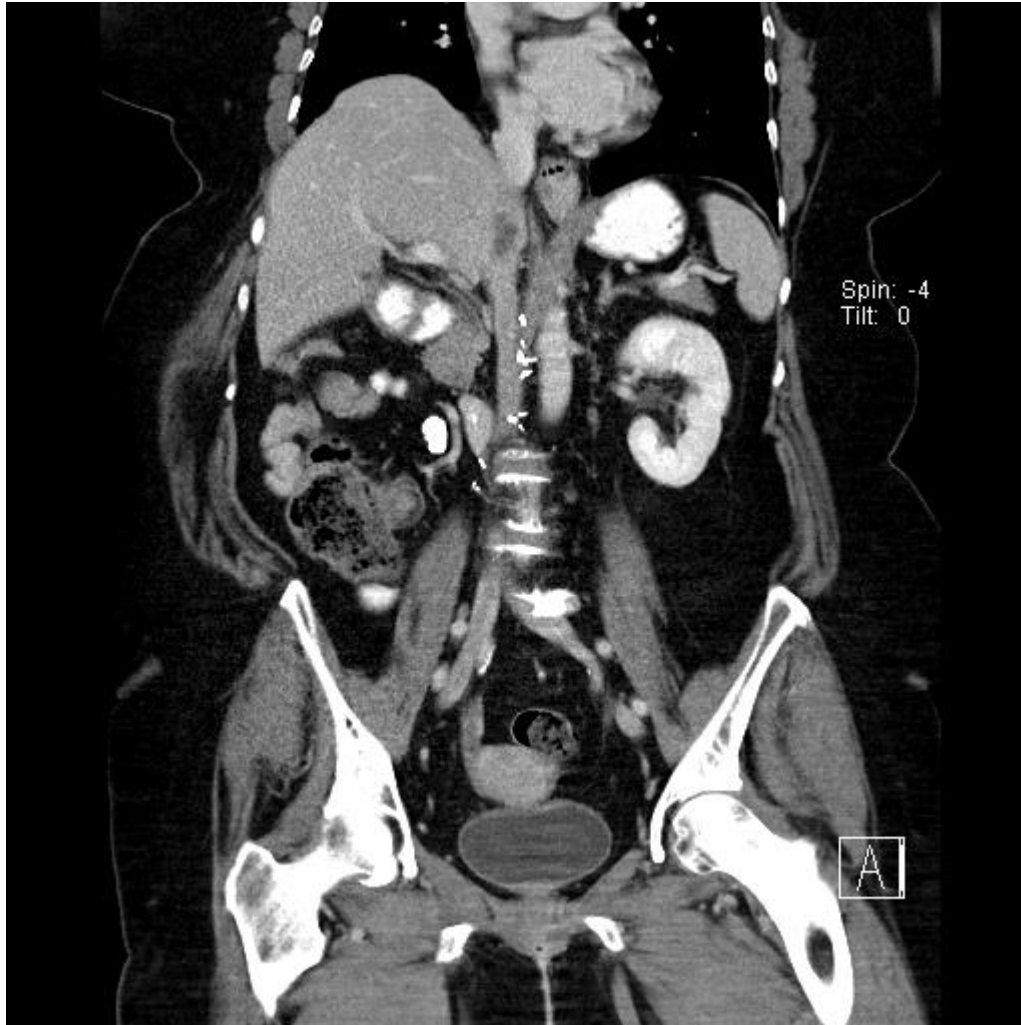
<sup>1</sup>Amiraliev A et al., Interact Cardiovasc Throac Surg 2012

<sup>2</sup>Staehler MD et al., World J Urol 2010

<sup>3</sup>Zerbi A et al., Ann Surg Oncol 2008



# Oligometastases – renal cell cancer





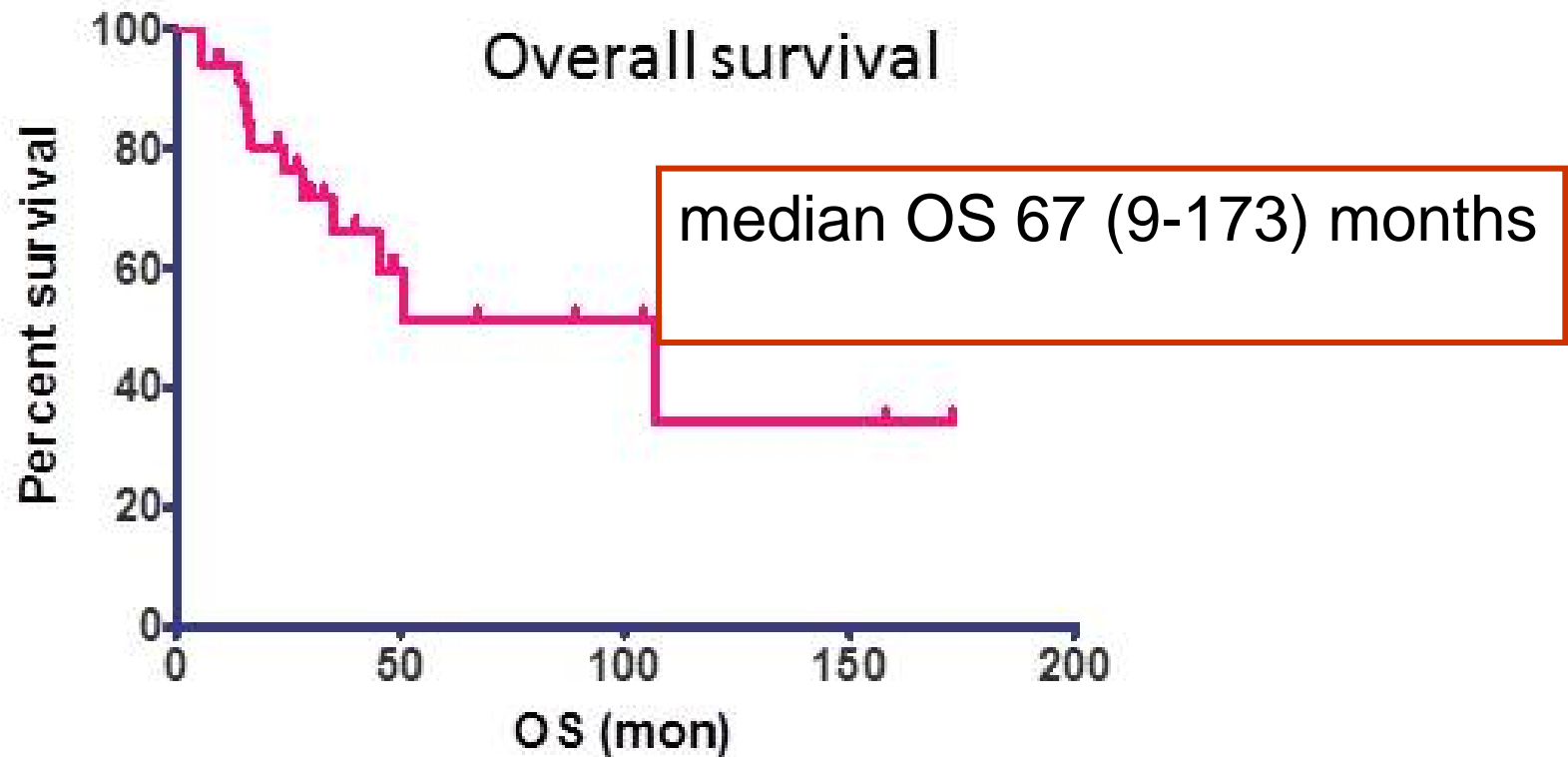


# Oligometastases – renal cell cancer

Patient	nephrectomy	Time to relapse, yrs	Thrombus level	Surgical approach	Vascular replacement	complications	Follow up (years)
F.H. * '40	right	7	III	thorako-abdominal	Resection if IVC, prothesis	none	3
A.L. * '32	right	9	II + apposition thrombus	abdominal	suture	none	1
G.V. * '39	right	1	IV	thorako-abdominal	suture	none	8
E.H. * '39	Right, caval thrombus	2	III	thorako-abdominal	suture	hernia	5
V.B. * '42	right	1	II + apposition thrombus	thorako-abdominal	suture	splenectomy	0,5

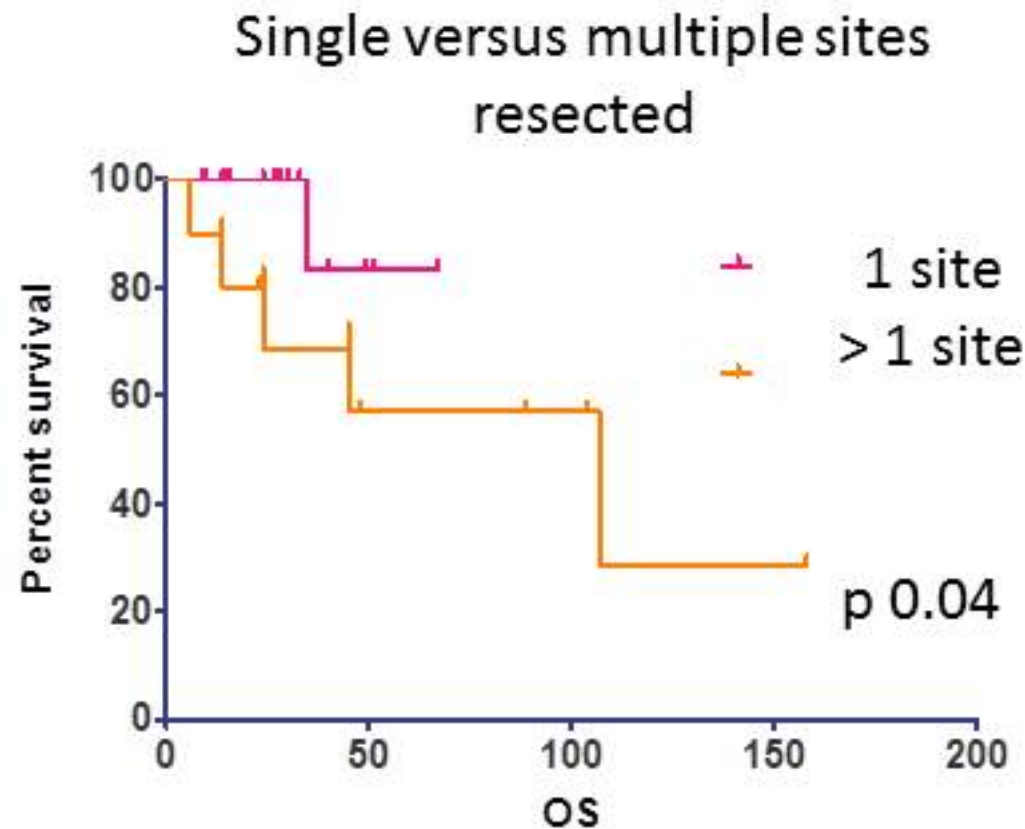


# Resection of metastasis and local recurrences of renal cell carcinoma after presurgical targeted therapy: Probability of complete local control and outcome.





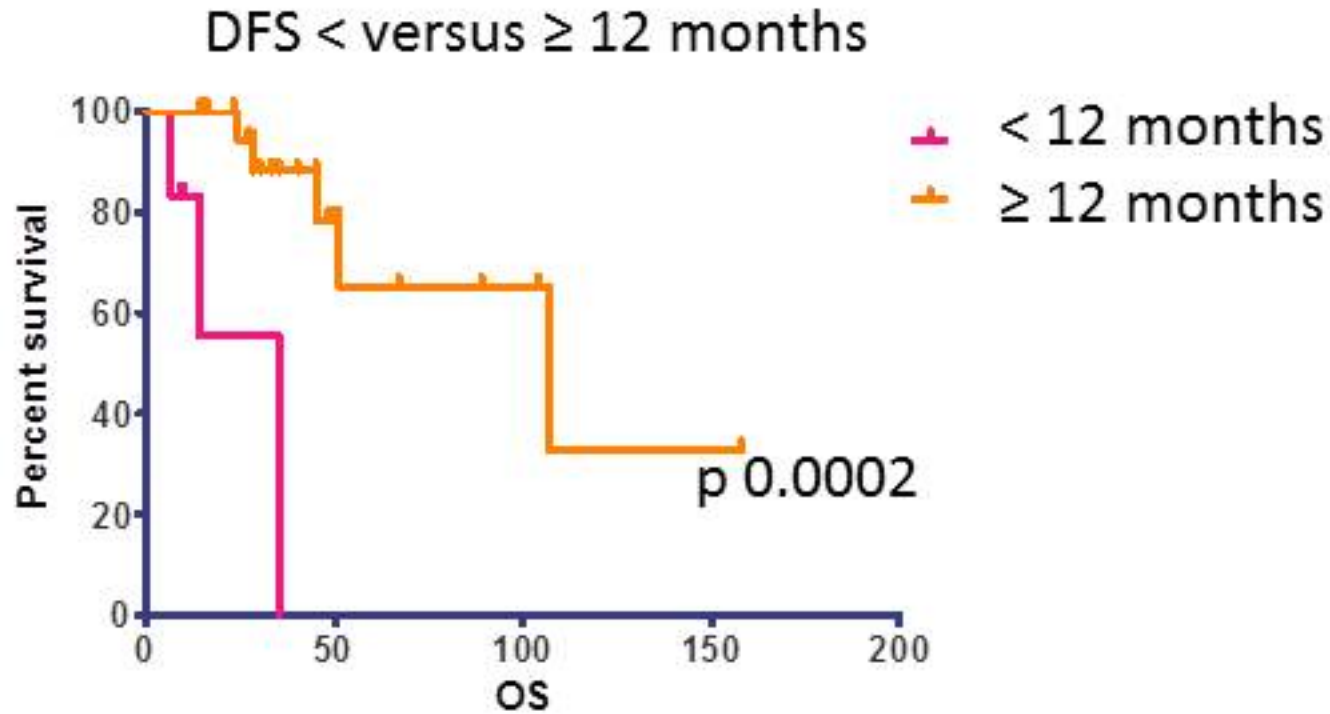
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










# Resection of metastasis and local recurrences of renal cell carcinoma after presurgical targeted therapy: Probability of complete local control and outcome.

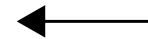


# Oligometastases – renal cell cancer

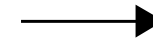
Study or subgroup	Log [hazard ratio]	SE		Hazard ratio (95% CI)*
Alt (2011) <sup>12</sup>	0.9594	0.1379		2.61 (1.99–3.42)
Pretalia (2010) <sup>†24</sup>	0.5365	0.2306		1.71 (1.09–2.69)
Staehler (2010) <sup>25</sup>	0.802	0.3825		2.23 (1.05–4.72)
Staehler (2009) <sup>26</sup>	0.7608	0.201		2.14 (1.44–3.17)
Eggerer (2008) <sup>27</sup>	0.9933	0.2606		2.70 (1.62–4.50)
Kwak (2007) <sup>30</sup>	0.9439	0.3826		2.57 (1.21–5.44)
Lee (2006) <sup>†32</sup>	1.2442	0.5171		3.47 (1.26–9.56)

Heterogeneity:  $\tau^2=0.00$ ;  $\chi^2=3.62$ ;  $df=6$ ;  $p=0.73$ ;  $I^2=0\%$

0.1 1 10 100



Favours no or  
incomplete  
metastasectomy



Favours  
metastasectomy

OS/CSS 40.8 versus 14.8 months



# Oligometastases – renal cell cancer

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Masking of participants and personnel (performance bias)	Masking of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Age	Sex	Fuhrman grade	Size or volume of metastases	Number of metastases	Previous treatment	Performance status	Different sites treated	Tumour histology
Alt et al (2011) <sup>12</sup>	-	-	-	-	?	?	-	+	+	-	-	+	-	+	-	+
Amiraliev et al (2012) <sup>23</sup>	-	-	-	-	?	?	-	-	-	-	-	-	-	-	-	-
Brinkmann et al (2007) <sup>29</sup>	-	-	-	-	-	?	-	+	+	-	-	+	-	+	-	+
Eggenger et al (2008) <sup>27</sup>	-	-	-	-	?	?	-	-	-	-	-	-	-	+	-	-
Fokas et al (2010) <sup>36</sup>	-	-	-	-	?	-	-	-	+	-	-	-	-	-	-	-
Fuchs et al (2005) <sup>35</sup>	-	-	-	-	-	?	-	-	-	-	-	-	-	-	-	-
Hunter et al (2012) <sup>34</sup>	-	-	-	-	?	?	-	+	+	-	-	-	-	+	-	-
Ikushima et al (2000) <sup>37</sup>	-	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-
Kwak et al (2007) <sup>30</sup>	-	-	-	-	?	?	-	+	+	+	-	+	+	+	-	+
Lee et al (2006) <sup>32</sup>	-	-	-	-	?	?	-	+	+	-	-	+	+	-	-	-
Pretalia et al (2010) <sup>24</sup>	-	-	-	-	?	?	-	-	-	-	-	-	+	-	+	-
Russo et al (2007) <sup>31</sup>	-	-	-	-	?	-	-	+	-	-	-	-	-	-	-	+
Staehler et al (2009) <sup>26</sup>	-	-	-	-	?	?	-	-	-	-	-	-	-	-	-	-
Staehler et al (2010) <sup>25</sup>	-	-	-	-	?	?	-	-	+	+	-	+	-	+	+	-
Zelevsky et al (2012) <sup>33</sup>	-	-	-	-	?	-	-	-	-	-	-	-	-	-	-	-
Zerbi et al (2008) <sup>28</sup>	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-

**high probability of bias and confounding**

- no prospective studies
- no randomized trials
- high risk of selective reporting





## Best candidates for metastasectomy

- single site of first recurrence
- solitary site of first metastases
- curative resection of first metastases
- long disease-free interval
- metachronous presentation



- definition of oligometastases
- goals of treatment
- **treatment options in**
  - renal cell cancer
  - **bladder cancer**
  - prostate cancer



# Oligometastases – bladder cancer: what about the primary?

**No data are available with regard to  
cytoreductive cystectomy**



# Surgery for metastatic urothelial carcinoma with curative intent: the German Experience (AUO AB 30/05). Eur Urol 2009; 55: 1293 - 1299

Jan Lehmann<sup>a,p,\*</sup>, Henrik Suttman<sup>p,q</sup>, Peter Albers<sup>b,c,k</sup>, Björn Volkmer<sup>d</sup>,  
 Jürgen E. Gschwend<sup>d,n</sup>, Guido Fechner<sup>b</sup>, Martin Spahn<sup>e</sup>, Axel Heidenreich<sup>f</sup>, Axel Odenthal<sup>g</sup>,  
 Christoph Seif<sup>h</sup>, Nils Nürnberg<sup>a,h</sup>, Christian Wülfing<sup>i</sup>, Christoph Greb<sup>j</sup>, Tilmann Kälble<sup>j</sup>,  
 Marc-Oliver Grimm<sup>k</sup>, Claus Friedrich Fieseler<sup>l</sup>, Susanne Krege<sup>m</sup>, Margitta Retz<sup>n</sup>,  
 Heiner Schulte-Baukloh<sup>o</sup>, Martin Gerber<sup>p</sup>, Markus Hack<sup>p</sup>, Jörn Kamradt<sup>p</sup>, Michael Stöckle<sup>h,p</sup>

	No. of Patients	%
Total	44	100
Men	29	65.9
Women	15	34.1
Primary tumor site		
Bladder	35	79.5
Upper urinary tract	9	20.5
Sequence of treatment for metastases		
Surgery only	9	20.5
Surgery + chemotherapy	13	29.5
Chemotherapy + surgery	16	36.4
Chemotherapy + surgery + chemotherapy	6	13.6
Metastatic sites resected		
Retroperitoneal lymph nodes (above aortic bifurcation)	25	56.8
Distant lymph nodes	5	11.3
Lung	8	18.2
Bone	2	4.5
Adrenal gland	1	2.3
Brain	1	2.3
Small intestine	1	2.3
Subcutaneous	1	2.3

- all patients underwent resection at one site only following chemotherapy
- only patients with complete resection of metastases were included
- median time from primary tumour to **detection** of metastases **15 months**
- median time from primary tumor and **resection** of metastases **18 months**





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	Median, mo (95% CI)	SE, %	2-yr survival rate, %	5-yr and 10-yr survival rate, %
Overall survival				
From diagnosis of metastases	34.7 (17.0–52.4)	9.0	60.9	28.0
From resection of metastases	27.2 (6.8–47.6)	10.4	50.9	27.7
Cancer-specific survival				
From diagnosis of metastases	38.2 (13.6–62.9)	12.6	64.2	33.8
From resection of metastases	34.3 (9.3–59.3)	12.6	53.7	32.5
Progression-free survival				
From diagnosis of metastases	19.0 (14.4–23.5)	2.3	42.0	23.6
From resection of metastases	14.6 (6.6–22.5)	4.0	35.6	24.0

- no predictive or prognostic risk could be identified  
 => all metastases at one organ site and completely resected  
 => might represent the most important risk factor already

# Outcome of metastasectomy for urothelial carcinoma: a multiinstitutional retrospective study in Japan.

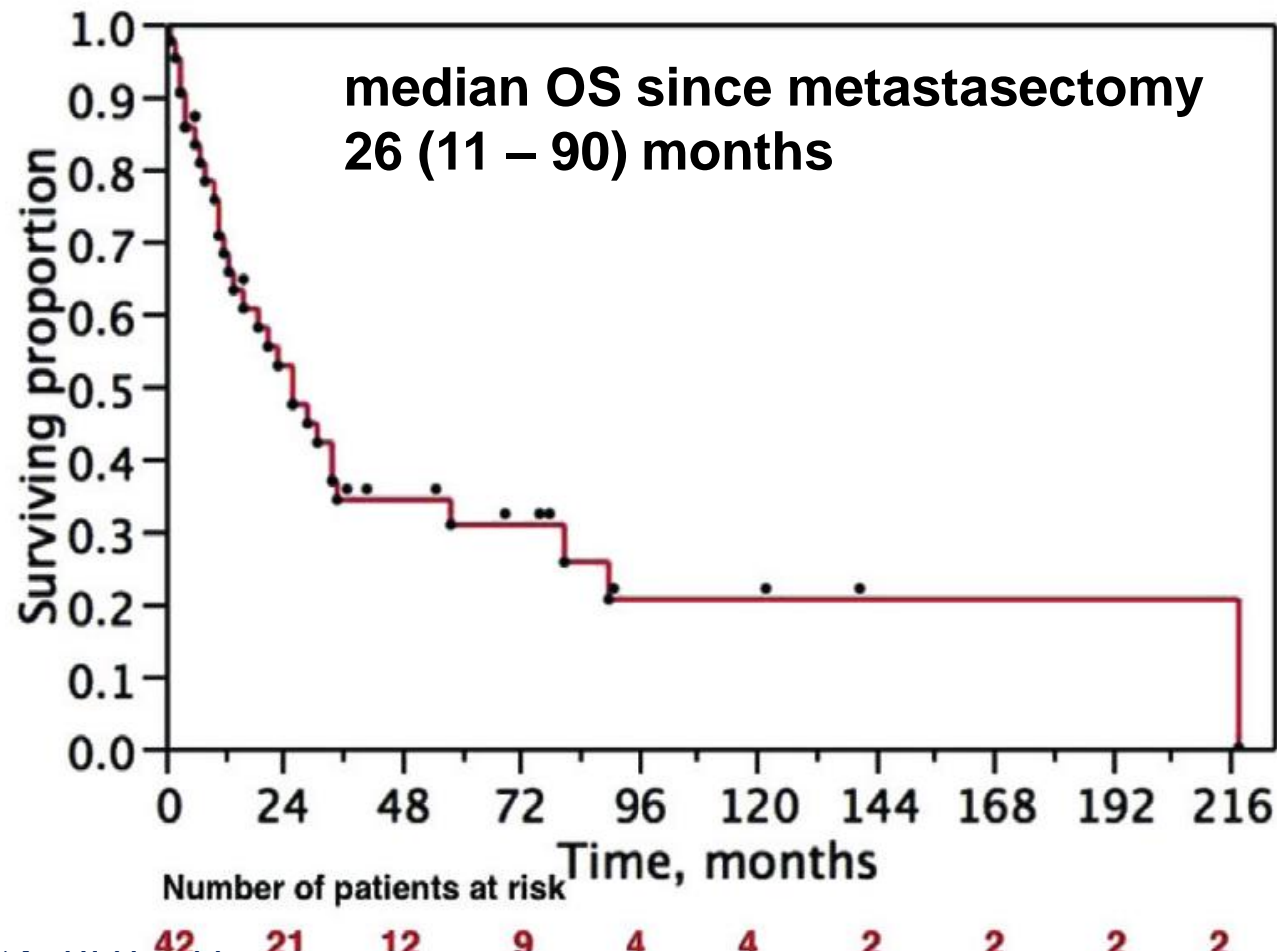
Abe T et al., J Urol 2014; 191: 932 - 936

**Table 1.** *Patient and metastasectomy characteristics*

Median age (range)	67.5 (36—80)
No. male	29
No. female	13
No. metastatic site:*	
Regional LN recurrence	8
Distant LNs	12
Lung	14
Bone	1
Liver	2
Adrenal gland	1
Local recurrence	5
No. treatment course:	
Metastasectomy after chemotherapy	34
Chemotherapy after metastasectomy	7
Metastasectomy only	1
Median mos followup (range):	
Overall	28 (3—218)
After metastasectomy	22 (1—218)

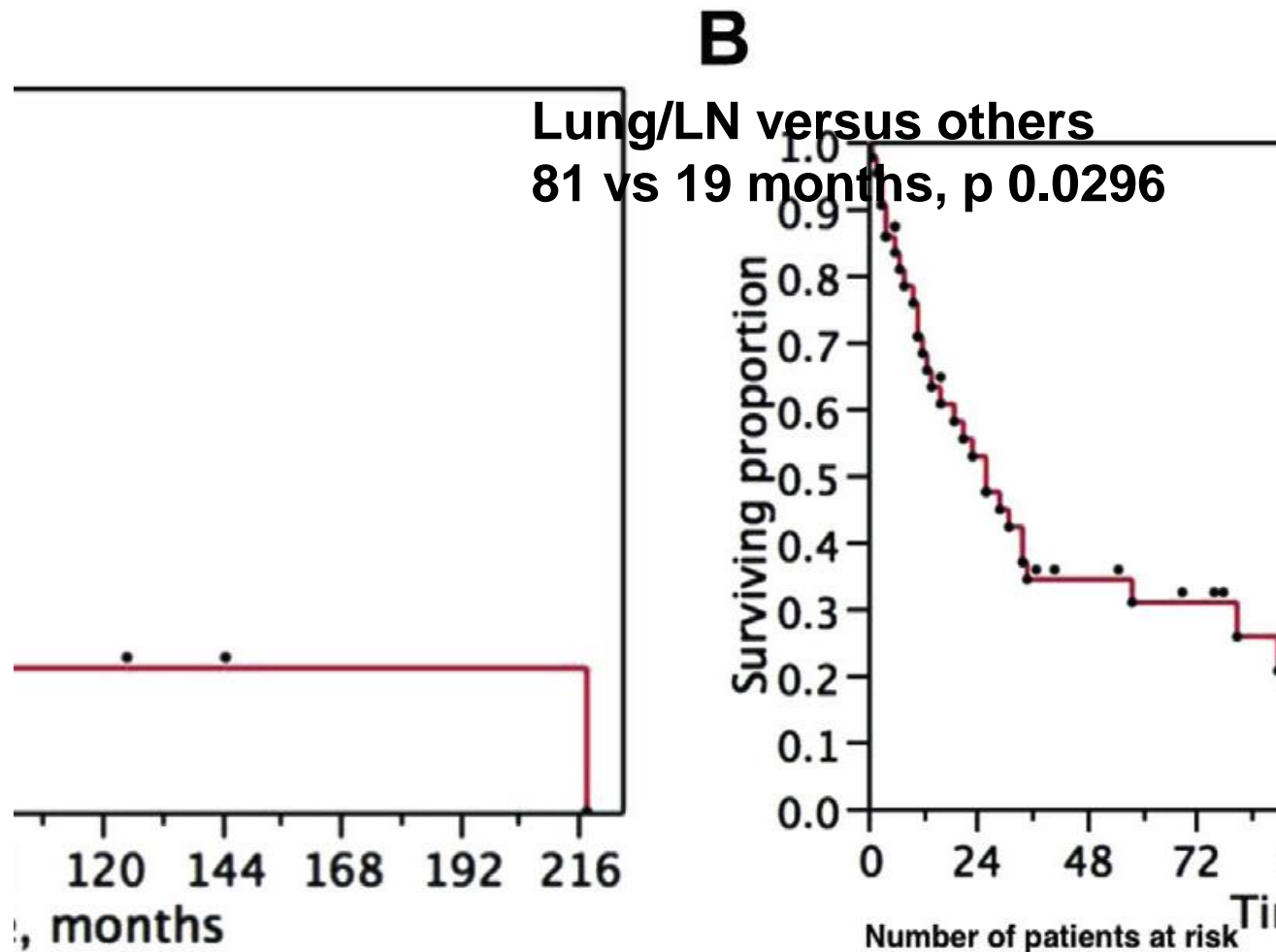
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## Outcome of metastasectomy for urothelial carcinoma: a multiinstitutional retrospective study in Japan.

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# Pulmonary metastasectomy could prolong overall survival in select cases of metastatic urinary tract cancer.

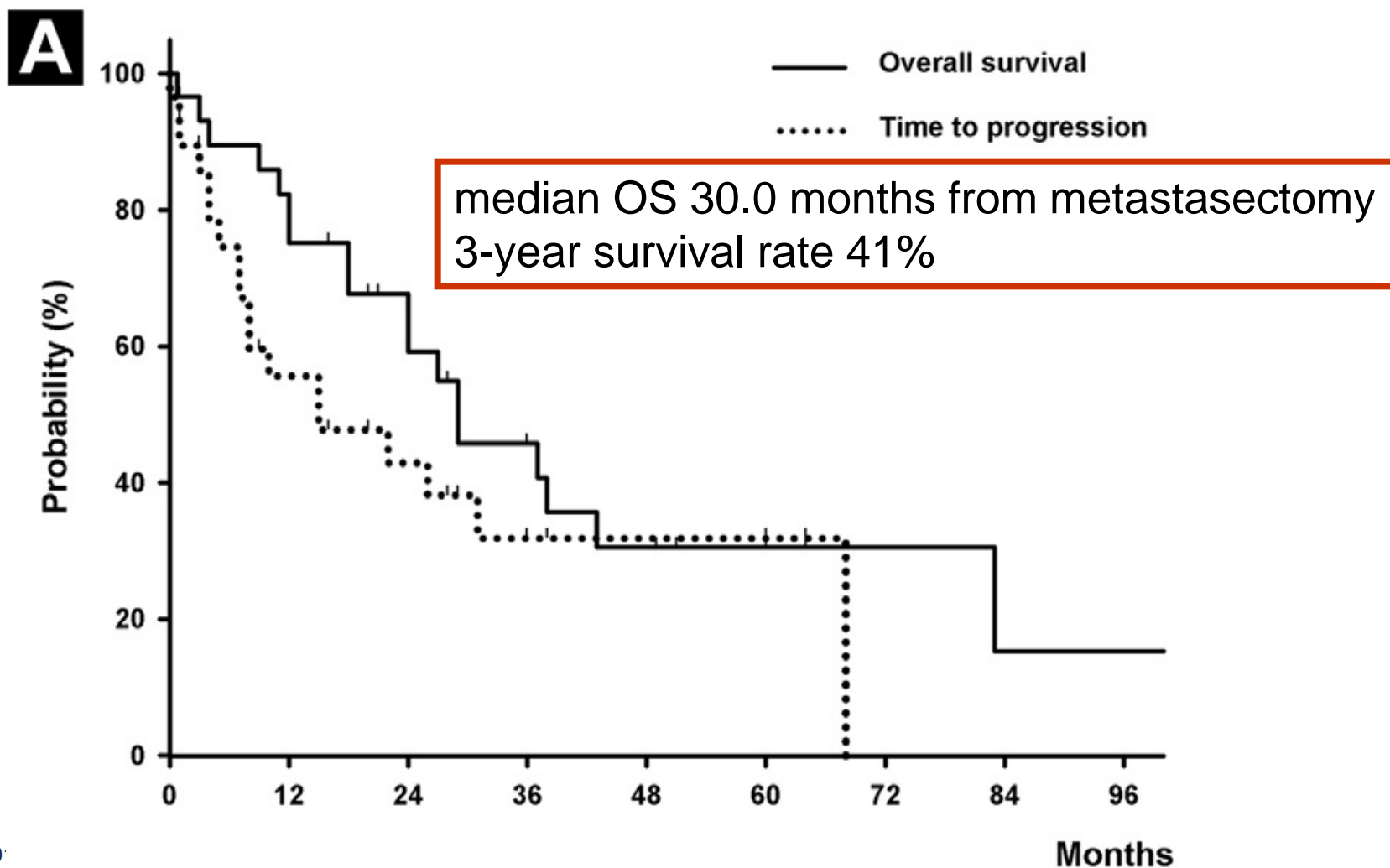
Kim T et al., Clin Genitourin Cancer 2015; 13: e297 - 304

Table 2 Sites and Characteristics of the Resected Metastases (n = 30)	
Characteristic	n (%)
<b>Resected Site</b>	
Lung	24 (80)
Liver	2 (7)
Bone	1 (3)
Lymph node	3 (10)
<b>Additional Metastasectomy</b>	
No	24 (80)
Yes	6 (20)
1 More <sup>a</sup>	2 (7)
2 More <sup>b</sup>	3 (10)
4 More <sup>c</sup>	1 (3)



# **Pulmonary metastasectomy could prolong overall survival in select cases of metastatic urinary tract cancer.**

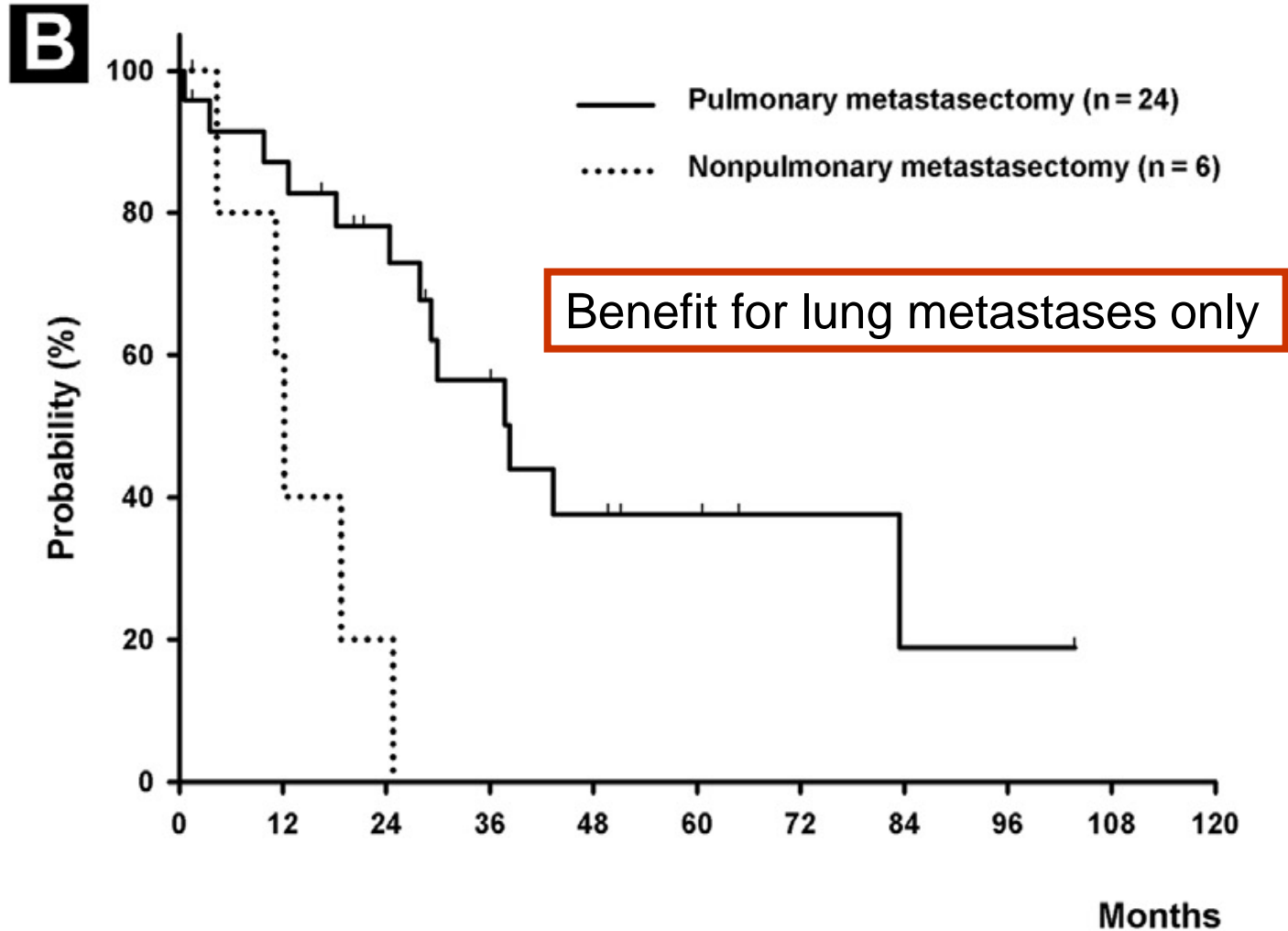
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## Pulmonary metastasectomy could prolong overall survival in select cases of metastatic urinary tract cancer.

Kim T et al., Clin Genitourin Cancer 2015; 13: e297 - 304





# Oligometastases – Bladder Cancer

- complete resection of solitary metastases at one single organ site after systemic therapy might result in prolonged survival
- lung and lymph nodes significantly better than other sites
- individual decision in the scenario of a multimodality approach



- definition of oligometastases
- goals of treatment
- **treatment options in**
  - renal cell cancer
  - bladder cancer
  - **prostate cancer**

## Rationale for local treatment

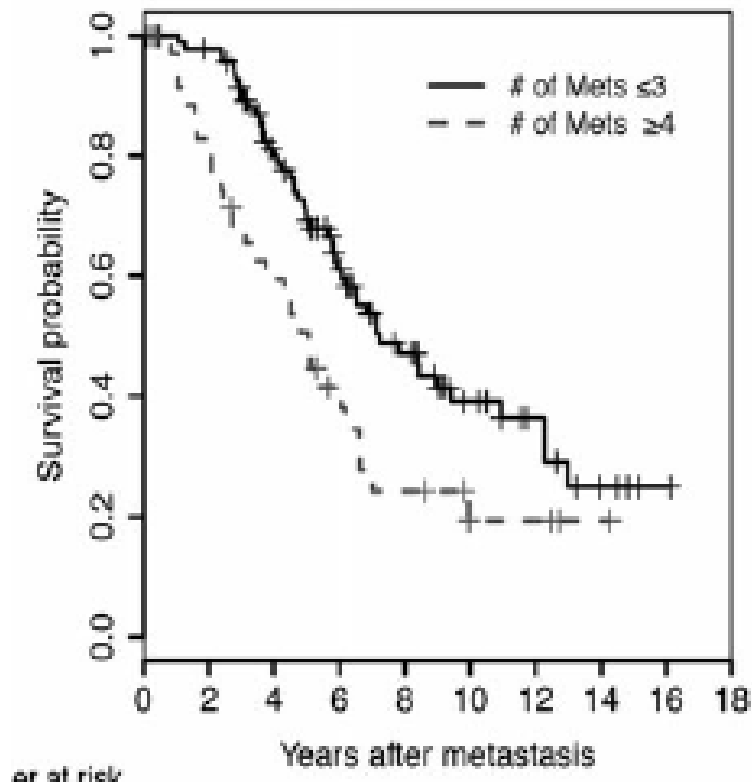
	1 LN vs $\geq 2$ LN	Gleason $\leq 7$ vs 8-10	$\leq pT3b$ vs pT3b
relapse	23% vs 85%	29% vs 95%	35% vs 89%

Lymph node metastases  $\neq$  lymph node metastases  
Long-term survival possible



# Metastasis-free survival is associated with overall survival in men with PSA-recurrent prostate cancer treated with deferred androgen deprivation therapy. Schweizer MT et al., Ann Oncol 2013; 24: 2881 - 2886

- N = 140 with metastatic PCA and ADT



Variables	HR for death (95% CI)	P-value
Log (MFS) <sup>a</sup>	0.77 (0.63, 0.94)	<b>0.012</b>
Number of metastases		
≥4	1 [reference]	
≤3	0.50 (0.29, 0.85)	<b>0.012</b>
Pain with metastases		
Yes	1	
No	0.43 (0.25, 0.72)	<b>0.002</b>
Bisphosphonate use		
No	1	
Yes	0.60 (0.37, 0.98)	<b>0.041</b>

# Cytoreductive radical prostatectomy in men with prostate cancer and low volume skeletal metastases.

Heidenreich A et al., J Urol 2015; 193: 832 - 838

## Inclusion Criteria CRP

- Locally resectable prostate cancer (=> mpMRI)
- ≤3 hot spots on bone scan
- Pelvic lymph node metastases ≤3 cm
- No retroperitoneal lymph node metastases
- No visceral metastases

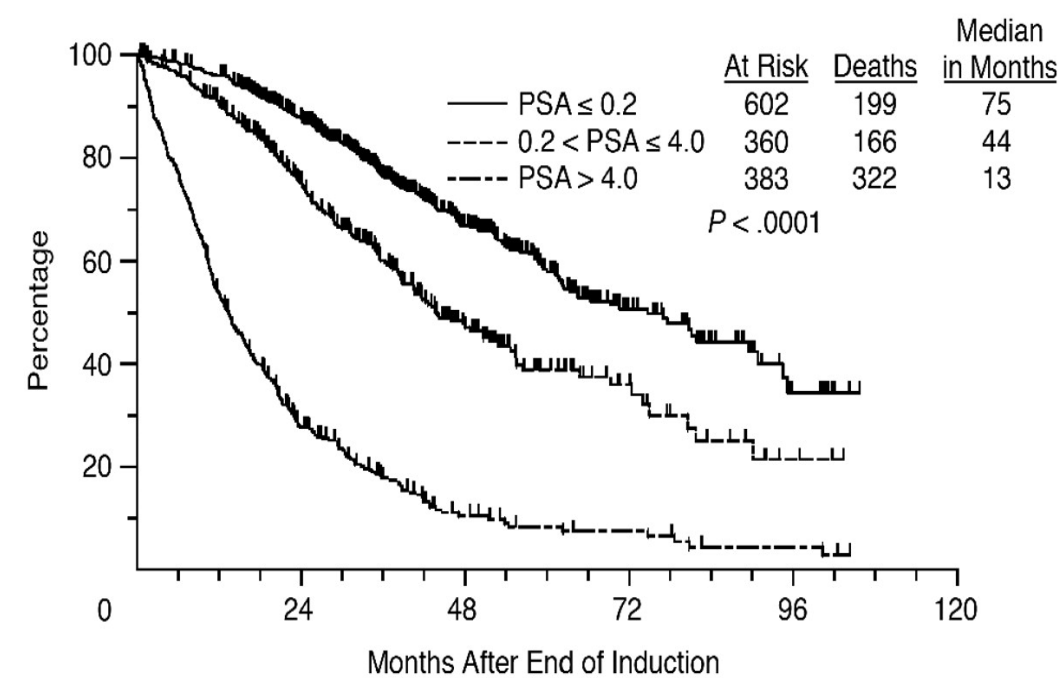
## Treatment design

- Neoadjuvant androgen deprivation (LHRH analogues) for 6 months
- PSA↓ < 0.4 ng/ml → extended radical prostatectomy and extended pelvic LAD
- Adjuvant ADT for 2 years

# Cytooreductive radical prostatectomy in men with prostate cancer and low volume skeletal metastases.

Heidenreich A et al., J Urol 2015; 193: 832 - 838

## PSA decrease after 6 months as surrogate marker of prognosis



At risk:

PSA ≤ 0.2 ng/mL	453	210	63
0.2 < PSA ≤ 4.0	219	77	20
PSA > 4.0	92	17	7

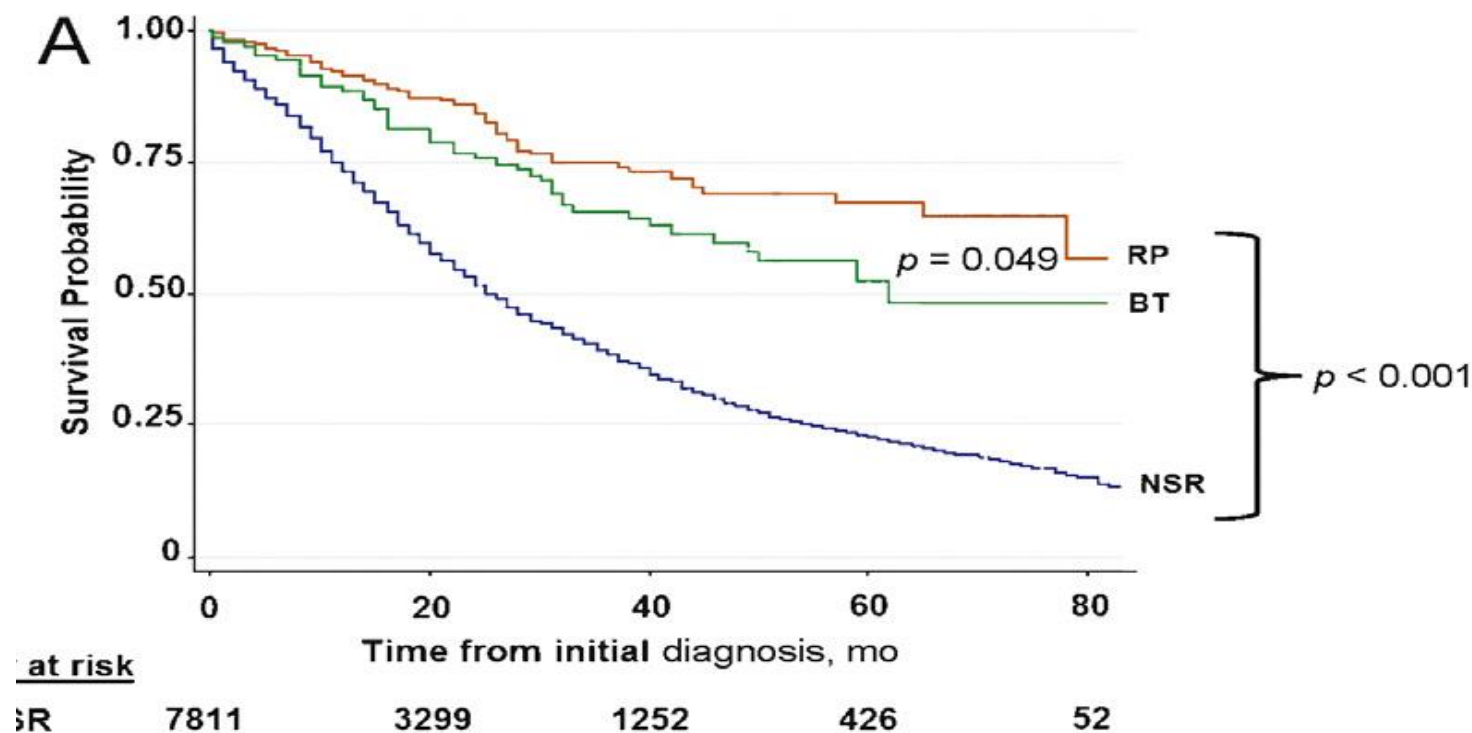
	CRP	Control	Adapted control group*	P value
Patients	32	38	26	
Mean follow-up, months (range)	40.6 (3–71)	44 (24–96)	42.3 (27–89)	NS
Median time, months (range)				
Clinical PFS	38.6 (22–52)	26.5 (12–48)	32.4 (19–48)	0.032
CRPC free survival	40 (9–65)	29 (16–54)	35.4 (22–47)	0.014
CSS	47 (9–71)	40.5 (19–75)	44.3 (21–75)	NS
Freedom from surgery, %	100	71.1		0.01
Overall survival, %	91.3	78.9		0.048
Cancer specific survival, %	95.6	84.2		0.043

# Might Men Diagnosed with Metastatic Prostate Cancer Benefit from Definitive Treatment of the Primary Tumor? A SEER-Based Study

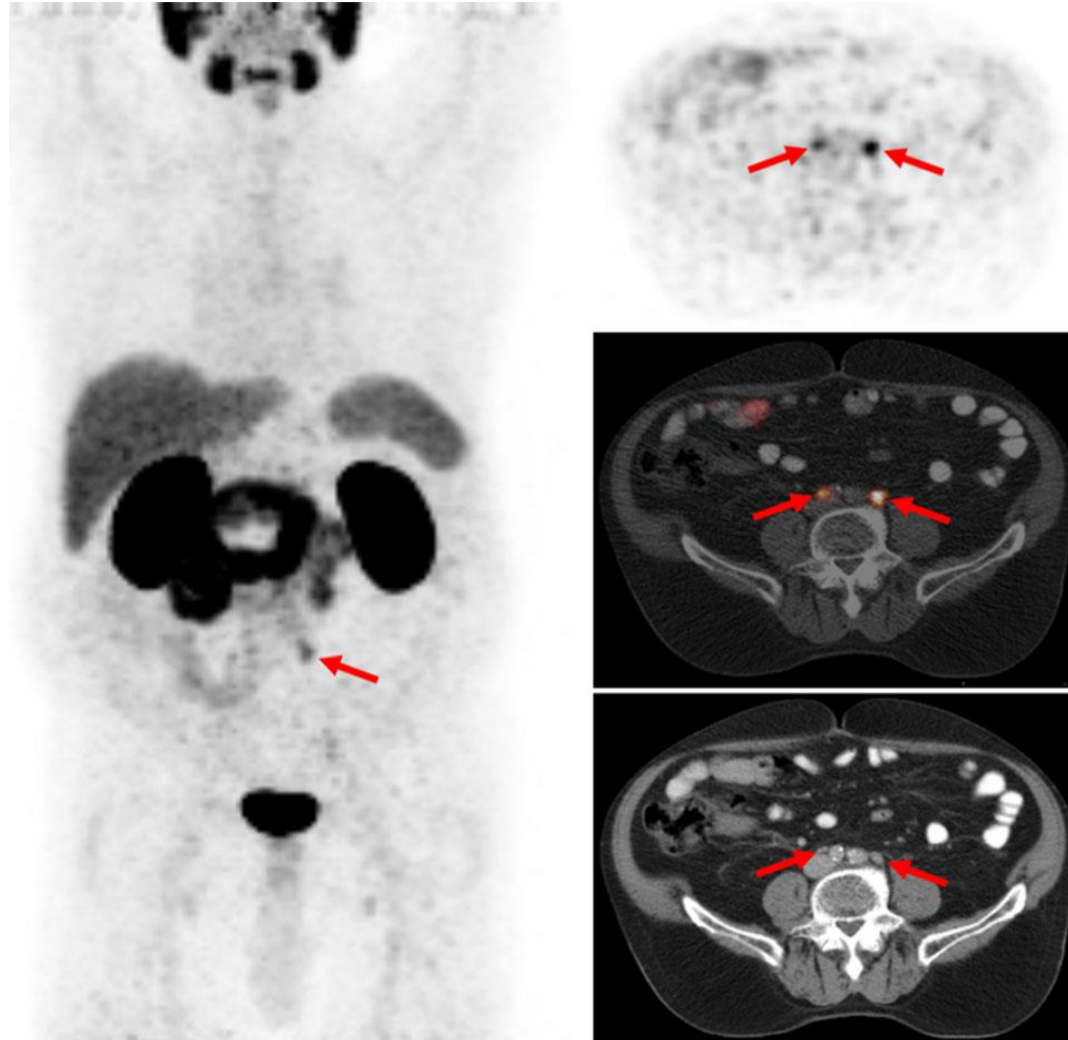
Stephen H. Culp<sup>a,\*</sup>, Paul F. Schellhammer<sup>b</sup>, Michael B. Williams<sup>b</sup>

## PCA-specific mortality

Adjusted for age, PSA, T-stage, tumor grade, year of diagnosis



# Oligometastases – Prostate Cancer - Imaging -





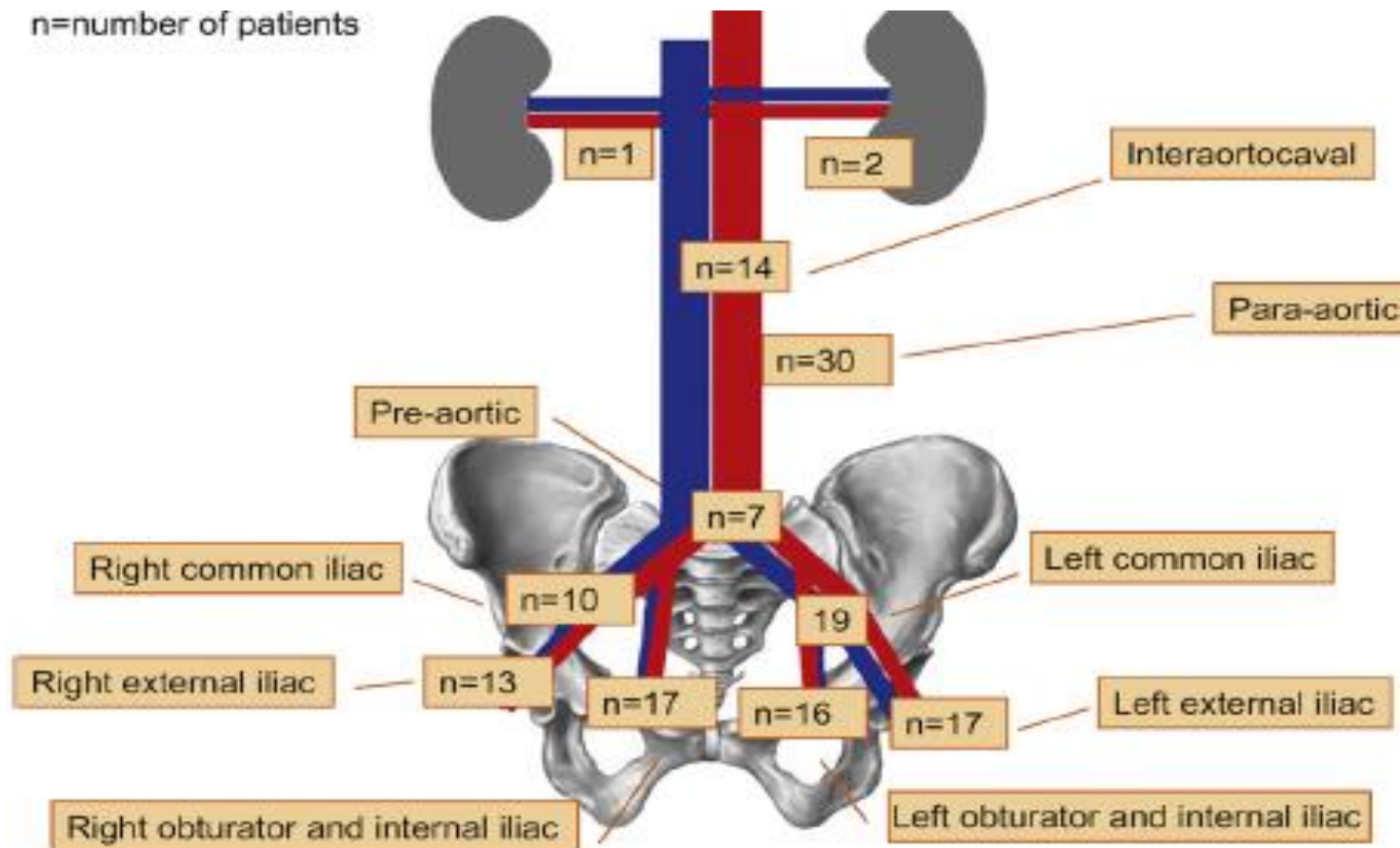


# Extent of disease in recurrent prostate cancer determined by <sup>68</sup>Ga-PSMA-HBED-CC PET/CT in relation to PSA levels, PSA doubling time and Gleason Score. Verburg FA, Pfister D, Heidenreich A, Vogg A, Drude NI, Vöö S, Mottaghy F, Behrendt FF. Eur J Nucl Med Mol Imaging 2015

	PSA (ng/ml)				PSA doubling time (months)				Gleason score		
	<1	1 – 2	≥2	<i>p</i> value	<6	6 – 12	≥12	<i>p</i> value	<8	8 – 10	<i>p</i> value
Total no. of patients	27	19	109		60	27	21		76	53	
Pathological tracer accumulation	12 (44 %)	15 (79 %)	97 (89 %)	<0.001	54 (90 %)	22 (81 %)	11 (48 %)	0.001	58 (76 %)	43 (81 %)	0.51
Local tumour <sup>a</sup>	4 (15 %)	3 (16 %)	35 (32 %)	0.10	14 (23 %)	6 (22 %)	7 (33 %)	0.61	18 (24 %)	16 (30 %)	0.41
Pelvic lymph node metastases (cN1)	10 (37 %)	7 (37 %)	51 (47 %)	0.53	27 (45 %)	17 (63 %)	5 (24 %)	0.026	29 (38 %)	30 (57 %)	0.039
Extrapelvic lymph node metastases (cM1a)	4 (15 %)	7 (37 %)	45 (41 %)	0.037	32 (53 %)	9 (33 %)	2 (10 %)	0.001	28 (37 %)	19 (36 %)	0.91
Bone metastases (cM1b)	4 (15 %)	3 (16 %)	43 (39 %)	0.013	32 (53 %)	9 (33 %)	0 (0 %)	<0.001	24 (32 %)	16 (30 %)	0.87
Visceral metastases (cM1c)	1 (4 %)	1 (5 %)	13 (12 %)	0.34	10 (17 %)	1 (4 %)	0 (0 %)	0.041	5 (7 %)	6 (11 %)	0.34

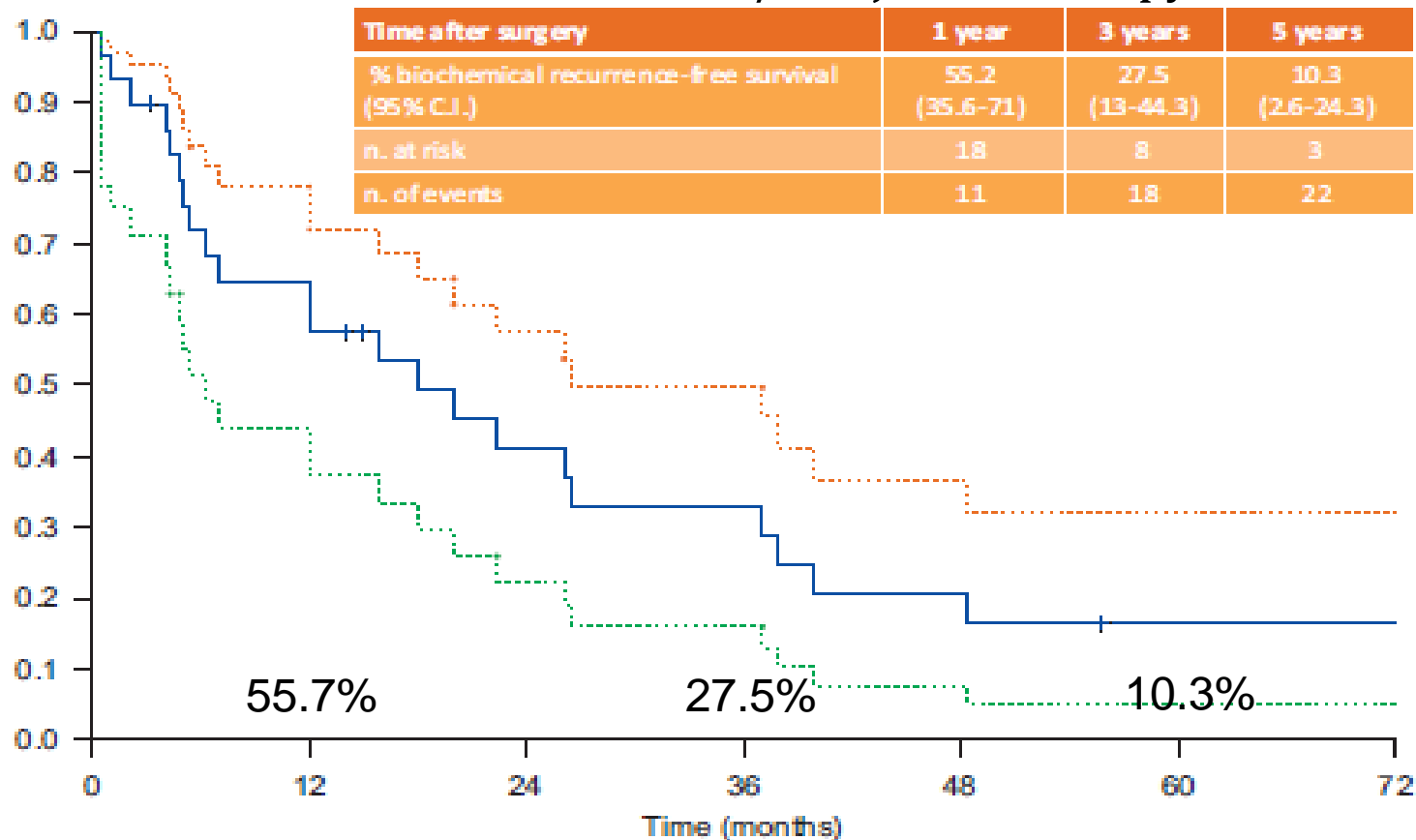
19/20 (95%) pts with PSA > 1 ng/ml & PSA-DT < 6 months **positive**  
09/14 (64%) pts with PSA < 1 ng/ml & PSA-DT > 6 months **negative**

# Pelvic/Retroperitoneal Salvage Lymph Node Dissection for Patients Treated With Radical Prostatectomy With Biochemical Recurrence and Nodal Recurrence Detected by [11C]Choline Positron Emission Tomography/Computed Tomography



# Pelvic/Retroperitoneal Salvage Lymph Node Dissection for Patients Treated With Radical Prostatectomy With Biochemical Recurrence and Nodal Recurrence Detected by [11C]Choline Positron Emission Tomography/Computed Tomography

Follow-up of n = 28 with PSA < 0.2 ng/ml  
After LAD and w/o adjuvant therapy





# Salvage Lymph Node Dissection - Cologne Experience -

- N=85 (2009-2015)
  - Cholin-PET: 38
  - PSMA-PET: 47
- extended pelvic LAD and/or retroperitoneal LAD
- median preop. PSA 2,29 (0,4-8,2) ng/ml
- median age 66 (55-75) years
- interval to primary RPE/RT 50 (9-163) months
- 21 Pat. with ADT/SRT
- 843 LN resected
- 216 pos LN (micrometastases to perforation of LN capsule)



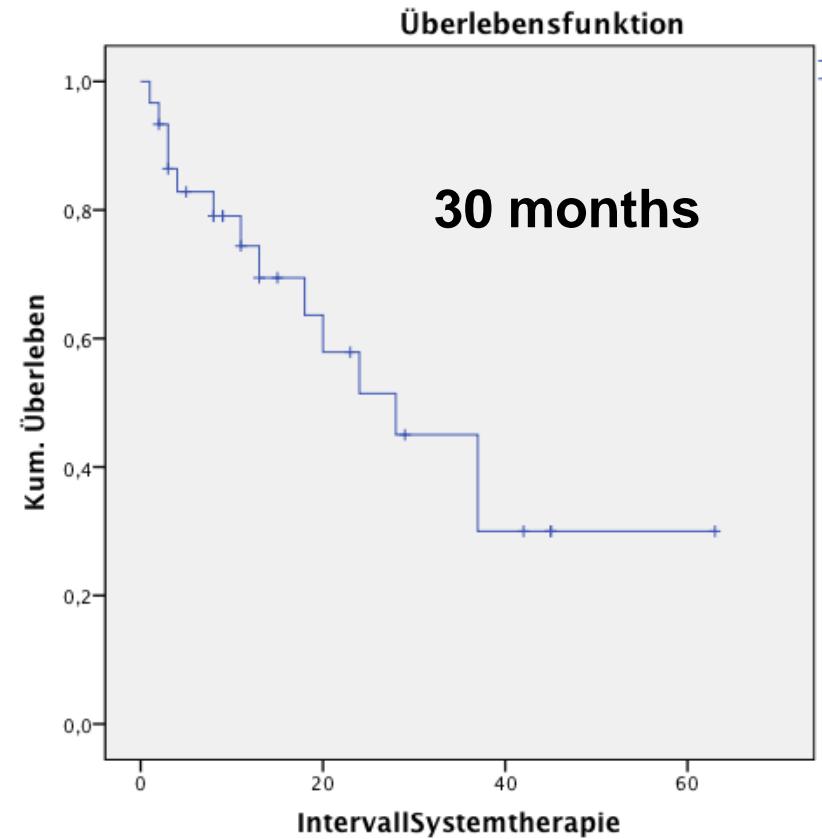
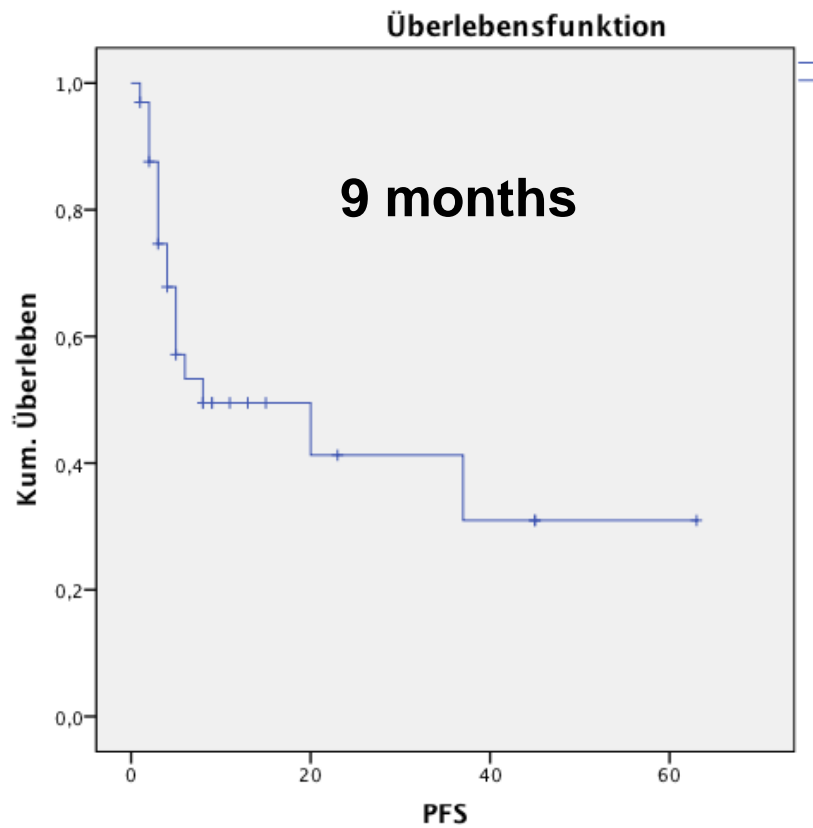
# Salvage Lymph Node Dissection - Cologne Experience -

## Choline versus PSMA – PET/CT

	PSMA	Cholin
Per Patient	18% false positive	22% false negative
Per LN		
Sensitivity	94%	73%
Specificity	94%	88%
Positive predictive value	80%	76%
Negative predictive value	98%	90%



# Salvage Lymph Node Dissection - Cologne Experience -



**median follow-up 18 (3-66) months**



Study	N	Mean FU (mo)	ADT prior to sLND (%)	ADT after sLND (%)	Complete response * (%)	5-yr BRFS *(%)	5-yr CPFS (%)	5-yr CSS (%)
Rinnab 2008	15	13.7	33	73	NA	NA	NA	NA
Rigatti 2011	72	39.4	56	65	57	19	34	75
Jilg 2012	47	35.5**	79	65	46	9	26	78
Suardi 2013	162	40**	NA	NA	41	40	47	86
Suardi 2014	59	81.1**	63	1-yr: 44 5-yr: 63	59	29	52	89
Osmonov 2014	22	NA	NA	41	64	NA	NA	NA





# Metastasis-directed Therapy of Regional and Distant Recurrences After Curative Treatment of Prostate Cancer: A Systematic Review of the Literature. Ost P et al., Eur Urol 2015; 67: 852 - 863

## Complications following lymphadenectomy

Complication type	Rinnab et al. [31] (n = 15), no. (%)	Busch et al. [37] (n = 6), no. (%)	Jilg et al. [34] (n = 47), no. (%)	Suardi et al. [36] (n = 59), no. (%)	Total (n = 127), no. (%)
Grade 1					
Lymphorrhea	0 (0)	0 (0)	4 (7.7)	12 (20.3)	16 (12.5)
Fever	0 (0)	0 (0)	3 (5.8)	18 (30.5)	21 (16.5)
Temporary weakness of the hip flexor	0 (0)	0 (0)	1 (1.9)	0 (0)	1 (0.8)
Wound dehiscence	0 (0)	0 (0)	3 (5.8)	0 (0)	3 (2.3)
Grade 2					
Deep vein thrombosis	0 (0)	0 (0)	0 (0)	1 (1.7)	1 (0.8)
Ileus	1 (7)	0 (0)	0 (0)	12 (20.3)	13 (10.2)
Grade 3a					
Lymphocele requiring drainage	1 (7)	0 (0)	2 (3.9)	7 (11.2)	10 (7.8)
Wound dehiscence	0 (0)	0 (0)	0 (0)	3 (5.1)	3 (2.3)
Hydronephrosis requiring stenting	1 (7)	0 (0)	0 (0)	0 (0)	1 (0.8)
Grade 3b					
Lymphocele requiring surgical drainage	0 (0)	0 (0)	0 (0)	1 (1.7)	1 (0.8)

# Long-term Outcomes of Salvage Lymph Node Dissection for Clinically Recurrent Prostate Cancer: Results of a Single-institution Series with a Minimum Follow-up of 5 Years

Nazareno Suardi<sup>a,†</sup>, Giorgio Gandaglia<sup>a,†</sup>, Andrea Gallina<sup>a</sup>, Ettore Di Trapani<sup>a</sup>, Vincenzo Scattoni<sup>a</sup>, Damiano Vizziello<sup>a</sup>, Vito Cucchiara<sup>a</sup>, Roberto Bertini<sup>a</sup>, Renzo Colombo<sup>a</sup>, Maria Picchio<sup>b</sup>, Giampiero Giovacchini<sup>b</sup>, Francesco Montorsi<sup>a</sup>, Alberto Briganti<sup>a,\*</sup>



## Prediction of Clinical Relapse

Preoperative model		
Variable	Univariable HR (95% CI); p value	Multivariable HR (95% CI); p value
PSA at LND, ng/ml	1.10 (0.03–1.17); <0.001	1.08 (1.00–1.15); 0.03
PSA at LND ≥4 vs <4 ng/ml	2.02 (1.00–4.19); 0.05	–
Gleason score at RP 7 vs 2–6	0.91 (0.37–2.22); 0.9	–
8–10 vs 2–6	0.88 (0.34–2.68); 0.8	–
Time to BCR, mo	1.00 (0.99–1.01); 0.3	–
Positive lymph nodes at RP	2.04 (1.01–4.13); 0.04	1.83 (0.86–3.91); 0.1
Site of positive spot at PET/CT scan Retroperitoneal vs pelvic	2.21 (1.12–4.36); 0.02	1.82 (0.84–3.92); 0.1
ADT after RP	1.87 (0.89–3.93); 0.09	–
RT after RP	1.36 (0.61–3.03); 0.44	–

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## Prediction of Clinical Relapse

- mean follow-up: 81.1 months
- 35/59 (59.3%) with PSA response after LAD

PSA↓	46.7% versus 27.1%	p < 0.001
PSA < 4 ng/ml	43.8% versus 23.5%	p = 0.05
positive LN	20.0% versus 44.8%	p = 0.8
LN at RP	22.4% versus 68.7%	p < 0.001
≤ 2 pos LN	63.2% versus 28.3%	p = 0.4



## Summary – oligometastases in prostate cancer

pre salvage LAD	post salvage LAD
PSA < 4 ng/ml	complete PSA response after surgery
positive nodes in the small pelvis only	≤ 2 positive nodes at salvage LAD
Gleason Score ≤ 7 at RP	positive lymph nodes in the small pelvis only

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

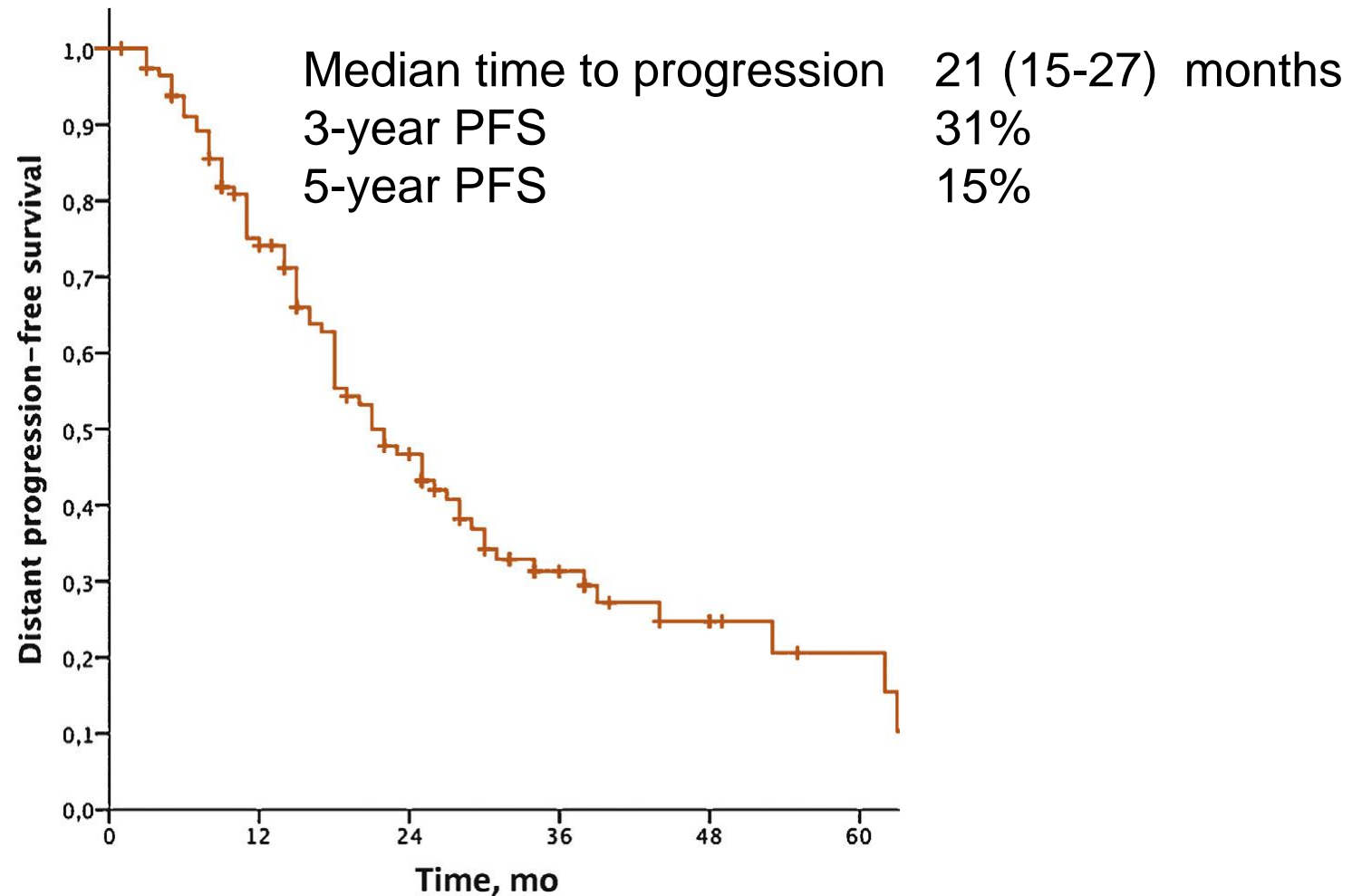
Ost P et al., Eur Urol 2015; 69: 9-12

Characteristics	All patients ( <i>n</i> = 119)
Primary site of metastases, <i>n</i> (%)	
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, <i>n</i> (%)	43 (36)
Axial	22 (18)
Appendicular	17 (14)
Both	4 (3)

Characteristics	All patients ( <i>n</i> = 119)
Node and/or bone and/or viscera, <i>n</i> (%)	2 (2)
Imaging modality at recurrence, <i>n</i> (%)	
Choline PET-CT	92 (77)
FDG PET-CT	24 (20)
MRI	3 (3)
Adjuvant ADT, <i>n</i> (%)	
No	59 (50)
Yes	60 (50)
Duration of ADT, mo, median (range)	2 mo (1–8 mo)

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

Ost P et al., Eur Urol 2015; 69: 9-12





# Metastasis-directed Therapy of Regional and Distant Recurrences After Curative Treatment of Prostate Cancer: A Systematic Review of the Literature. Ost P et al., Eur Urol 2015; 67: 852 - 863

## Complications following radiation therapy

Complication type	Muacevic et al. [24] (n = 40), no. (%)	Würschmidt et al.* [25] (n = 15), no. (%)	Ahmed et al. [26] (n = 17), no. (%)	Jereczek-Fossa et al. [27] (n = 19), no. (%)	Decaestecker et al. [29] (n = 50), no. (%)	Total (n = 141), no. (%)
Grade 1						
Bone pain	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	3 (2)
Asymptomatic fracture	1 (2.5)	0 (0)	0 (0)	0 (0)	1 (2)	2 (1.4)
Fatigue	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (0.7)
Rectal toxicity	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	2 (1.4)
Urinary toxicity	0 (0)	0 (0)	0 (0)	2 (11)	0 (0)	2 (1.4)
Grade 2						
Nausea requiring antiemetics	5 (12.5)	0 (0)	0 (0)	0 (0)	0 (0)	5 (3.5)
Rectal toxicity	0 (0)	2 (13.3)	0 (0)	1 (5)	2 (4)	5 (3.5)
Urinary toxicity	0 (0)	0 (0)	0 (0)	1 (5)	1 (2)	2 (1.4)
Grade 3						
Urinary toxicity	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	1 (0.7)

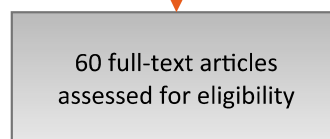
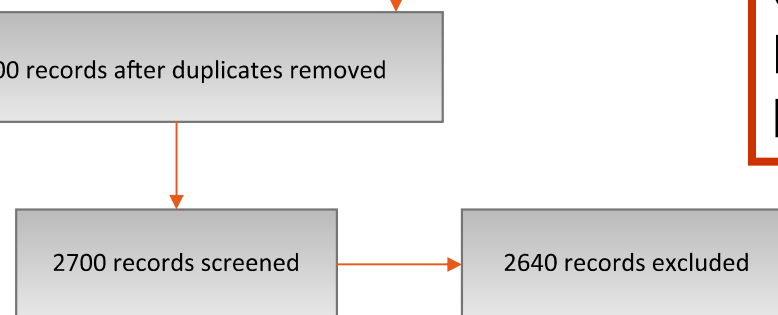


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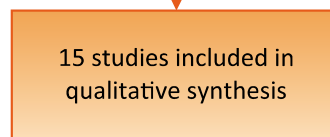
**Drawback**  
Choline-PET/CT or FDG  
PET/CT  
**LOW EVIDENCE**

**n = 450 patients**  
n = 299 radiotherapy  
n = 151 surgery

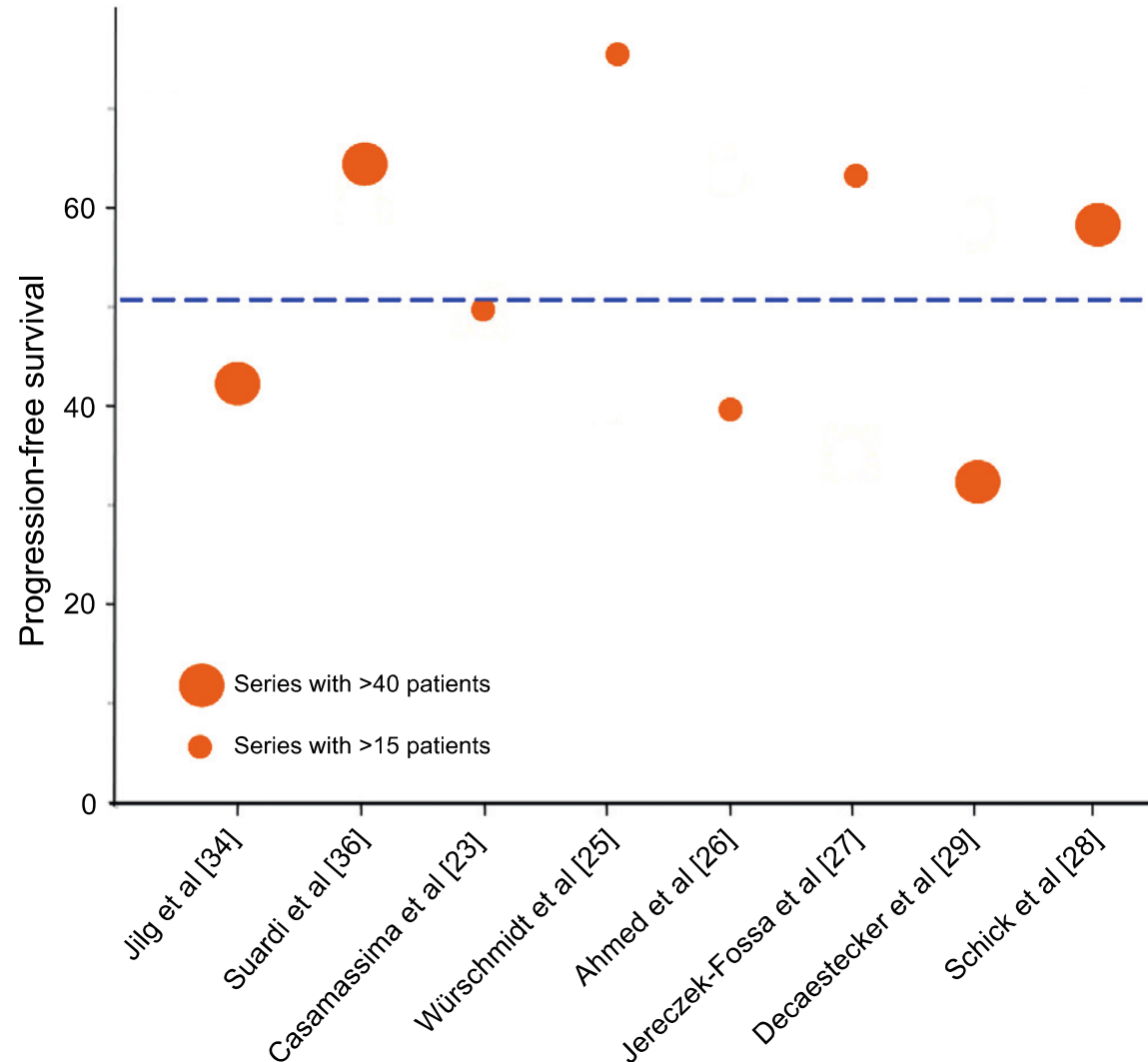


45 full-text articles excluded, with reasons:

- Abstracts/meetings/editorial: 18
- Case reports: 1
- Previous reports of the same research group: 4
- No details on outcome and toxicity: 10
- No or <5 PCa patients included: 12



# Metastasis-directed Therapy of Regional and Distant Recurrences After Curative Treatment of Prostate Cancer: A Systematic Review of the Literature. Ost P et al., Eur Urol 2015; 67: 852 - 863





# Oligometastases – Prostate Cancer: Future Perspectives

## Primary goal

Biochemical failure rate

Clinical failure rate

### Inclusion criteria :

1. PS 0-1
4. Prior radical prostate treatment (surgery or radiotherapy)
5.  $\leq 5$  metastatic pelvic lymph nodes detected by FCH PET.
6. Upper limit of metastatic lymph nodes: aortic bifurcation
7. Respect of dosimetric constraints to organs at risk
8. If ADT was previously administered to the patient (e.g. neoadjuvant ADT prior to surgery or adjuvant ADT in locally-advanced prostate cancer treated with radiotherapy), a time-interval without ADT of a minimum of 6 months between the predictable duration of the last injection and inclusion of the patient has to be respected.

Consent and inclusion

### Androgen Depriving Therapy

Eligard@ 45 mg, 1 injection on day 1 or  
maximum 3 months prior to RT

*or*

Any other ADT (LH-RH  
agonists/antagonists)

*During 6 Months*

### IG-IMRT

Whole Pelvis Irradiation (54 Gy in 30  
fractions)

*and*

Simultaneous Integrated Boost on PET-  
positive pelvic ( $\leq 5$ ) oligometastatic  
lymph nodes (66 Gy in 30 fractions)

*+/- Prostate bed Irradiation possible* (66  
Gy in 33 fractions )

*+ /- boost to any PET-positive prostate bed  
relapse* (72 Gy 36 fractions)

*6-7 weeks*



- local treatment of oligometastases in genitourinary malignancies
  - is typically performed after systemic therapy in renal & bladder cancer and prior to ADT in PCA
  - is reserved to well selected patients with minimal disease, a low probability of early systemic relapse and complete resectability
  - might have a benefit in terms of progression-free survival and systemic treatment-free survival
  - has not been proven in randomized trials
  - represents an individual decision