

FACULTY OF MEDICINE
AND HEALTH SCIENCES

LOCAL TREATMENT OF PROSTATE CANCER IN METASTATIC SETTING

Prof. Dr. Nicolaas Lumen
Dept. Of Urology
Ghent University Hospital (Belgium)

GHENT UNIVERSITY

DISCLOSURES

- Consultant for Bayer, Janssen, AstraZeneca, Astellas
- Receiving grants from Bayer, Janssen and Ipsen
- PI Ipatiential, Translate, Propel, Lomp1, Lomp2, Vespar, Poirot trial
- Member of EAU panel trauma and urethra

RATIONALE: ANALOGY WITH OTHER TUMORS

- Breast
- CRC
- Testis
- Renal

Table 1 Phase III trials of IFN with nephrectomy

Trial	No. patients	Median survival (months)		Response to therapy (%)		Unable to receive post-surgery immunotherapy n (%)	Operative Mortality n (%)	
		IFN alone	Surgery + IFN	IFN alone	Surgery + IFN			
SWOG 9504 ^a	241	8.1	11.1	0.05	3.3	3.6	NR	1 (0.8)
EWIC 3045 ^b	85	8.9	17	0.05	12	19	0.38	1 (1.2)
Combined analysis ^c	331	7.8	19.6	0.0002	5.7	6.9	0 (0.0)	2 (1.4)

^aEWIC: European Organization for the Research and treatment of Cancer; ^bIFN: interferon; ^cNR: not reported; NS: not significant; SWOG: Southwest Oncology Group.

GHENT UNIVERSITY → Polcari AJ et al. Int J Urol. 2009 Mar;16(3):227-33.

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RATIONALE: ANALOGY WITH N1 PC

(n = 19 each)

- M1
- Cx
- re
- RT
- R1

Study	Year	Source	Number of patients	Study outcome	Design	Treatment	Median (I)	Treatment detail	Survival	Study outcome	
Sonne et al. [14]	2007	NCDB	1087	All cause mortality	Observational	LT + ADT vs LT	NP and RT	78.8% (74.5-83.0%) for LT vs 60% (21-81.3%) for ADT alone > 5 yr OS	HR = 0.31, 95% CI = 0.13-0.74 $p < 0.001$		
Jani et al. [15]	2010	Control arm of the STAMPEDE	177	Fallen-free survival (PSA level, local, regional, or distant metastasis)	Observational	RT + ADT vs ADT	EBRT to the prostate + pelvic	78.8% (74.5-83.0%) for RT vs 53% (40-66%) for ADT alone > 5 yr OS	HR = 0.35, 95% CI = 0.11-0.64 $p < 0.001$		
Beuthowes et al. [16]	2014	SEER	796	Overall and cause-specific survival	Observational	RT vs no RT	5.2 yr	EBRT	73.5% (70.4-76.6%) for RT vs 65% (62-68%) for no RT 65% vs 58% 5-yr OS 71.5% vs 72% 5-yr CSS 70.5% vs 68% 5-yr RFS	HR = 0.31, 95% CI = 0.08-0.52 $p < 0.001$	
Tewari et al. [14]	2010	SEER	1000	Overall and cause-specific survival	Observational	RT vs no RT	9.0 mo	EBRT brachytherapy	78.3% for RT vs 71.5% for CSS	HR = 0.66, 95% CI = 0.41-0.91 $p < 0.001$	14-15 yr
Lee et al. [17]	2009	NCDB	3540, 639 after propensity score matching	All cause mortality	Observational	RT + ADT vs ADT	EBRT	73.5% (72.5-75%) for RT vs 65% (62-68%) for ADT alone 5-yr OS	HR = 0.31, 95% CI = 0.13-0.72 $p < 0.001$		

GHENT UNIVERSITY → Engel J et al. Eur Urol. 2010 May;57(5):742-41
→ Vervenne E et al. Eur Urol Oncol. 2019 May;2(5):294-301

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RATIONALE

- Primary tumor = mother of all evil
- Premetastatic niche
 - TDSF
 - Exosomes
- Maintenance of met's
 - Cytokines, chemokines

GHENT UNIVERSITY → Alharbi et al. Adv Anat Pathol. 2019
→ Gueron et al. Prostate Cancer Prostatic Dis 2012

LOCAL TREATMENT M1 PC: RETROSPECTIVE

- SEER database 2004-2010

	No LT	BT	RP
5y OS (%)	22.5	52.6	67.4
5y CSM (%)	51.3	38.7	24.2

A. Survival Probability

B. Cumulative Incidence of Metastasis

Culy et al. Eur Urol 2014

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RP FOR Σ0 M1 PC: PROSPECTIVE				
	Total (n = 46)	Group A (n = 17)	Group B (n = 29)	P value
Patient/tumor				
Age, yr	69 ± 10	64 ± 8	72 ± 10	.005
Initial PSA, µg/L	45 (4.0-3092)	10 (4.6-75)	156 (5.2-3092)	.002
CT stage, n (%)				
T1a	11 (24)	8 (47)	3 (10)	
T1b	12 (26)	2 (12)	10 (35)	
T2	10 (22)	1 (6)	3 (10)	
T3	13 (29)	0 (0)	13 (45)	
CM positive, n (%)	34 (74)	17 (77)	22 (76)	.7
CM stage, n (%)				
1a	13 (28)	0 (0)	4 (14)	
1b	29 (63)	8 (47)	21 (72)	
2a	4 (8.7)	0 (0)	4 (14)	
Grade group, n (%)				.2
1	12 (27)	1 (6)	11 (38)	
2	4 (9.3)	2 (12)	0 (0)	
3	3 (6.5)	2 (12)	1 (3.4)	
4	3 (6.5)	0 (0)	0 (0)	
5	27 (59)	8 (47)	19 (66)	
Metastatic burden				
Low volume, n (%)	25 (54)	16 (94)	9 (31)	<.001
Medium volume lesions	1 (2.2)	1 (6)	11 (38)	.002
Follow-up, mo	15 ± 9	13 ± 8	16 ± 10	.29
Total (n = 46)				
Group A (n = 17)				
Group B (n = 29)				
P value				.014
Local symptom, n (%)				
Continent and no local symptoms				
Urinary obstruction	7 (15)	5 (29)	0 (0)	
Obstructive voiding (α-moderate)	8 (17)	0 (0)	8 (28)	
Obstructive voiding (α>PSA/CW)	3 (6.5)	0 (0)	3 (10)	
Urinary tract infection (α-moderate)	1 (2.2)	0 (0)	1 (3.4)	
Urinary obstruction (β-symptomatic)	1 (2.2)	0 (0)	1 (3.4)	



Poelaert et al. Urology 2017

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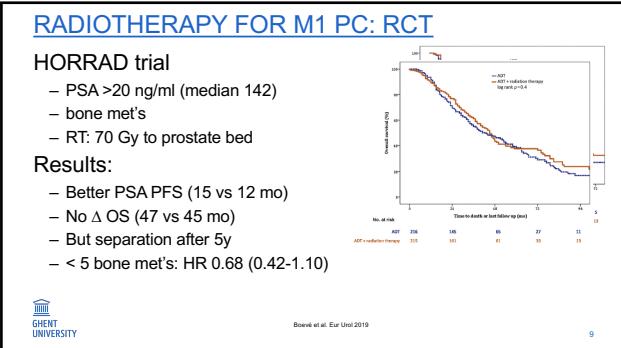
RP FOR OLIGO M1 PC: PROSPECTIVE

- ≤ 3 bone met's
- PSA <1ng/ml after 6mo ADT
- Matched-control
- Less local symptoms (surgery-free survival)
- (marginal) better survival data

	Group 1	Group 2 (all)	Group 2 (adapted)*	p Value
No. pt.	20	64	42 (37-89)	
Median mos followup (range)	40.6 (3-71)	44.0 (24-96)	42.3 (27-89)	0.014
Median mos to extraction in distant PCA (range)	40 (9-65)	29 (16-54)	35.4 (22-47)	
Median mos to distant PS (range)	47 (9-71)	40.5 (19-75)	44.3 (21-75)	
Surgery-free survival rate (%)	100	71.1	73.1	<0.01
Overall survival rate (%)	91.3	78.9	80.4	0.048
CSS rate (%)	95.6	84.2	84.3	0.043

Heiderreich et al. J Urol 2014

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Boeve et al. Eur Urol 2019

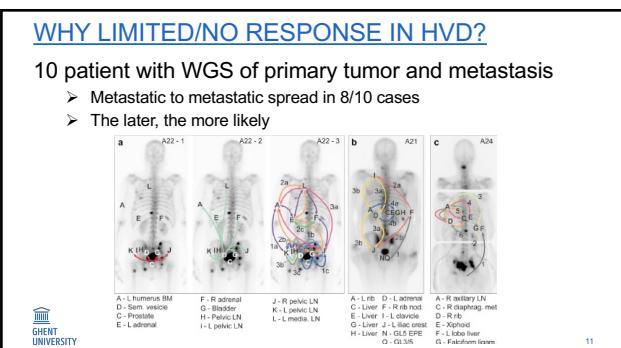
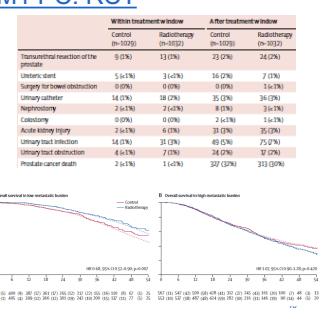
RADIOTHERAPY FOR M1 PC: RCT

STAMPEDE

- Overall population (n=2061)
 - No difference
- High-volume (n=1120)
 - No difference
- Low-volume (n=819)
 - Survival benefit (=Horrad <5 bone met's)
- No difference in local events



Parker et al. Lancet 2018

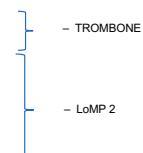


KNOWLEDGE GAPS

- RCT in low volume M1 PC
 - RP vs SOC
 - RT vs RP (cf SEER; local events?)
- RCT in high volume M1 PC:
 - RP vs SOC
- Can we cure M1 PC: LT + MDT?



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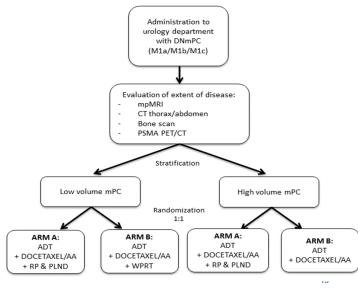


LOMP-2

Incl: eligible for LT (<T4 on MRI)

Primary endpoint:

- Feasibility of randomization
- CRPC free survival
- CSS
- OS
- Acute and late toxicity due to the local treatment:
- QoL
- Skeletal related event (SRE)
- Local event (LE)



CAN WE CURE M1 PCA?

– 31-3-17: cT3b N1 M1a

- WHO 5
- iPSA 140

– 2-5-2017: RALP + PLND

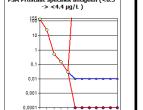
pT3b R1 N1

- Postop PSA 24.2

– WPRT + RPRT + ADT (till 04/2019)

– 11/2019:

- PSA < 0.01
- No incontinence
- Complete ED



CONCLUSION

- Low volume disease: SOC includes RT
- Cytoreductive surgery: RCTs needed
- Combination LT + MDT: explore!



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Nicolaas Lumen
M.D., Ph.D.

Department of Urology

E Nicolaas.lumen@ugent.be
T +32 9 332 22 76

- f Universiteit Gent
v @ugent
e @ugent
n Ghent University

www.ugent.be

