12ème Biennale Monégasque de Cancérologie

Cours Francophone d'Oncologie

GRIMALDI FORUM ~ 3 – 6 Février 2016

MONACO

SOUS LE HAUT PATRONAGE DE SAS LE PRINCE ALBERT II DE MONACO

Cancers de la Prostate
Patient oligometastatique
Place des traitements locaux

Alberto Bossi

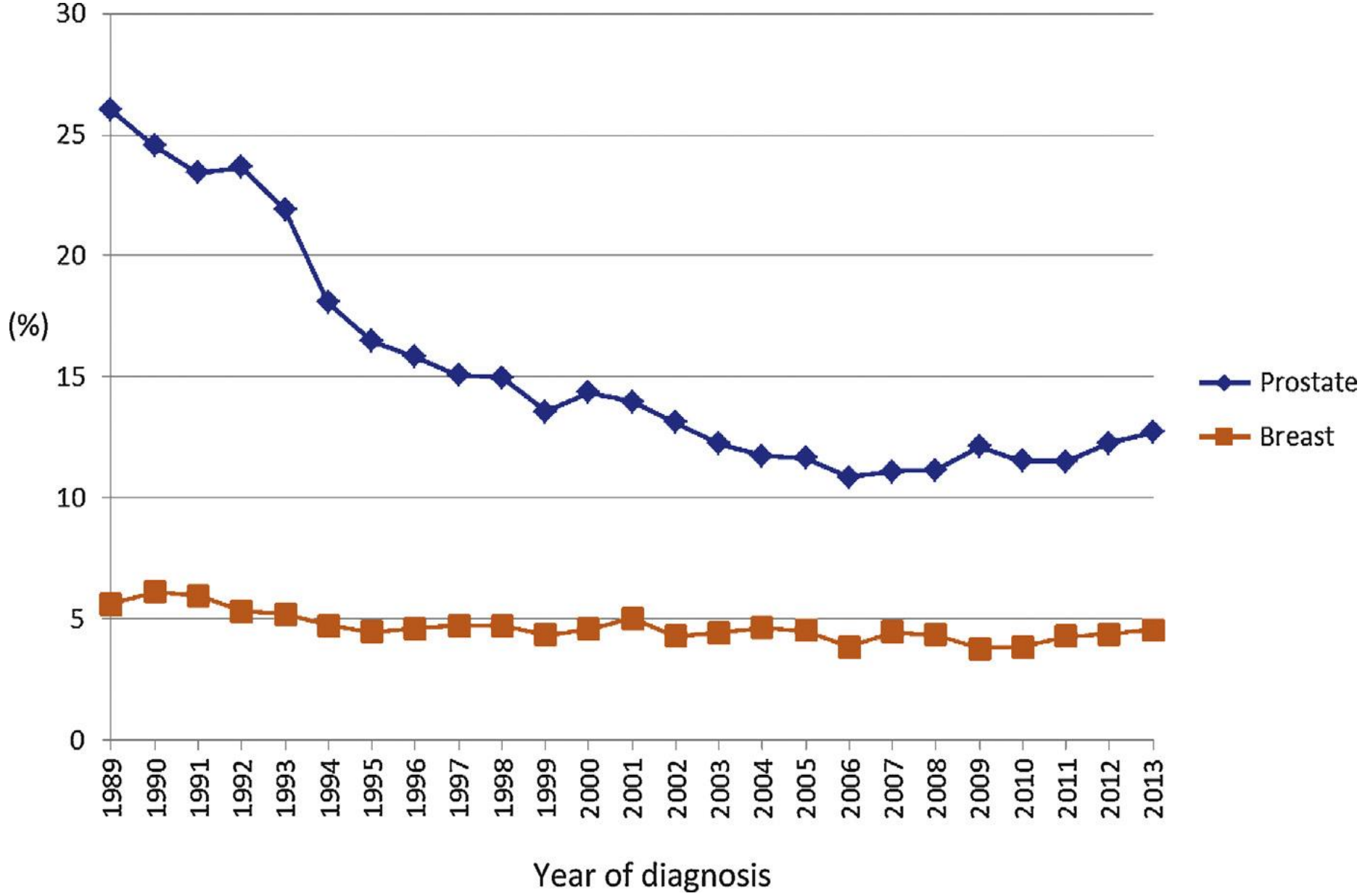
GUSTAVE ROUSSY

CANCER CAMPUS
GRAND PARIS

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

disclosures:

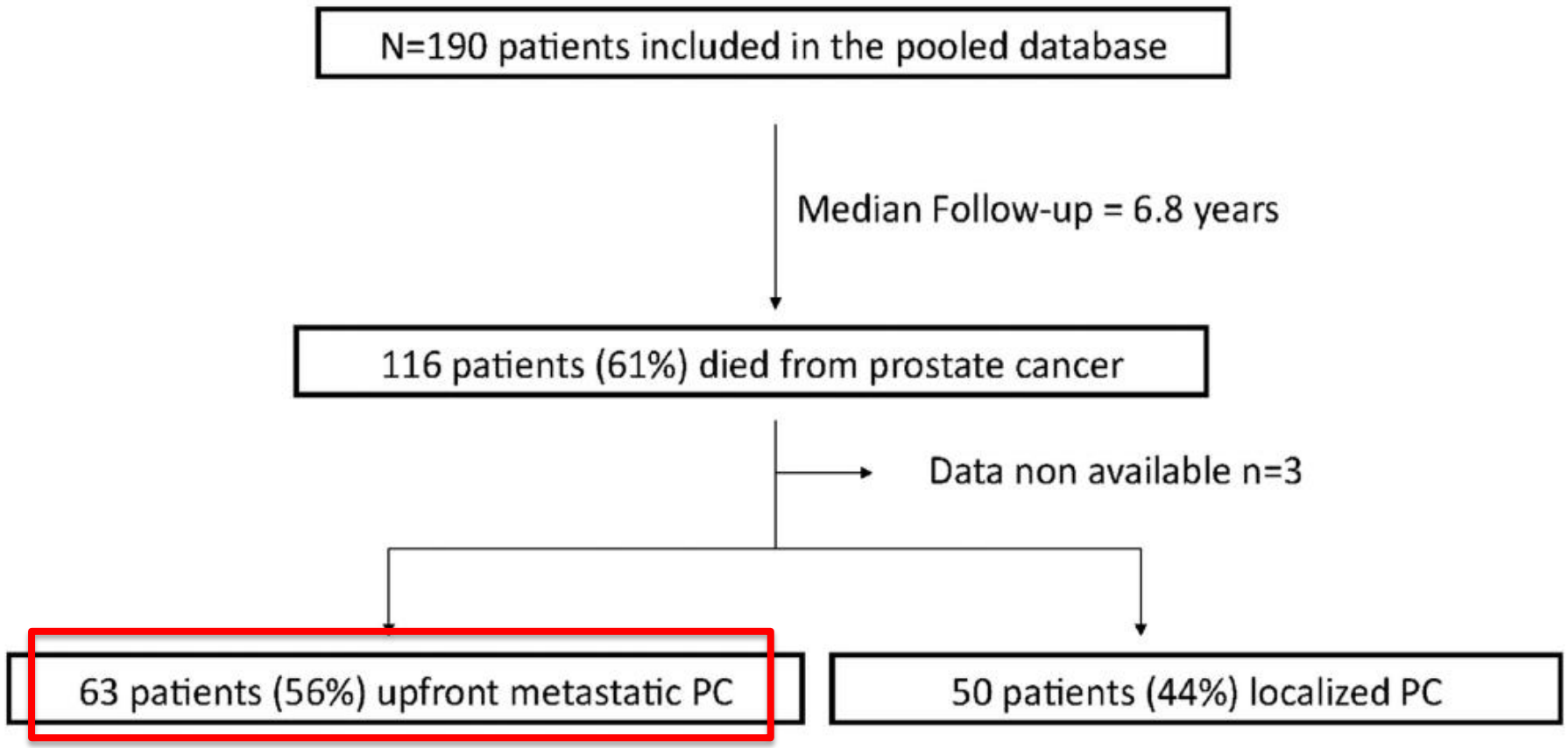
Astellas
Bard
BMS
Elekta-Brachytherapy
Ferring
Ipsen
Janssen
Sanofi



The Netherlands Cancer Registry www.cijfersoverkanker.nl.

2008 – 2011, mCRPC

Who dies from prostate cancer?
A Patrikidou *et al*



Patrikidou et al, Prostate, 2014

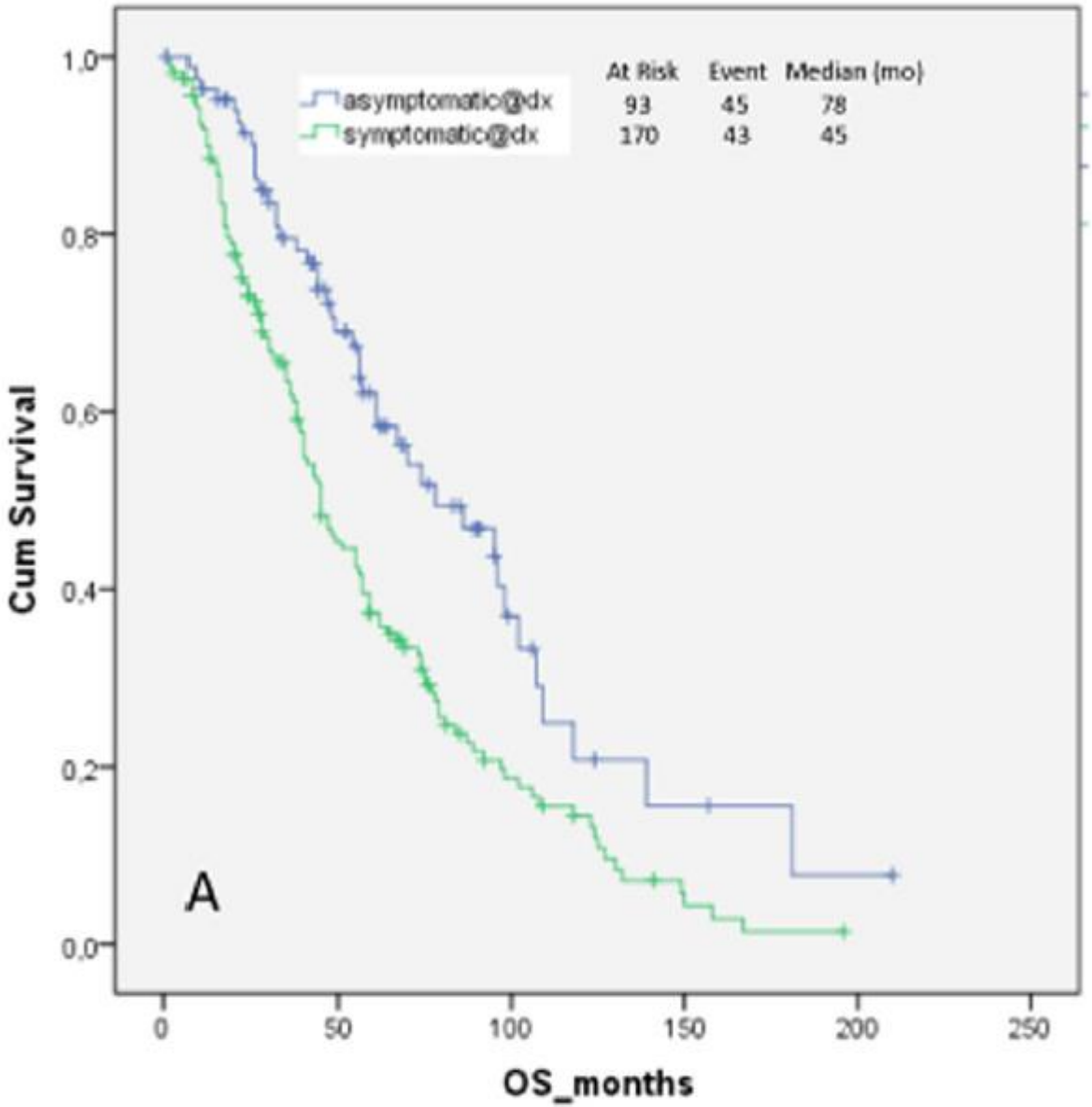
2008 – 2011, mCRPC

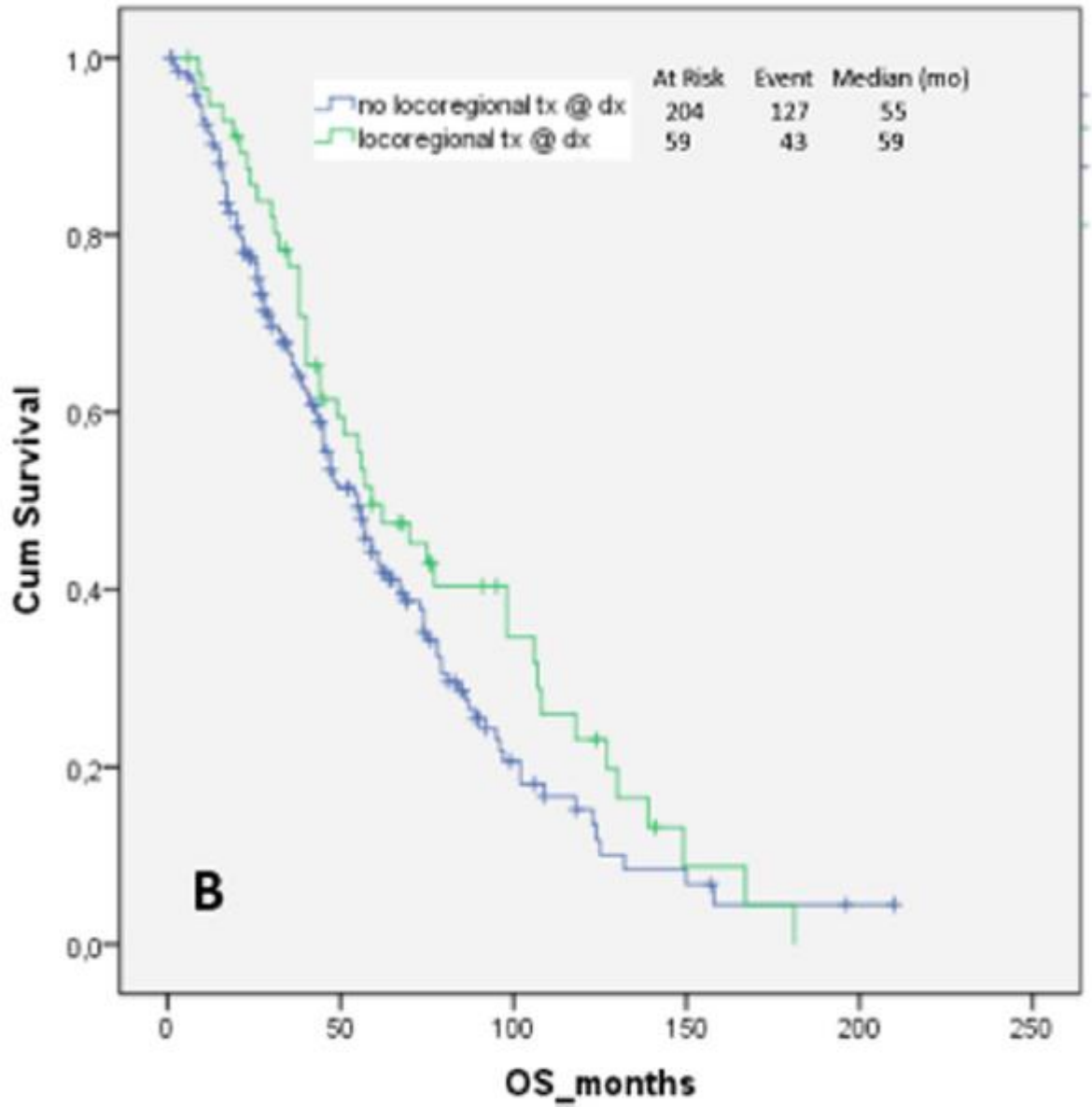
Who dies from prostate cancer?
A Patrikidou *et al*

N=190 patients included in the pooled database

63 patients (56%

Characteristics	*Metastatic patients* (n = *63*)
Age (years)	
Median (range)	63 (47–81)
Unknown (*n*, %)	1 (1.6)
Metastatic sites (n, %)	
Bone	42 (66.7)
Lymph node	27 (42.8)
N1	25 (39.7)
M1a	2 (3.2)
Visceral	7 (11.1)
Multiple sites	9 (14.3)
Unknown	0 (0.0)





Patrikidou et al, Urol Oncol, 2015

Table 13.1: Prognostic factors for the heterogeneous M1 population for patients with advanced prostate cancer (3)

Prognostic factors	Good		Intermediate		Poor
Axial bone metastasis and/or nodes	X				
Appendicular bone or visceral metastasis		X	X	X	X
Performance status < 1		X	X		
Performance status ≥ 1				X	X
Gleason score < 8		X			
Gleason score ≥ 8			X		
PSA < 65				X	
PSA ≥ 65					X
Median survival (months)	54		30		21

PSA = prostate specific antigen.

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

European Association of Urology

Review – Prostate Cancer

Does Local Treatment of the Prostate in Advanced and/or Lymph Node Metastatic Disease Improve Efficacy of Androgen-Deprivation Therapy? A Systematic Review

Paul C.M.S. Verhagen [a,*], *Fritz H. Schröder* [a], *Laurence Collette* [b], *Chris H. Bangma* [a]

[a] *Department of Urology, Erasmus MC, Rotterdam, The Netherlands*
[b] *European Organisation of Research and Treatment of Cancer Headquarters, Statistics Department, Brussels, Belgium*

Eur Urol, 2010

…analogy with other cancers

…seed and soil uni-directional hypothesis

…self-seeding multidirectional hypothesis

…intratumoral synthesis of testosterone

…second wave of distant mets by uncontrolled primary

…reduction of CTC

Aoun et al, Biomed Research Int, 2014

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

Platinum Priority – Prostate Cancer

Editorial by Brian F. Chapin, Sean E. McGuire and Ana Aparicio on pp. 1067–1068 of this issue

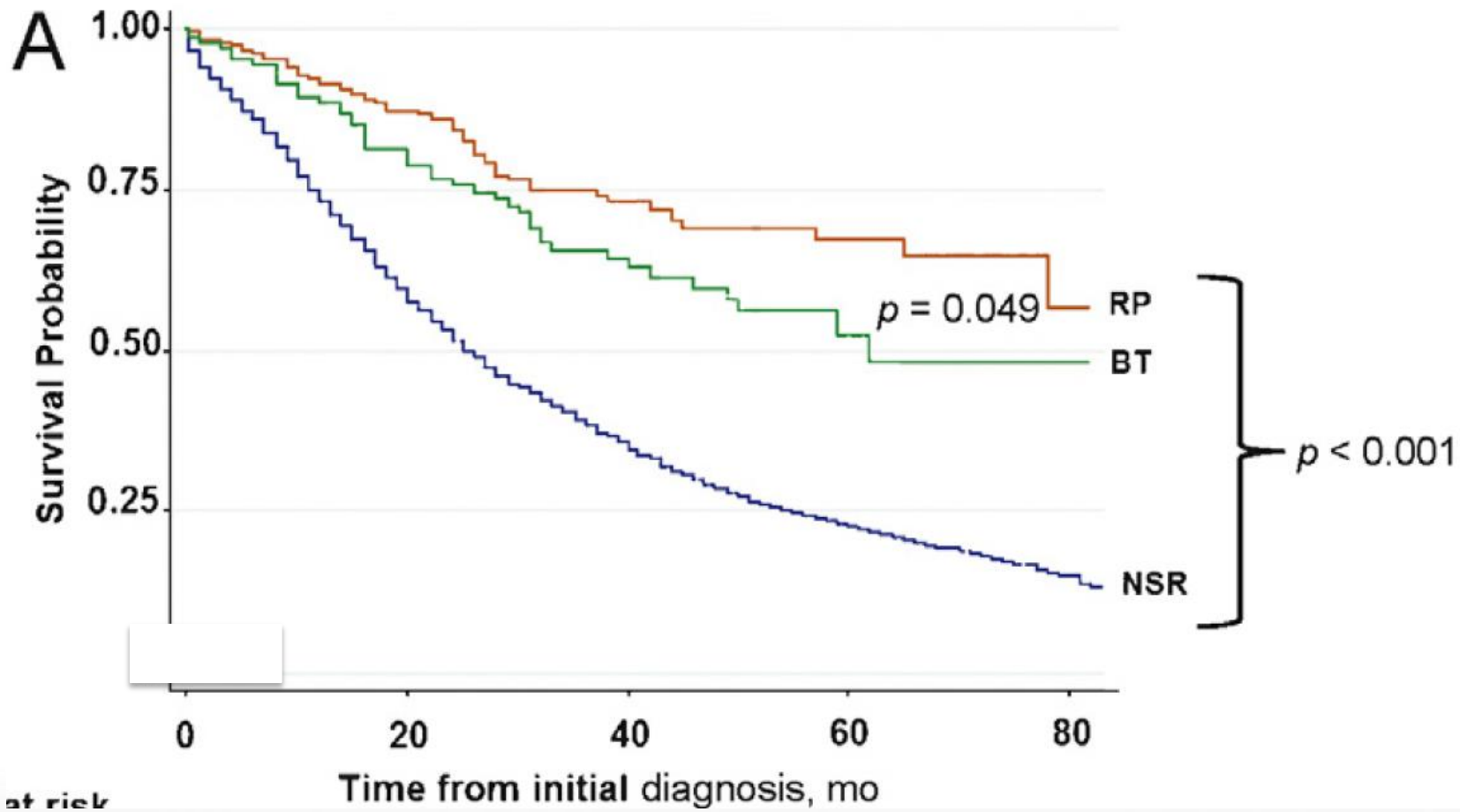
Might Men Diagnosed with Metastatic Prostate Cancer Benefit from Definitive Treatment of the Primary Tumor? A SEER-Based Study

Stephen H. Culp[a,*], *Paul F. Schellhammer*[b], *Michael B. Williams*[b]

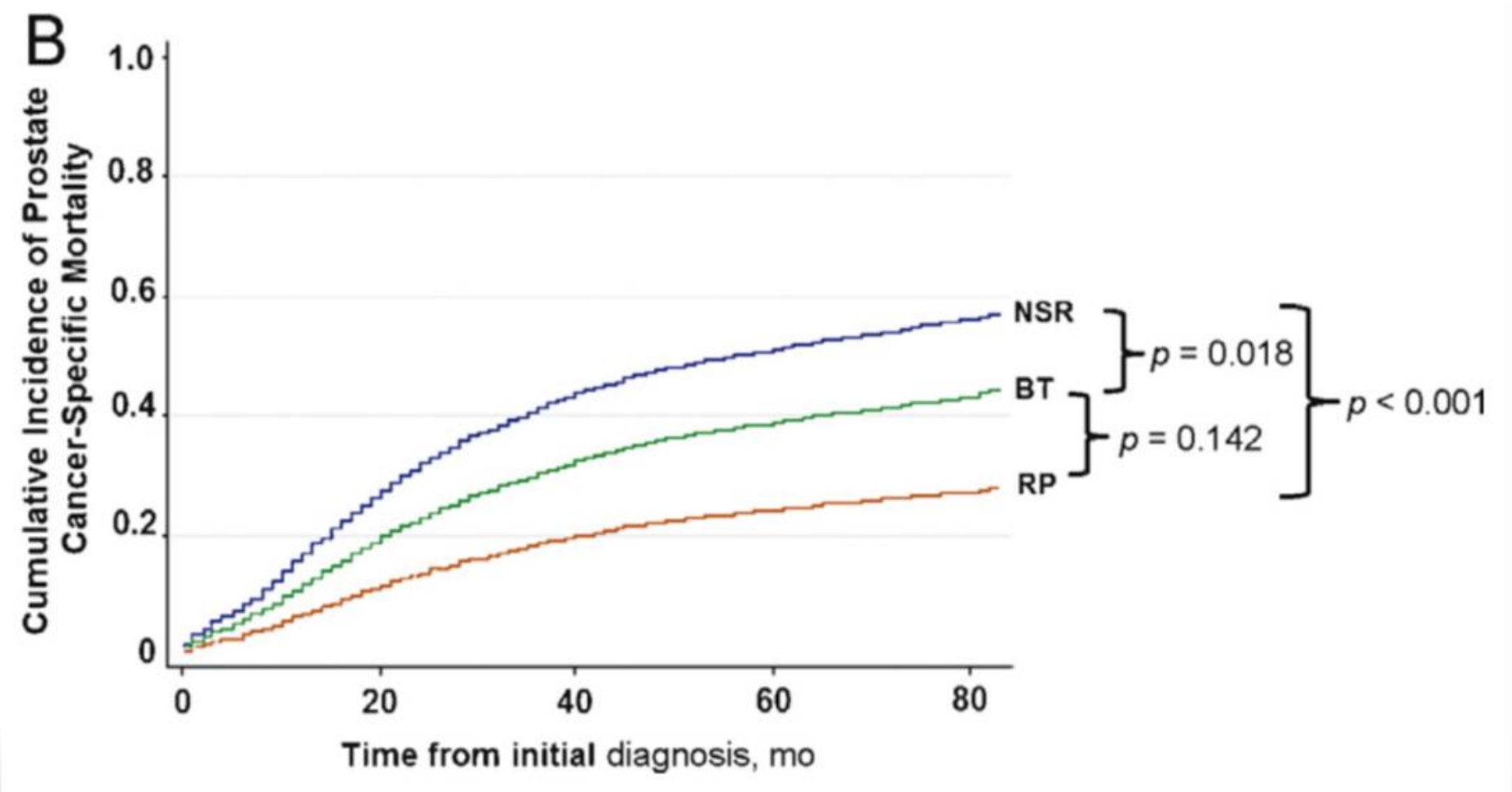
Table 1 – Patient characteristics

Characteristic	No surgery or radiation therapy (n = 7811)	Radical prostatectomy (n = 245)	p value[a]	Brachytherapy (n = 129)	p value[b]
Median age, yr (IQR)^	72 (63–80)	62 (58–67)	<0.001	68 (61–74)	<0.001
AJCC M stage, no. (%)^			0.004		0.002
M1a	463 (5.9)	24 (9.8)		16 (12.4)	
M1b	5469 (70.0)	150 (61.2)		75 (58.1)	
M1c	1879 (24.1)	71 (29.0)		38 (29.5)	

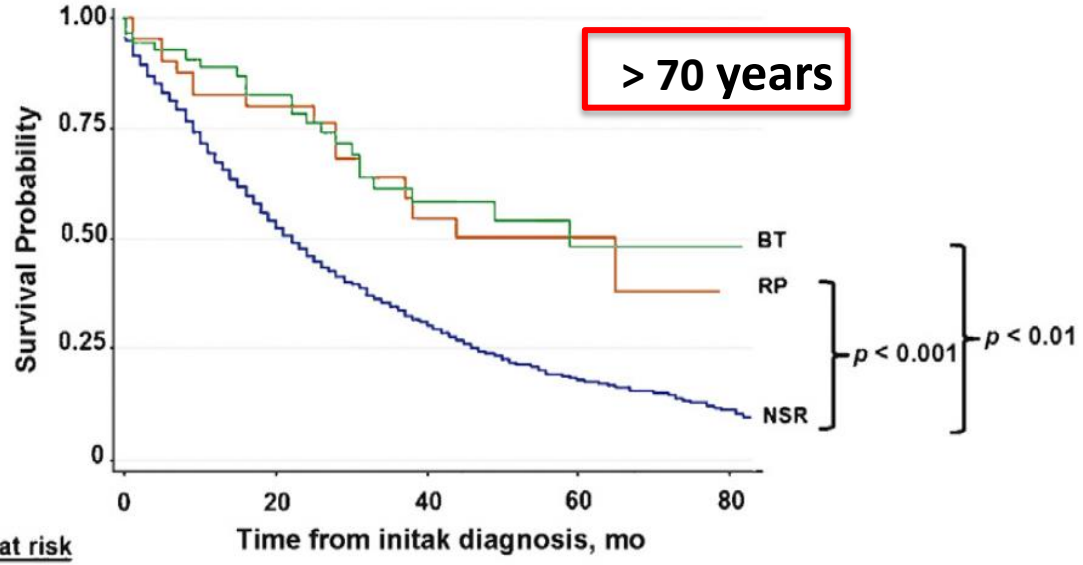
Survie globale



Survie specifique



B

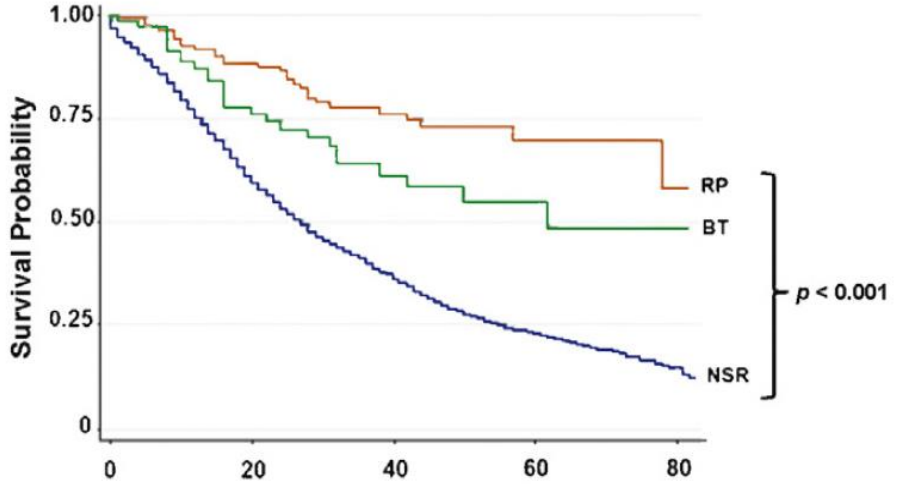


> 70 years

Number at risk

NSR	4487	1760	664	212	22
RP	43	26	12	5	0
BT	55	39	17	8	2

M1b



Number at risk

NSR	5469	2365	902	304	39
RP	150	98	49	19	3
BT	75	45	23	9	2

EUROPEAN UROLOGY 65 (2014) 1058–1066

As such, we do not advocate LT based on these data alone but instead in the context of organized prospective clinical trials designed not only to demonstrate a survival benefit with LT of the primary tumor but also to identify patients most likely to benefit.

Brief Correspondence

Identifying Optimal Candidates for Local Treatment of the Primary Tumor Among Patients Diagnosed with Metastatic Prostate Cancer: A SEER-based Study

Nicola Fossati [a,b], *Quoc-Dien Trinh* [c], *Jesse Sammon* [d], *Akshay Sood* [d], *Alessandro Larcher* [b,e], *Maxine Sun* [e], *Pierre Karakiewicz* [e], *Giorgio Guazzoni* [b], *Francesco Montorsi* [b], *Alberto Briganti* [b], *Mani Menon* [d], *Firas Abdollah* [d,*]

we found that LT conferred a survival benefit at 3 yr after diagnosis only in patients with a CSM risk ≤40%.

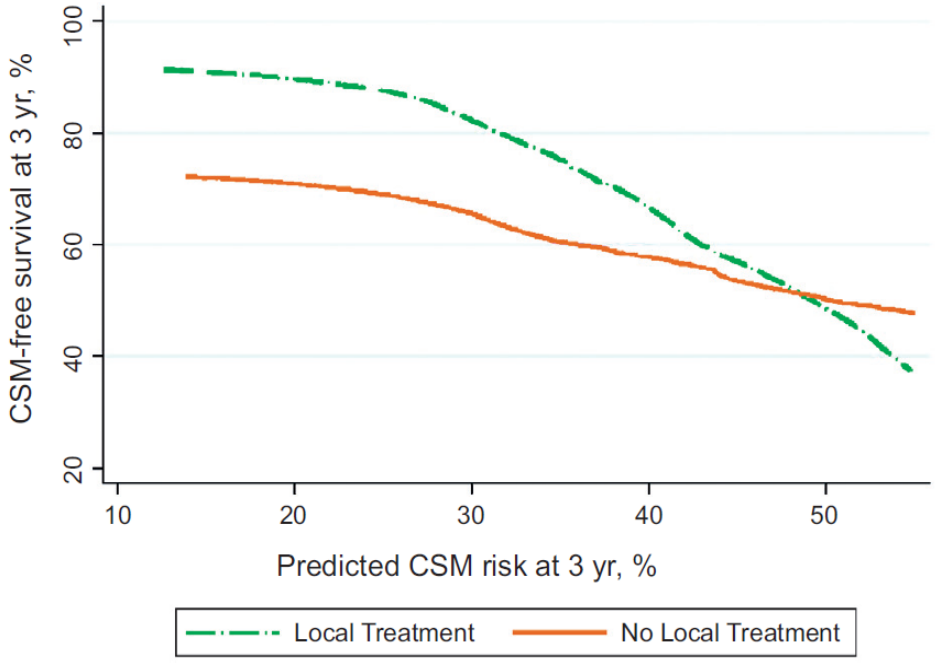


Fig. 1 – Cancer-specific mortality (CSM)–free survival rate plotted against predicted probability of CSM at 3 yr after diagnosis. Dashed green line indicates local treatment of the primary tumor. Solid orange line indicates no local treatment of the primary tumor.
CSM = cancer-specific mortality.

Fossati et al, Eur Urol, in press

Brief Correspondence

Identifying Optimal Candidates for Local Treatment of the Primary Tumor Among Patients Diagnosed with Metastatic Prostate Cancer: A SEER-based Study

Nicola Fossati [a,b], *Quoc-Dien Trinh* [c], *Jesse Sammon* [d], *Akshay Sood* [d], *Alessandro Larcher* [b,e], *Maxine Sun* [e], *Pierre Karakiewicz* [e], *Giorgio Guazzoni* [b], *Francesco Montorsi* [b], *Alberto Briganti* [b], *Mani Menon* [d], *Firas Abdollah* [d,*]

$$X\beta = -0.0077575 * \mathbf{age} + 0.0000027 * \mathbf{sp[age]1} + 0.0000378 * \mathbf{sp[age]2} + 0.0043901 * \mathbf{psa} + 0.2845397 * \mathbf{gleason7} + 0.6852518 * \mathbf{gleason8} + 0.1021685 * \mathbf{Tstage3} + 0.1372309 * \mathbf{Nstage1} + 0.4461924 * \mathbf{Mstage1b} + 0.7113211 * \mathbf{Mstage1c}$$

$$Risk = 1 - 0.8067804^{e^{X\beta}}$$

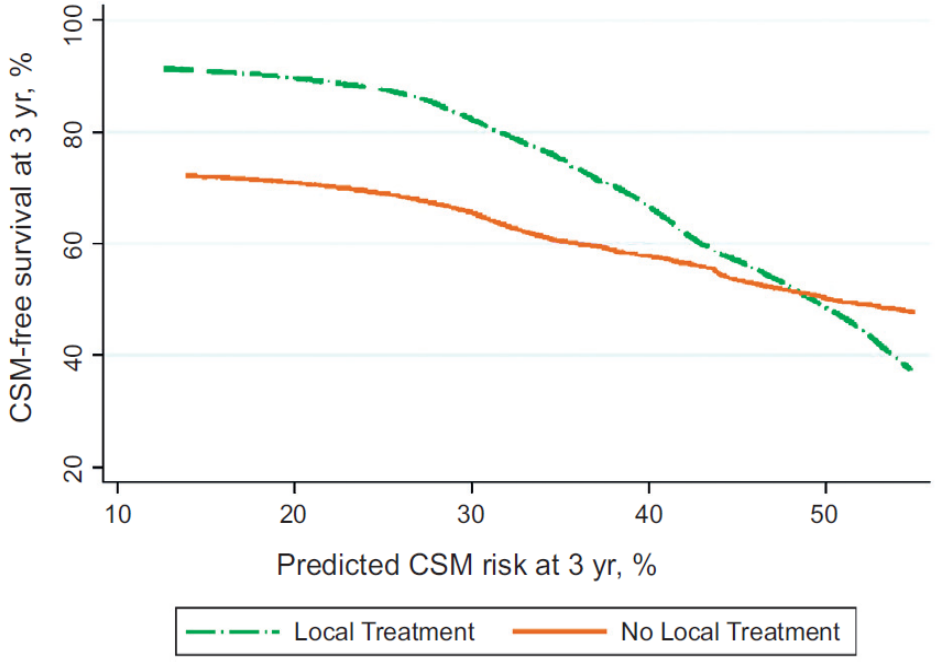
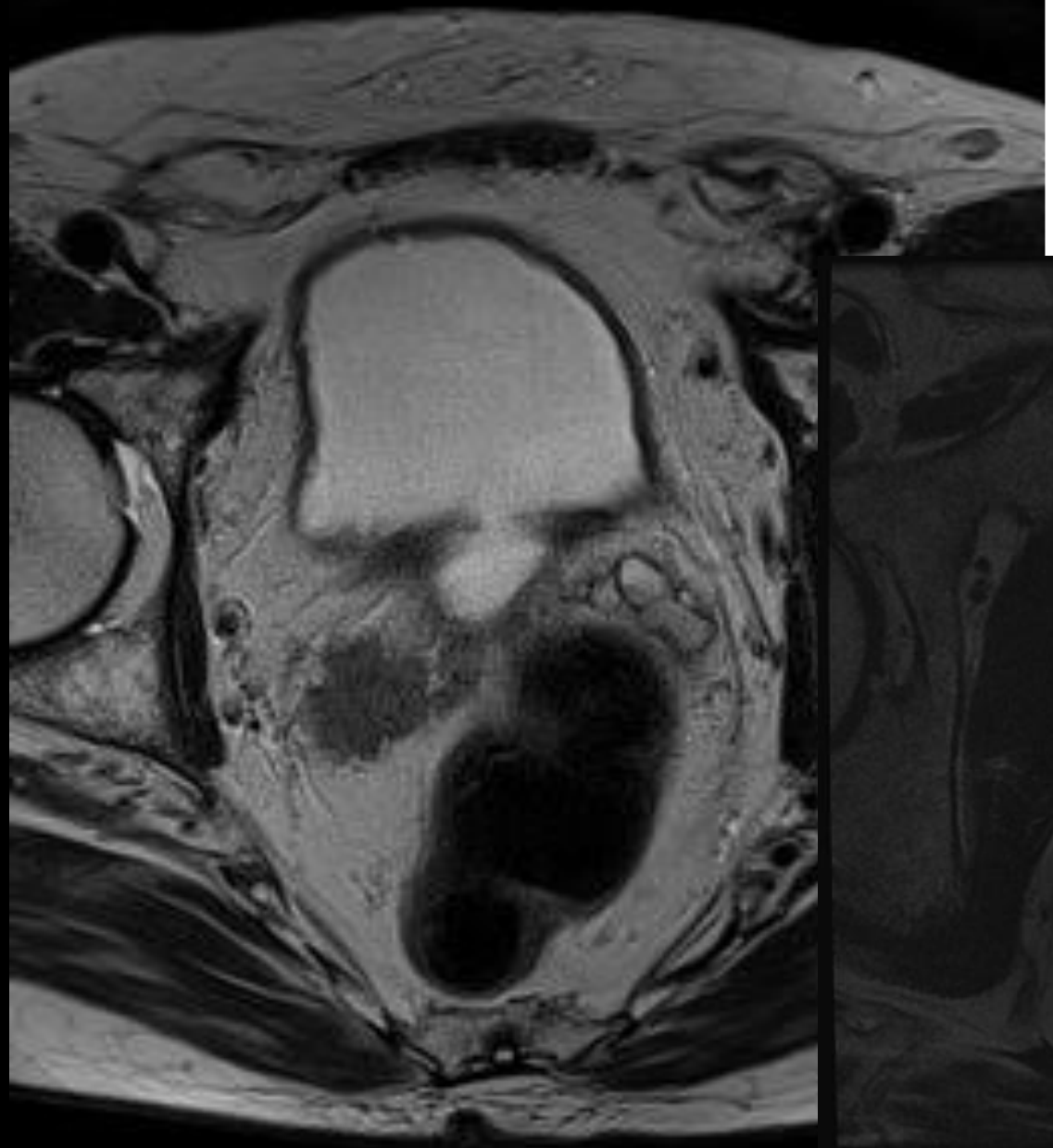
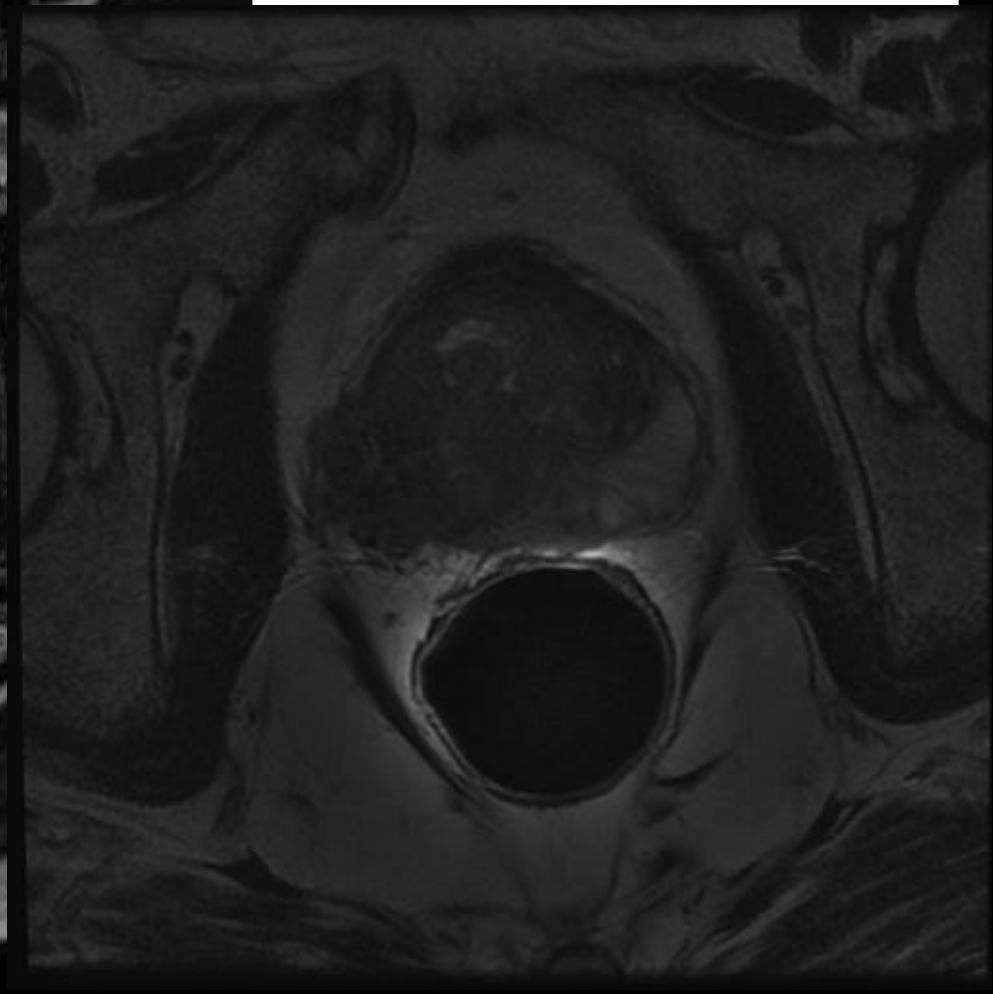


Fig. 1 – Cancer-specific mortality (CSM)–free survival rate plotted against predicted probability of CSM at 3 yr after diagnosis. Dashed green line indicates local treatment of the primary tumor. Solid orange line indicates no local treatment of the primary tumor.
CSM = cancer-specific mortality.

Fossati et al, Eur Urol, in press





cT3

PSA = 19 ng/ml

GPS = 4+4

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

European Association of Urology

Platinum Priority – Prostate Cancer
Editorial by XXX on pp. x–y of this issue

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

Prasanna Sooriakumaran[a,b], Jeffrey Karnes[c], Christian Stief[d], Bethan Copsey[e], Francesco Montorsi[f], Peter Hammerer[g], Burkhard Beyer[h], Marco Moschini[c], Christian Gratzke[d], Thomas Steuber[h], Nazareno Suardi[f], Alberto Briganti[f], Lukas Manka[g], Tommy Nyberg[b], Susan J. Dutton[e], Peter Wiklund[b,i], Markus Graefen[h,]*

106 pts
6 high-volume Prostate surgery Centres

Table 2 – Preoperative comorbidity scores and staging for the whole cohort

	n (%)
Charlson comorbidity index	
0	58 (77.3)
1	17 (22.7)

Sooriakumaran, Eur Urol, in press

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

European Association of Urology

106 pts
6 high-volume Prostate surgery Centres

Platinum Priority – Prostate Cancer
Editorial by XXX on pp. x–y of this issue

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

Prasanna Sooriakumaran[a,b], Jeffrey Karnes[c], Christian Stief[d], Bethan Copsey[e], Francesco Montorsi[f], Peter Hammerer[g], Burkhard Beyer[h], Marco Moschini[c], Christian Gratzke[d], Thomas Steuber[h], Nazareno Suardi[f], Alberto Briganti[f], Lukas Manka[g], Tommy Nyberg[b], Susan J. Dutton[e], Peter Wiklund[b,i], Markus Graefen[h,]*

PRE-operative STAGE	n (%)
T0 – 2	67 (62,2)
T3a – T3b	17 (16)
T4	13 (12,3)
N0 - X	61 (57,5)
N1	45 (42,5)

Table 2 – Preoperative comorbidity scores and staging for the whole cohort

	n (%)
Charlson comorbidity index	
0	58 (77.3)
1	17 (22.7)

Sooriakumaran, Eur Urol, in press

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

European Association of Urology

106 pts
6 high-volume Prostate surgery Centres

Platinum Priority – Prostate Cancer
Editorial by XXX on pp. x–y of this issue

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

Prasanna Sooriakumaran[a,b], Jeffrey Karnes[c], Christian Stief[d], Bethan Copsey[e], Francesco Montorsi[f], Peter Hammerer[g], Burkhard Beyer[h], Marco Moschini[c], Christian Gratzke[d], Thomas Steuber[h], Nazareno Suardi[f], Alberto Briganti[f], Lukas Manka[g], Tommy Nyberg[b], Susan J. Dutton[e], Peter Wiklund[b,i], Markus Graefen[h,]*

Table 2 – Preoperative comorbidity scores and staging for the whole cohort

	n (%)
Charlson comorbidity index	
0	58 (77.3)
1	17 (22.7)

PRE-operative STAGE	n (%)
T0 – 2	67 (62,2)
T3a – T3b	17 (16)
T4	13 (12,3)
N0 - X	61 (57,5)
N1	45 (42,5)

POST-operative STAGE	n (%)
pT0 – 2	23 (21,7)
pT3a – T3b	71 (67)
pT4	12 (11,3)
pN0 – X	30 (28,3)
pN1	76 (71,7)
Positive Margins	57 (54,3)

Sooriakumaran, Eur Urol, in press

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

European Association of Urology

106 pts
6 high volume Prostate surgery Centres

Platinum Priority – Prostate Cancer
Editorial by XXX on pp. x–y of this issue

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

Prasanna Sooriakumaran[a,b], Jeffrey Karnes[c], Christian Stief[d], Bethan Copsey[e], Francesco Montorsi[f], Peter Hammerer[g], Burkhard Beyer[h], Marco Moschini[c], Christian Gratzke[d], Thomas Steuber[h], Nazareno Suardi[f], Alberto Briganti[f], Lukas Manka[g], Tommy Nyberg[b], Susan J. Dutton[e], Peter Wiklund[b,i], Markus Graefen[h,]*

Table 2 – Preoperative comorbidity scores and staging for the whole cohort

	n (%)
Charlson comorbidity index	
0	58 (77.3)
1	17 (22.7)

Table 3 – Operative approach, overall complications, operative time, and length of hospital stay stratified by center

Center	Patients (*n*)	Approach		Operative time (min)	Length of stay
		Open, *n* (%)	Robotic (*n*)		
1	31	31 (100)	0	190 (164–247)	3 (3–5)
2	31	27 (87.1)	4	79.5 (67–140)	11 (9–13)
3	25	25 (100)	0	180 (156–212.5)	7 (6–8)
4	11	11 (100)	0	170 (160–380)	13 (7–19)
5	5	0 (0)	5	147 (130–180)	3 (3–3)
6	3	3 (100)	0	159 (147–170)	9 (7–10)

Data for operative time and length of stay are presented as median (interquartile range).

COMPLICATIONS	n (%)
Blood Transfusion	15 (14,2)
Hematoma / Lymphocele	11 (10,4)
Re-admission	6 (5,7)
Infection / Sepsis	6 (5,7)

Sooriakumaran, Eur Urol, in press

Urinary continence recovery after Radical Prostatectomy

Fig. 4 Kaplan–Meier analysis depicting urinary continence recovery after radical prostatectomy according to preoperative risk groups.

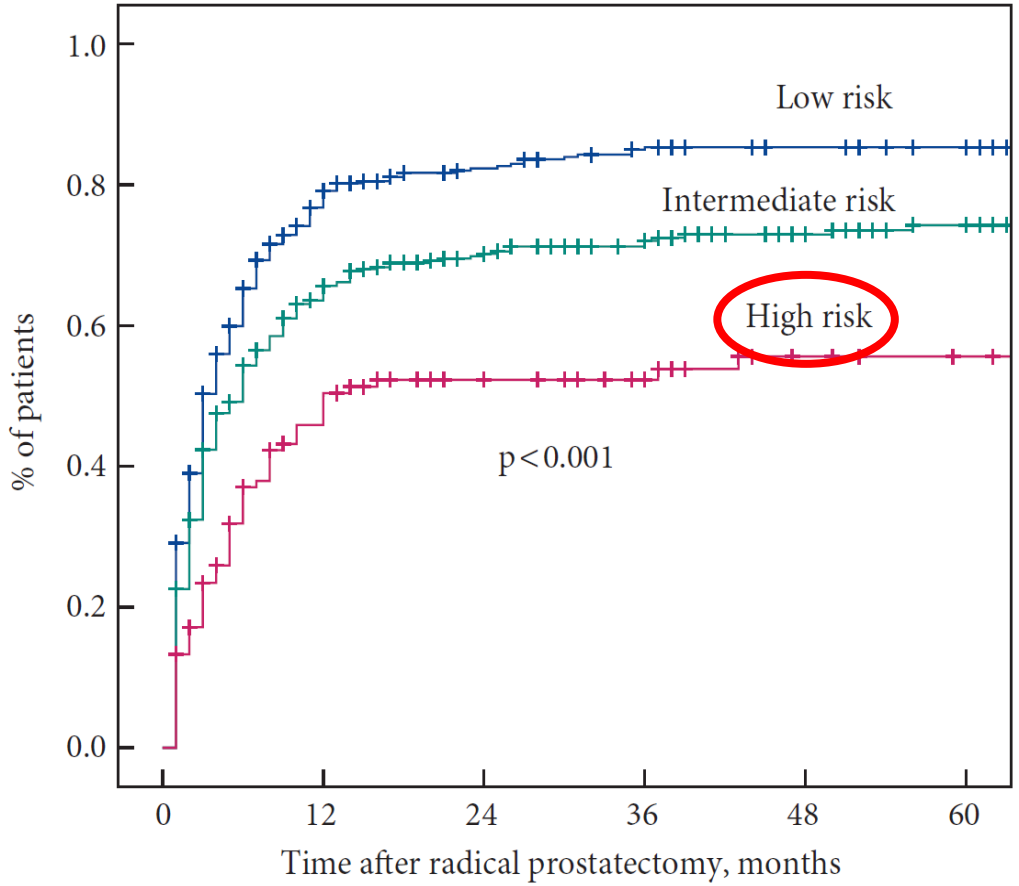
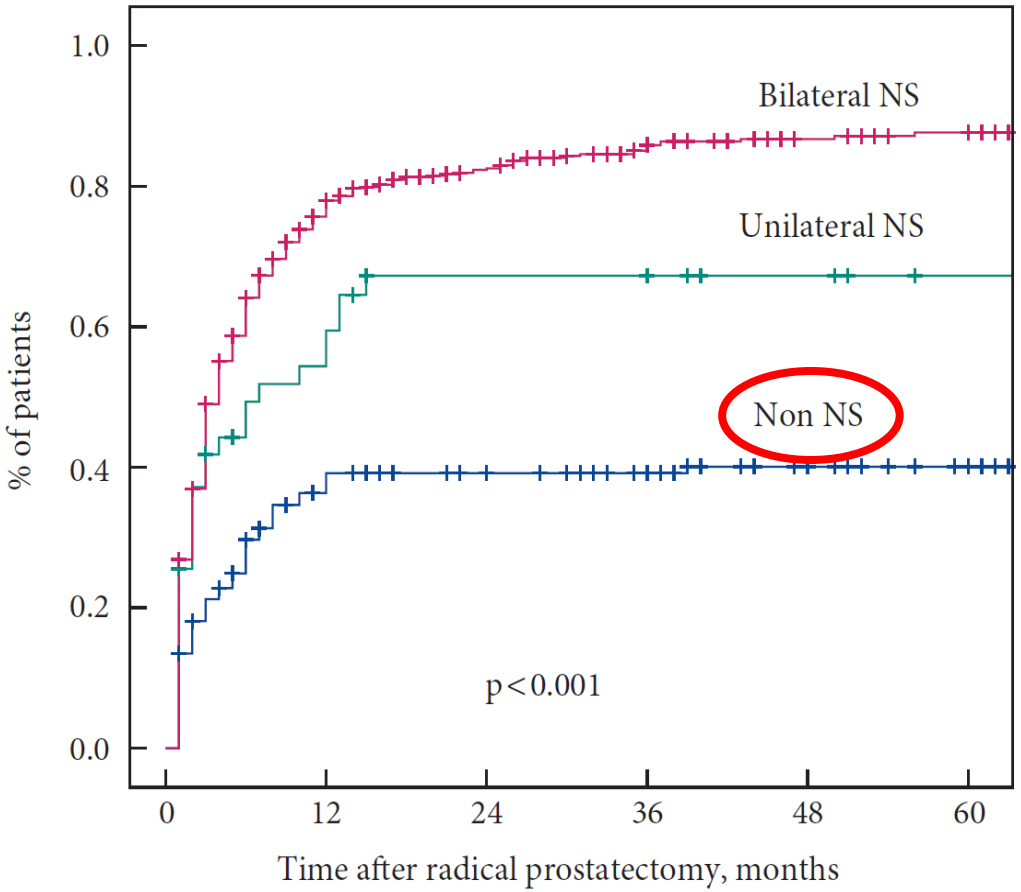


Fig. 2 Kaplan–Meier analysis depicting urinary continence recovery after radical prostatectomy according to nerve-sparing status.



Suardi et al, BJUI, 2012

A prospective, randomised study into the effect on survival of hormonal treatment versus hormonal treatment plus local external radiotherapy in patients with primary metastatic (bone) prostate cancer.

- *the HORRAD study* -

6. Study set-up

It is a prospective, comparative, open study whereby the patients are randomised into two groups:

Group 1: hormone treatment by means of an analogous LHRH (Eligard) every 3 months and an anti-androgen (Casodex 50 mg 1 dd 1) for 4 weeks, to start 1-2 weeks before the first administering of the analogous LHRH.

Group 2: hormone treatment by means of an analogous LHRH (Eligard) every 3 months and an anti-androgen (Casodex 50 mg 1 dd 1) for 4 weeks, to start 1-2 weeks before the first administering of the analogous LHRH, combined with local external radiotherapy of the prostate.

Courtesy of F. van den Bergh

A prospective, randomised study into the effect on survival of hormonal treatment versus hormonal treatment plus local external radiotherapy in patients with primary metastatic (bone) prostate cancer.

- *the HORRAD study* -

Within 3 months of the first injection of Eligard a start is made on the radiotherapy treatment. Hereby a curative dose is given with a dose equivalent to 70 Gy in 35 fractions of 2 Gy, assuming a constant normal tissue damage (a/b = 3). The dose is specified at the isocentrum. The proposed dose scheme is 24 parts of 2.6 Gy in 5 weeks, but a conventional scheme of 70 Gy in 7 weeks is permitted. The overall time may thus vary from 5 to 7 weeks, and the daily parts from 2 to 2.6 Gy. The target area consists of the prostate with any demonstrable extraprostatic tumour expansion including the base of the vesicula seminales (CTV). It is permitted as standard to choose the entire vesiculum as CTV. The target area to be planned (PTV) consists of the CTV including 1 cm margin in all directions. The CTV/PTV must be marked with a CT scan. The irradiation must be carried out by means of conformance with the planning. No elective target areas will be irradiated. For other possible dose schemes discussions can be held with the study co-ordinator.

A prospective, randomised study into the effect on survival of hormonal treatment versus hormonal treatment plus local external radiotherapy in patients with primary metastatic (bone) prostate cancer.

- the HORRAD study -

Aims of the study	Primary – survival Secondary – biochemical progression, quality of life (24 months)

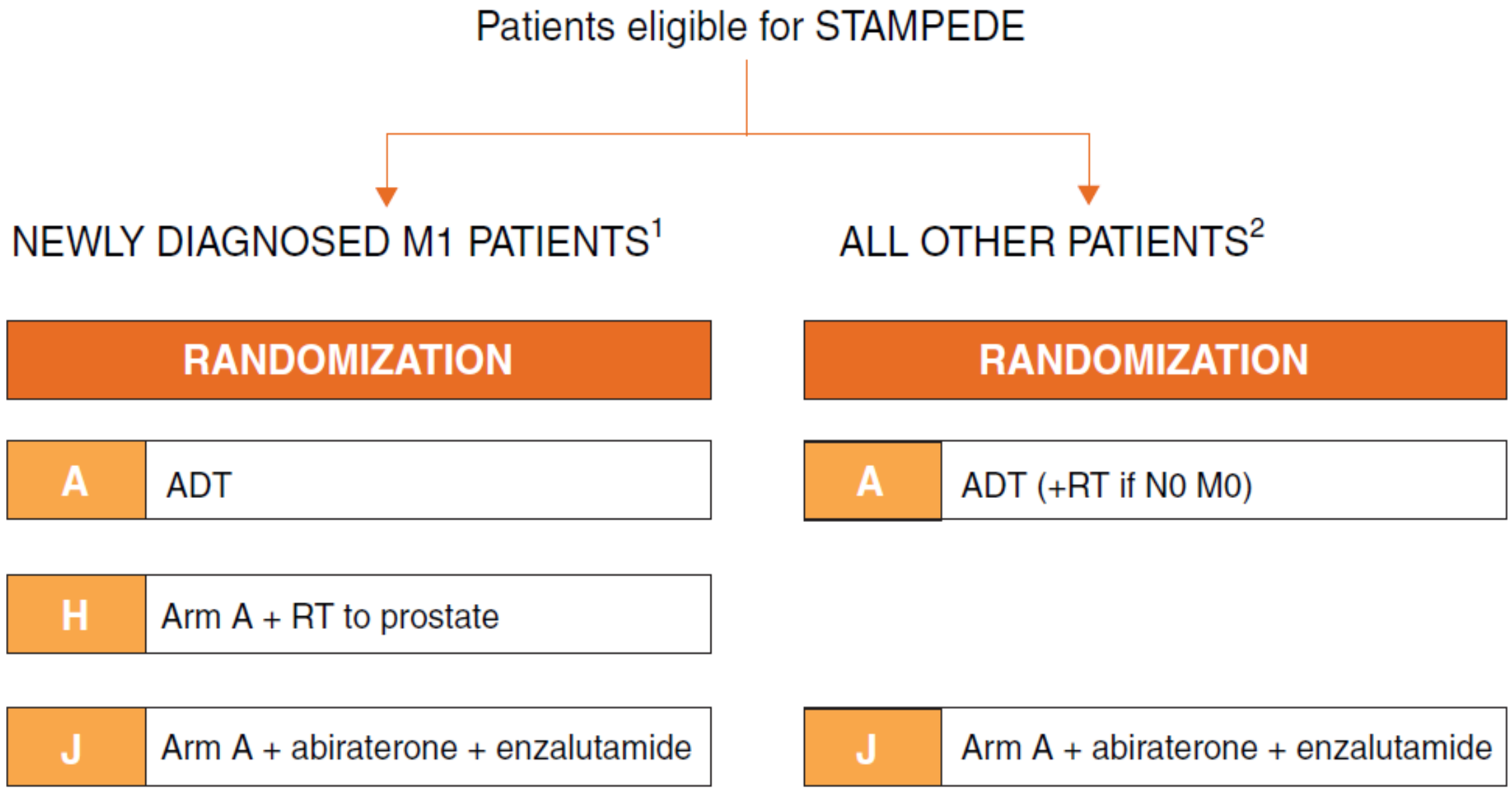
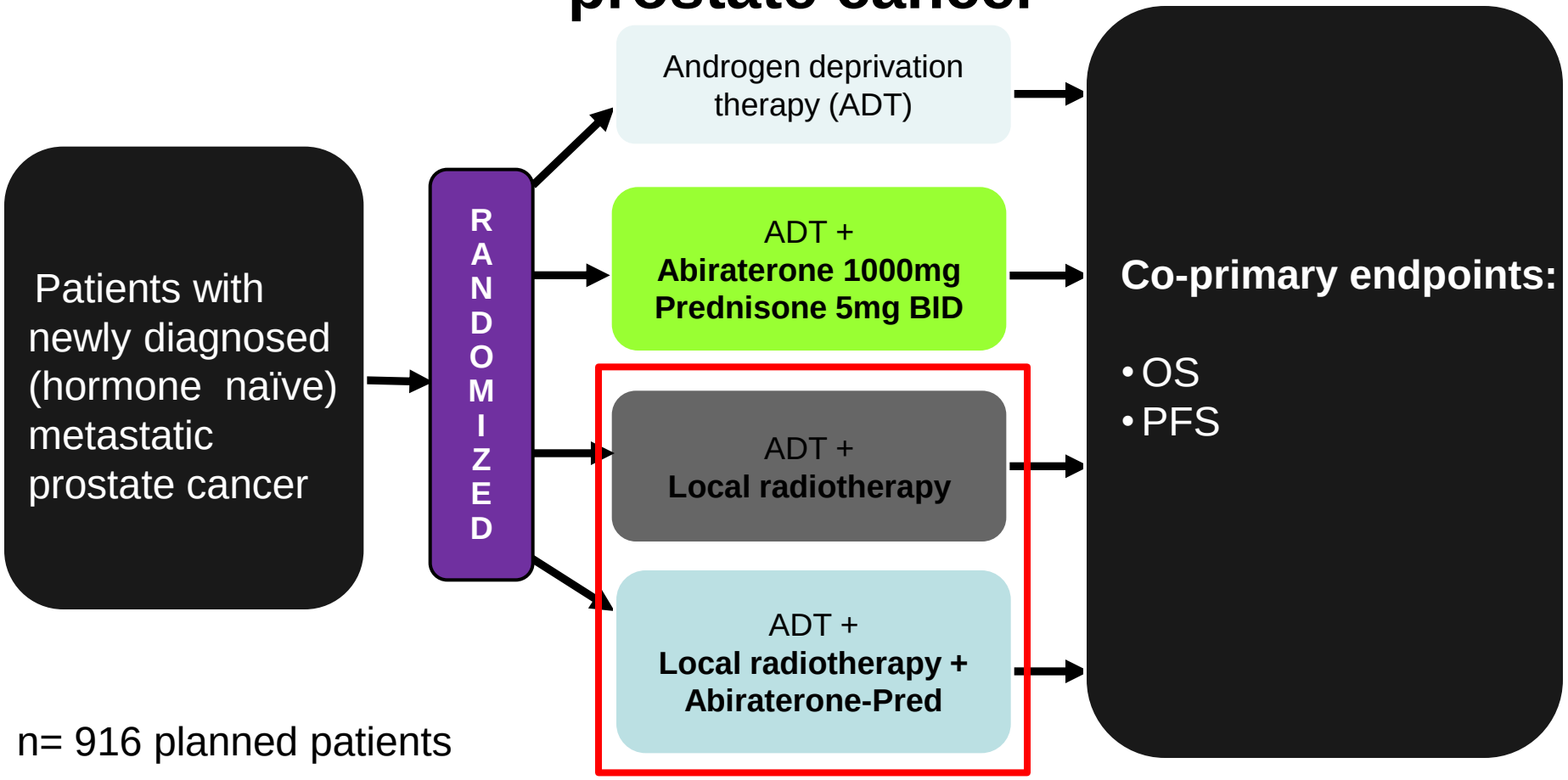


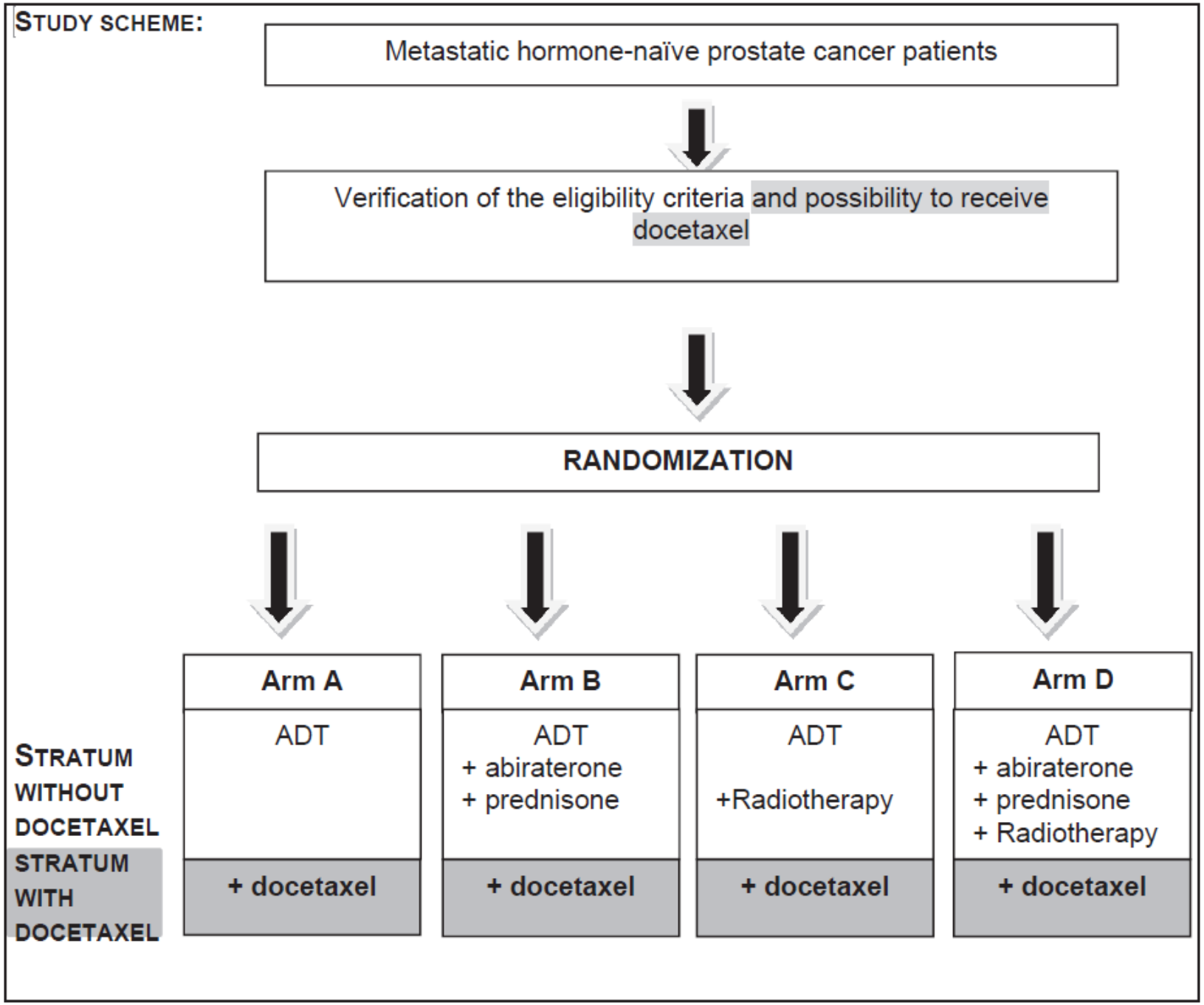
Fig. 1 – Study design for the STAMPEDE trial (protocol version 12.0 with inclusion of enzalutamide + abiraterone comparison). Source: STAMPEDE trial. Protocol version 12.0. http://www.stampedetrial.org/PDF/STAMPEDE_Protocol_v12.0_clean.pdf

GETUG-EORTC-PEACE-1: European Phase III Trial of Abiraterone and Radiotherapy in patients with newly diagnosed metastatic prostate cancer



n= 916 planned patients

Study sponsor: Unicancer, EORTC



Octobre 2015

SECONDARY OBJECTIVES:

- PSA response rate, as defined by an undetectable serum PSA level at 8 months
- Prospective correlative study of PSA response/progression at 8 months and overall survival
- Radiological progression-free survival (as defined by RECIST criteria or by the appearance of at least 2 new bone metastases on bone scan)
- Time to pain progression
- Time to next skeletal-related event
- Time to chemotherapy
- Time to severe local symptoms
- Toxicity (with a specific focus on the use of long-term low-dose steroids)
- Prostate cancer specific survival

EBRT

volumes : **prostate (+/- SV)**
pelvis ?

total dose/fraction (Gy): **74 / 37 fr**

55 / 20 fr ?

60,5 / 22 fr ?

57 / 19 fr ?

SBRT: 32,5 / 5 ?

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

…conclusions…