


  
**BAU2018**  
 18<sup>th</sup> ANNUAL CONGRESS  
 BELGIAN ASSOCIATION OF UROLOGY  
Doker - La Hulst/Terhulpen 7 & 8 DECEMBER 2018

CASE 2


Dr. Filip Poelaert




GHENT UNIVERSITY

CASE 2

Male, 69 years old

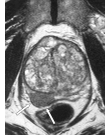


9/2015 Prostate cancer

cT3, iT2a iN0

GG4 (G1 4+5, 3/12+)

PSA 7.38



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WHAT TO DO?

1. Watchfull waiting
2. CT + bone scan
3. PSMA PET-CT
4. RP
5. EBRT
6. ADT

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CASE 2

Male, 69 years old



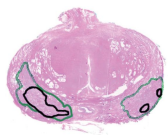
09/2015 PCa iT2a cN0M0 GG4 iPSA 7.38

> RA radical prostatectomy + PLND (10/2015):

pT2c pN1 (1/15)

GG4 (G1 4+4)

RO



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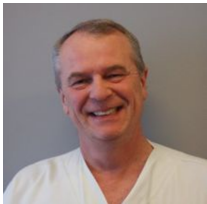
WHAT TO DO?




1. ADT
2. Adjuvant wpRT
3. Adjuvant wpRT + ADT
4. ADT + abiraterone
5. PSA surveillance
6. Watchfull waiting

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• The view of the Urologist



### The Role of Radical Prostatectomy and Lymph Node Dissection in Lymph Node-Positive Prostate Cancer: A Systematic Review of the Literature



Table 3 - Overview of most recent trials reporting survival in patients with high-risk prostate cancer according to treatment regimen

Author	Treatment	Overall survival		Cause-specific survival		Biochemical progression-free survival	
		5 yr	10 yr	5 yr	10 yr	5 yr	10 yr
Choudhry et al. (2015) n = 2463	RP vs. RP + LN	82	87	77	82	88	92
	RP + LN vs. RP + LN + BTLN	84	85	74	84	88	94
	RP + LN + BTLN vs. RP + LN	84	84	84	84	88	92
Bosch et al. (2015) n = 2325	RP vs. RP + LN	84	78	75	81	89	93
	RP + LN vs. RP + LN + BTLN	84	78	75	81	89	93
	RP + LN + BTLN vs. RP + LN	84	78	75	81	89	93
Mehanna et al. (2015) n = 58 with pN1	RP vs. RP + LN	74	84	70	80	80	86
	RP + LN vs. RP + LN + BTLN	74	84	70	80	80	86
	RP + LN + BTLN vs. RP + LN	74	84	70	80	80	86
Nigam et al. (2015) n = 588	RP vs. RP + LN	80	74	84	75	88	91
	RP + LN vs. RP + LN + BTLN	80	74	84	75	88	91
	RP + LN + BTLN vs. RP + LN	80	74	84	75	88	91
Choudhry et al. (2015) n = 122	RP vs. RP + LN	81.5	82.5	84.5	85.5	88.5	91.5
	RP + LN vs. RP + LN + BTLN	81.5	82.5	84.5	85.5	88.5	91.5
	RP + LN + BTLN vs. RP + LN	81.5	82.5	84.5	85.5	88.5	91.5
Mehanna et al. (2015) n = 588	RP vs. RP + LN	84	87	80	83	79	84
	RP + LN vs. RP + LN + BTLN	84	87	80	83	79	84
	RP + LN + BTLN vs. RP + LN	84	87	80	83	79	84
De Franco et al. (2015) n = 100	RP vs. RP + LN	81	81	73	73	80	81
	RP + LN vs. RP + LN + BTLN	81	81	73	73	80	81
	RP + LN + BTLN vs. RP + LN	81	81	73	73	80	81
Nigam et al. (2015) n = 588	RP vs. RP + LN	80	80	75	80	85	88
	RP + LN vs. RP + LN + BTLN	80	80	75	80	85	88
	RP + LN + BTLN vs. RP + LN	80	80	75	80	85	88
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Georgios Gakis<sup>1,2</sup>, Stephen A. Boorjian<sup>3</sup>, Alberto Briganti<sup>4</sup>, Steven Janina<sup>5</sup>, Guram Kanjanzashvili<sup>6</sup>, R. Jeffrey Karnes<sup>7</sup>, Agostino Mattei<sup>8</sup>, Shahrokh F. Shariat<sup>9</sup>, Arnulf Stenzl<sup>10</sup>, Manfred Wirth<sup>11</sup>, Christian G. Stief<sup>12</sup>, Eur Urol 2016

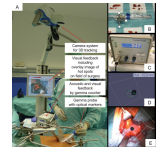
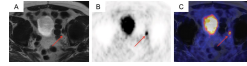
### HOW TO IMPROVE LYMPH NODE DISSECTION: Radio-guided surgery?



<sup>111</sup>In-PSMA has been used as a radiotracer for sLND

Maurer Eur Urol 2015

Similarly as in breast cancer surgery, intraoperative gamma probe



Robotic probe currently available

Results awaited

### CASE 2



Male, 69 years old

> RALP+PLND 10/2015: pT2c pN1 (1/15) R0 GG4



3wk postop: 1 pad /d, no erections

3mo postop: fully continent, no erections

PSA evolution:

12/2015	0.02
03/2016	0.04
07/2016	0.10

### WHAT TO DO?



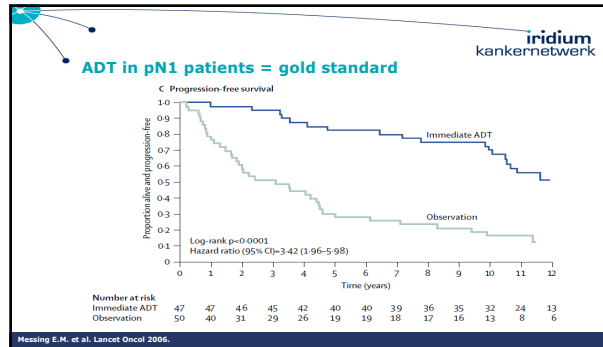
1. ADT
2. Salvage wpRT
3. Salvage wpRT + ADT
4. ADT + abiraterone
5. PSA surveillance
6. Watchfull waiting
7. PSMA PET-CT

### CASE 2



- The view of the Radiation Oncologist

Early or Salvage?



**RT could be added in a subset of patients**

**iridium kankernetwork**

**Table 1 - Univariable and multivariable Cox proportional hazards regression analyses testing the relationship between adjuvant treatment status: androgen deprivation therapy (ADT; reference category) versus adjuvant radiation therapy (aRT) + ADT on overall mortality in 5498 patients with non-metastatic lymph node-positive prostate cancer, treated with radical prostatectomy and pelvic lymph node dissection between 2004 and 2015 within the National Cancer Database. Patients were divided into groups based on previously published algorithm [5]**

Risk groups <sup>a</sup>	Treatment		Univariable analysis		Multivariable analysis	
	aRT + ADT (n)	ADT only (n)	HR (95% CI)	HR (95% CI)		
Group 1	6	13	1.46 (0.13-16.21)	-		
Group 2	205	320	1.35 (0.93-2.22)	1.27 (0.84-2.05)		
Group 3	1316	1742	0.72 (0.60-0.87)	0.75 (0.62-0.91)		
Group 4	289	531	0.55 (0.36-0.83)	0.57 (0.38-0.86)		
Group 5	202	396	0.88 (0.56-1.32)	0.92 (0.58-1.48)		

<sup>a</sup> ADT = androgen deprivation therapy; aRT = adjuvant radiotherapy; CI = confidence interval; HR = hazard ratio.

<sup>b</sup> Covariates included age and Charlson comorbidity score. The multivariable analysis was adjusted for interaction between groups (groups 2-5) and treatment (aRT + ADT vs ADT only); p value for interaction term was 0.03. Group 1 was excluded from this analysis because of a very small number of patients (n = 19) and notable hazard rates.

<sup>c</sup> Details of risk groups are as follows:  
 Group 1: patients with one to two positive nodes and pathological Gleason score 2-6.  
 Group 2: patients with one to two positive nodes, pathological Gleason score 7-10, pT2pT3a disease, and negative surgical margins.  
 Group 3: patients with one to two positive nodes, pathological Gleason score 7-10, pT2pT3a disease, or positive surgical margins.  
 Group 4: patients with three to four positive nodes.  
 Group 5: patients with more than four positive nodes.

Abdollah F, et al. Eur Urol 2018. 13

**Adjuvant vs. (early) salvage RT**

**iridium kankernetwork**

Study	Arms	RT dose	No	endpoint
RADICALS RT	Adjuvant vs. salvage (PSA failure)	66 Gy in 33 fractions	1150	Prostate cancer mortality
GETUG-17	Adjuvant vs. early salvage (PSA > 0.2)	66 Gy in 33 fractions + 6 months ADT	2000	PFS
RAVES	Adjuvant vs. early salvage (PSA > 0.2)	64 Gy in 32 fractions	470	PFS
EORTC 22043	Adjuvant vs. early salvage (0.1 < PSA > 0.5)	64 - 74 Gy + ADT	600	bPFS

**Salvage RT is best initiated as early as possible**

**iridium kankernetwork**

**Group 4 - High risk**

Metastasis-free survival at 5 yr (MFS5) (%)

PSA at SRT (ng/ml)

$p < 0.0001$

Fossati N, et al. Eur Urol 2018. 15

**GETUG-AFU 16: primary endpoint = PFS**

**iridium kankernetwork**

Progression-free survival (%)

Time since randomisation (months)

Number at risk:  
 Radiotherapy alone: 367, 338, 315, 294, 280, 266, 252, 228, 188, 140, 79, 61, 31, 19, 5, -  
 Radiotherapy plus goserelin: 363, 350, 349, 342, 319, 298, 285, 269, 236, 185, 111, 87, 46, 14, 5, -

Carrie C, et al. Lancet Oncol 2016. 16

**RTOG 96-01: primary endpoint = OS**

**iridium kankernetwork**

**A Overall Survival, All Patients**

Patients Who Survived (%)

Years since Randomization

No. of Deaths:  
 Placebo Group: 131  
 Bicalutamide Group: 108

Hazard ratio, 0.77 (95% CI, 0.59-0.99)  
 $P=0.04$

No. at Risk:  
 Placebo: 376, 359, 319, 280, 203, 25  
 Bicalutamide: 384, 368, 337, 294, 223, 32

Shibley W.U, et al. NEJM 2017. 17

**CASE 2**

**GHENT UNIVERSITY**

Male, 69 years old

> RALP+PLND 10/2015: pT2c pN1 (1/15) R0 GG4  
 > Salvage wpRT 08/2016

PSA evolution:

07/2016	0.10
12/2016	0.03
03/2017	0.10
07/2017	0.13
01/2018	0.20

**WHAT TO DO?**



1. ADT
2. ADT + abiraterone
3. PSA surveillance
4. Watchfull waiting
5. PSMA PET-CT
6. CT + Bone scan

**CASE 2**

Male, 69 years old

> RALP+PLND 10/2015: pT2c pN1 (1/15) R0 GG4  
> Salvage wpRT 08/2016

PSMA PET-CT 02/2018: bone lesion 4<sup>th</sup> right rib


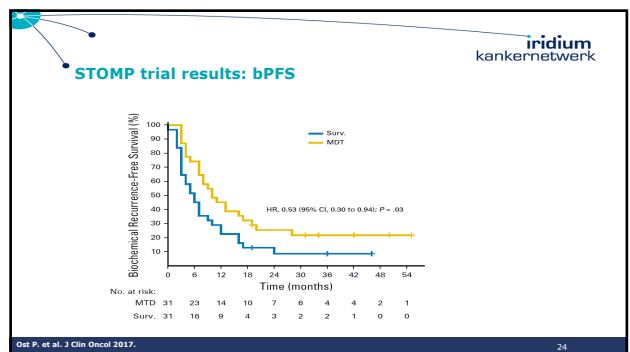
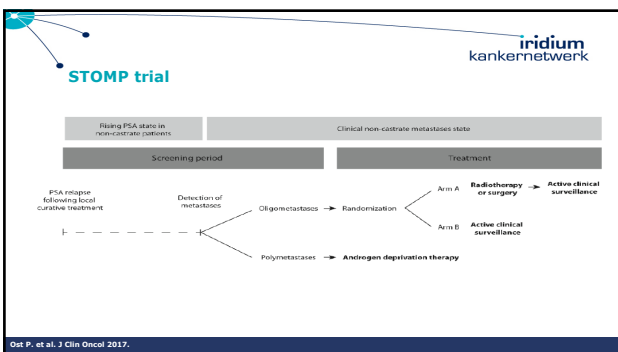
**WHAT TO DO?**

1. ADT
2. ADT + abiraterone
3. ADT + docetaxel
4. SBRT
5. SBRT + ADT
6. PSA surveillance
7. Watchfull waiting

**CASE 2**

•The view of the Radiation Oncologist

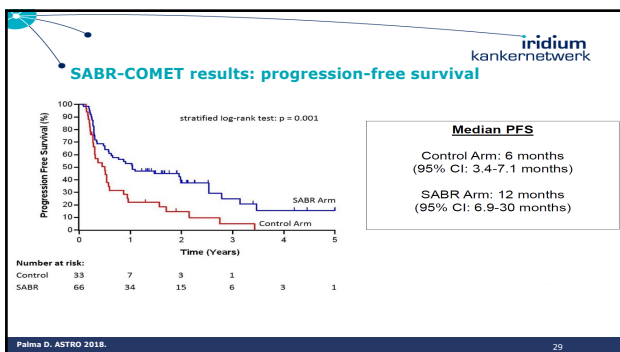
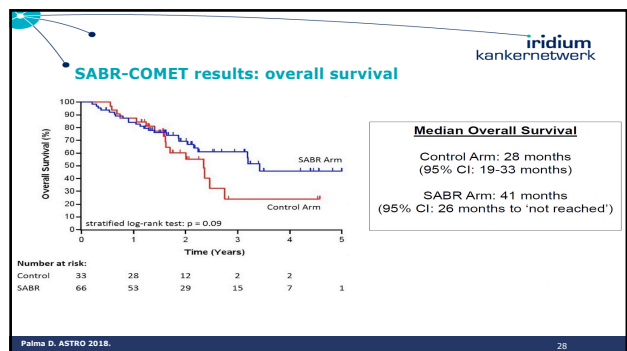
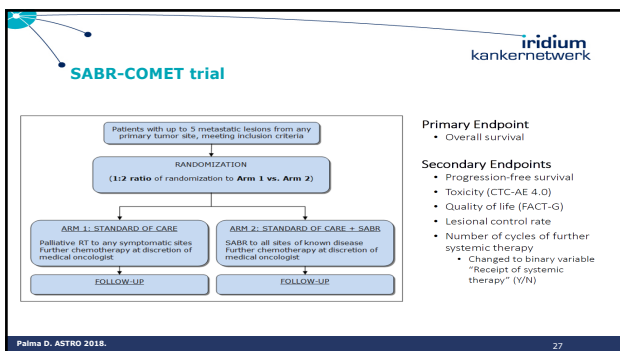
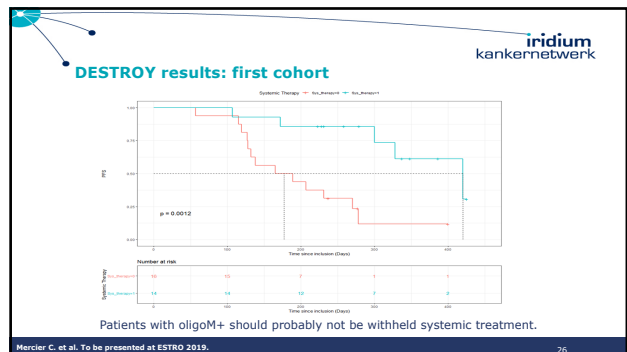
**You said SBRT?**

### DESTROY trial

Level	Fractions	Interval	Dose/fraction	Total	BED <sub>2Gy</sub>	BED <sub>10Gy</sub>	EQD <sub>2Gy</sub>
1	5	48h	7	35	59.5	96.25	78.75
2	3	48h	10	30	60.0	105	90
3	1	NA	20	20	60.0	120	110

Mercier C. et al. Radiat Oncol 2018. 25



### CASE 2

Male, 69 years old

> RALP+PLND 10/2015: pT2c pN1 (1/15) R0 GG4

> Salvage wpRT 08/2016

> SBRT 03/2016: 4<sup>th</sup> right rib

PSA evolution:

01/2018	0.20
05/2018	0.40
09/2018	0.69

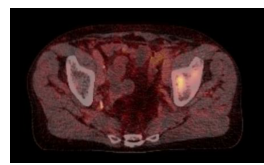
Ghent University logo

**WHAT TO DO?**

1. ADT
2. ADT + abiraterone
3. PSA surveillance
4. Watchfull waiting
5. PSMA PET-CT
6. CT + Bone scan
7. Whole body MRI

**CASE 2**

Bone scan 09/2018: new bone lesion left acetabulum  
 PSMA PET-CT 09/2018:




**WHAT TO DO?**

1. ADT
2. ADT + abiraterone
3. ADT + docetaxel
4. SBRT
5. SBRT + ADT
6. PSA surveillance
7. Watchfull waiting

**CASE 2**

**WHAT TO DO?**



**Systemic treatment or not?**

- Secondary M1,
- (very) low volume,
- low PSA,
- PSA dt 4-6 mo
- asymptomatic

Recommendations	Strength rating
In M1 symptomatic patients, offer immediate systemic treatment to palliate symptoms and reduce the risk for potentially serious sequelae of advanced disease (spinal cord compression, pathological fractures, ureteral obstruction, extra-skeletal metastasis).	Strong
Offer subcutaneous hormone-releasing hormone (LHRH) antagonists, especially to patients with an impending spinal cord compression or bladder outlet obstruction.	Weak
In M1 asymptomatic patients, offer immediate systemic treatment to improve survival, defer progression to a symptomatic stage and prevent serious disease progression-related complications.	Strong
In M1 asymptomatic patients, discuss deferred castration with a well-informed patient since it lowers the treatment side effects, provided the patient is closely monitored.	Weak
In M1 patients treated with a LHRH agonist, offer short-term administration of anti-androgens to reduce the risk of the 'flare-up' phenomenon.	Weak
Do not offer anti-androgen monotherapy for M1 disease.	Strong
Offer castration combined with chemotherapy (docetaxel) to all patients whose first presentation is M1 disease and who are fit enough for docetaxel.	Strong
Offer castration combined with abiraterone acetate plus prednisone to all patients whose first presentation is M1 disease and who are fit enough for the regimen.	Strong
Offer castration alone, with or without an anti-androgen, to patients unfit for, or unwilling to consider, castration combined with docetaxel or abiraterone acetate plus prednisone.	Strong

Metzler N et al. EAU guidelines 2018 retrieved from [https://uroweb.org/guidelines/ prostate\\_cancer/](https://uroweb.org/guidelines/ prostate_cancer/) accessed 02.12.2018