OLIGOMETASTATIC HORMONE SENSITIVE PROSTATE CANCER
DEFINITION - INCIDENCE - TREATMENT

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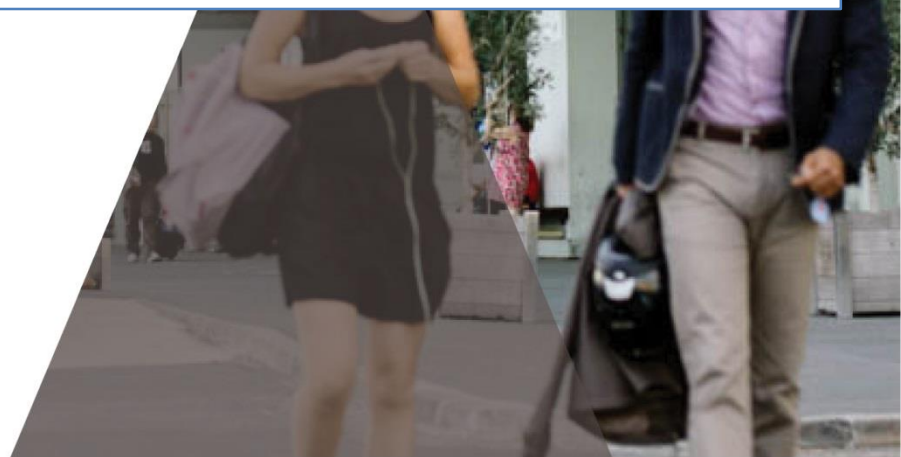


GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

Case report 1

Mr. F., born 1938.

LDR Brachytherapy in 2003 for low risk prostate cancer (PSA nadir 0.4 ng/mL in 2007)

Biochemical recurrence in 2011, PSA 2.15 ng/mL

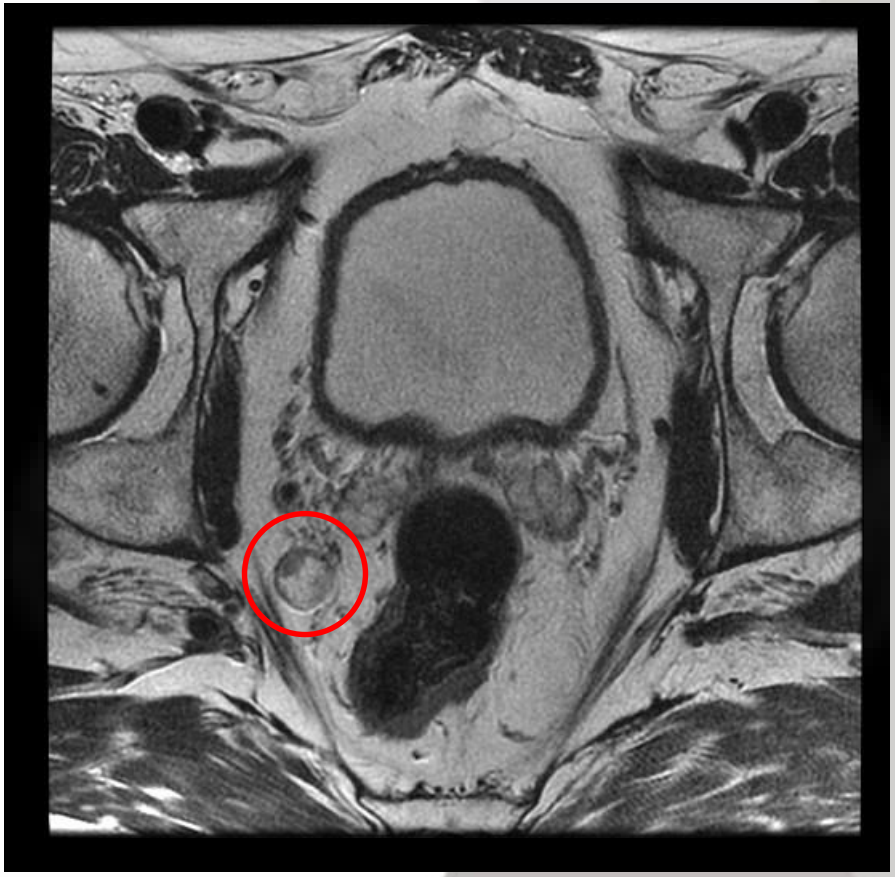
(PSA DT ~ 18 months)

Negative CT/Bone scan

Choline PET/CT in 2011 : single nodal hyperfixation

2012: SBRT – no ADT

Since 2012, PSA<0.2 ng/mL



What is an oligometastatic prostate cancer?

- **Initial definition of oligometastatic state by Weichselbaum and Hellman (JCO 1995)**

- Continuum between purely local disease and widespread systemic disease
- Oligometastatic state – only a limited number of metastatases, without a widespread distribution of cancer.

Case report 2

Mr. B., born 1950.

3y RT-HT (80 Gy) in 2012 for high risk prostate cancer (T3b, Gleason 8, PSA 16)

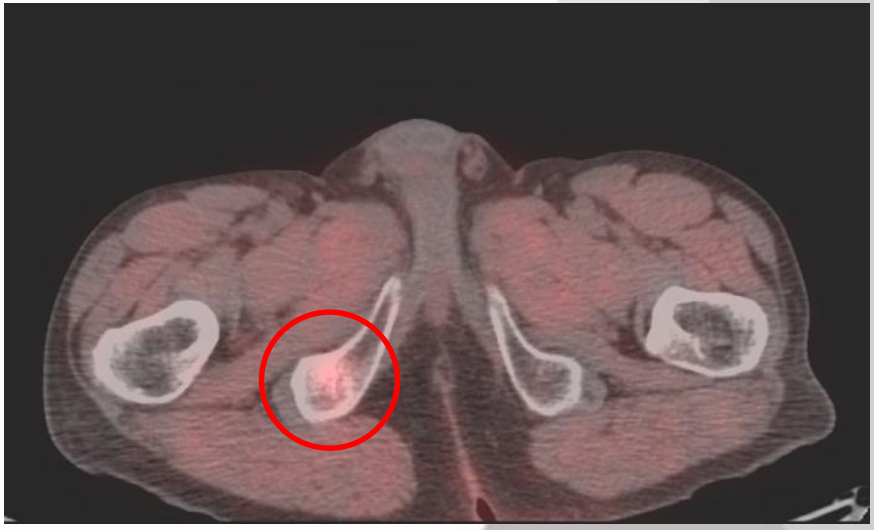
Biochemical recurrence in

2016 – one injection of goserelin 10.8 mg, with good PSA response.

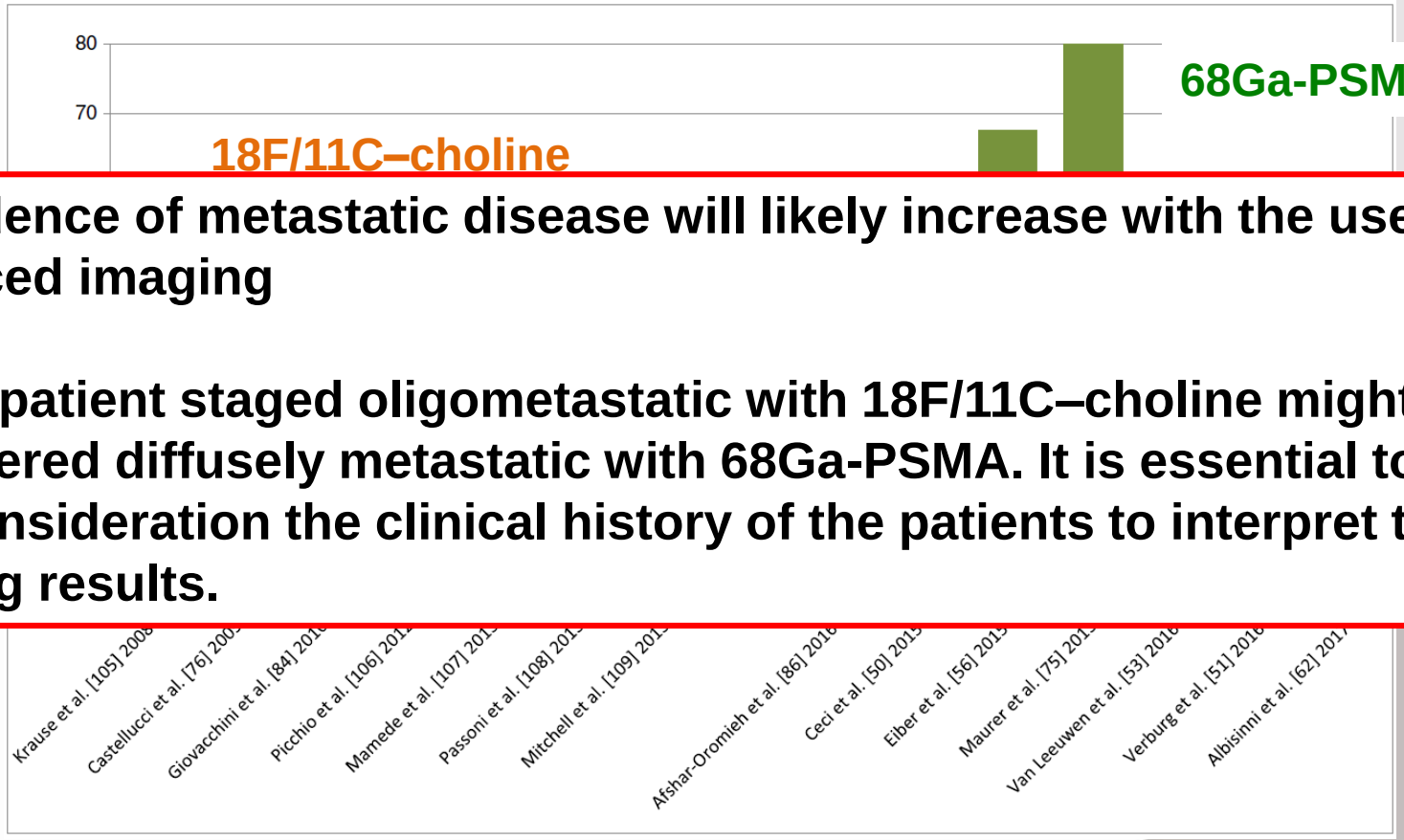
December 2017 PSA 1.26

March 2018 PSA 13.4

Choline PET/CT in March 2018 : single bone hyperfixation (right ischion)



Definition highly dependent on the imaging tools used



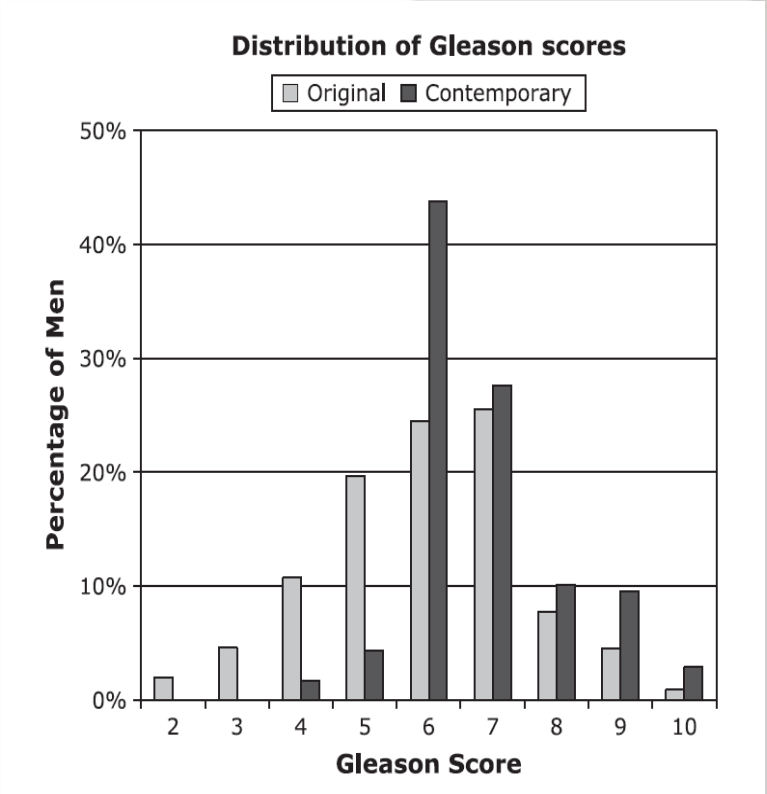
1. Incidence of metastatic disease will likely increase with the use of advanced imaging

2. One patient staged oligometastatic with 18F/11C–choline might be considered diffusely metastatic with 68Ga-PSMA. It is essential to take into consideration the clinical history of the patients to interpret the imaging results.

Detection rate in PC patients with low biochemical relapse of PSA < 1.0 ng/ml
Virgolini et al, EJNMMI 2018

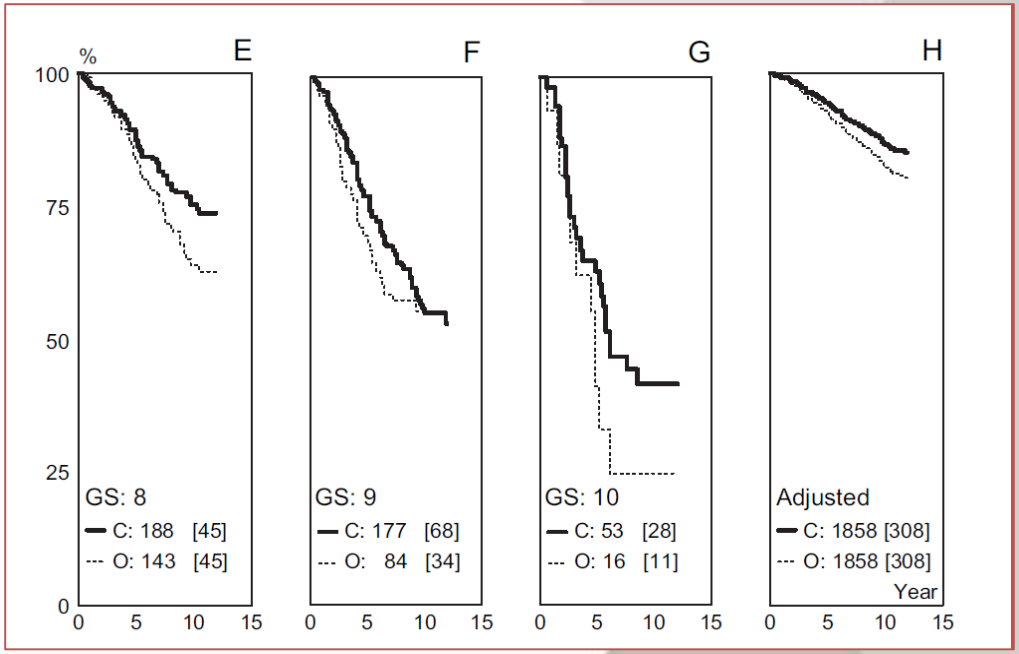
Will Rogers phenomenon and associated issues

- **“When the Okies left Oklahoma and moved to California, they raised the average intelligence level in both states.”**
- **Stage migration:**
  - **Gleason score**
  - **T-stage**
- **Albertsen et al, JNCI 2005**



Will Rogers phenomenon and associated issues

- **Mean Gleason score increase: 0.85 (0.79-0.91) P <.001**
- **Adjusted mortality rate ratio between contemporary reading and historic reading: 0.74 (0.69-0.80)**
- **Albertsen et al, JNCI 2005**
- **Other non-discussed issues include**
  T-stage classification (MRI),
  PSA screening



Cause specific survival curves comparing Original (O) and Contemporary (C) staging

Current standard and treatment options for Oligometastatic hormone sensitive PCa

- **Lifelong androgen deprivation therapy**
- **Intensified systemic therapy**
  - Docetaxel, abiraterone
  - To be discussed, but mostly for patients with higher disease burden
- **Role of local treatment of the primary? Of the metastatic disease?**

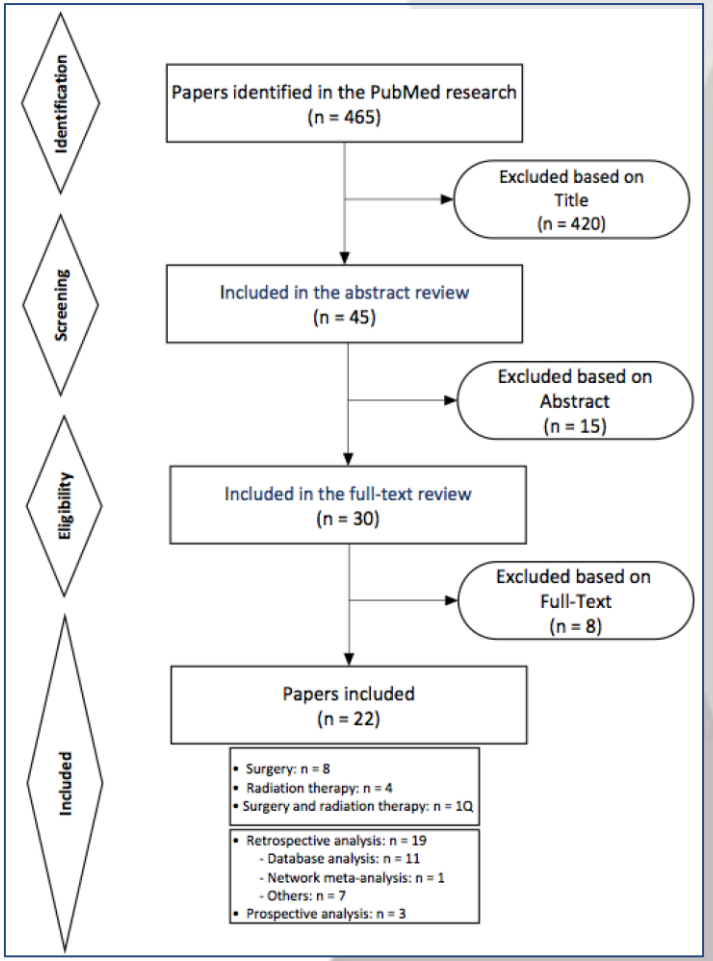
Benefit of local treatment in M1 Pca – many questions, no answer, yet…

Systematic review
22 papers identified
Almost all **retrospective**
Major confounding biases

All conclude that local treatment improves survival

RCT awaited (PEACE 1, STAMPEDE, HORRAD, TromBone, SWOG…)

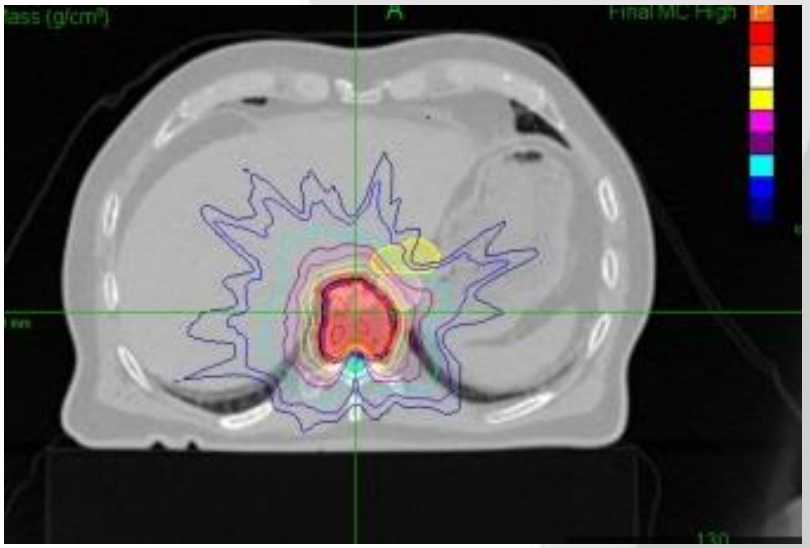
Schernberg, Blanchard et al, submitted



Benefit of additional local therapy in OM Pca – rationale and goals

- Reduce the tumor burden
- Prolong hormone sensitivity
- Delay hormone therapy introduction
- Delay symptoms secondary to local or metastatic progression
- Cure metastatic patients?

Case report 3



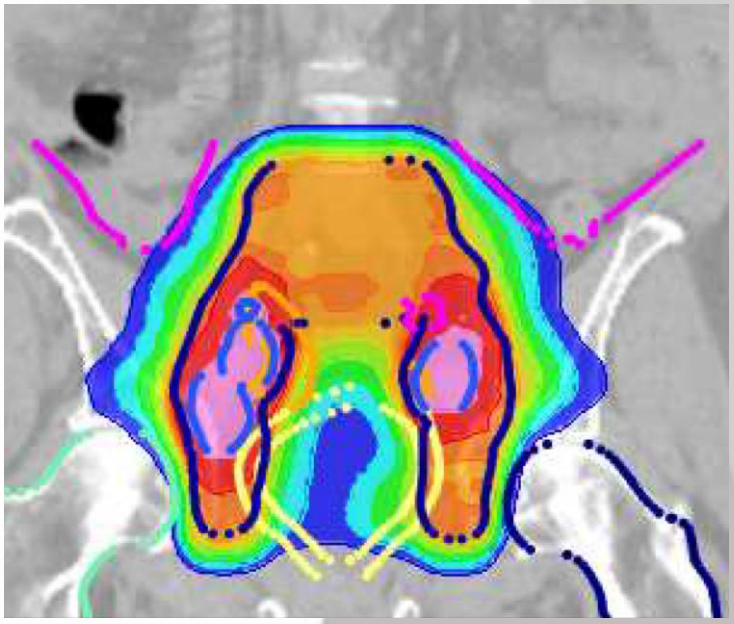
Mr. G. born 1943.

Prostatectomy in 2007 (pT2aN0/2R0)

Biochemical recurrence in

2015 – no treatment until january 2018 (PSA 3.49 ng/mL)

Choline PET/CT in 2017 : single bone hyperfixation (T10) and two pelvic lymph nodes

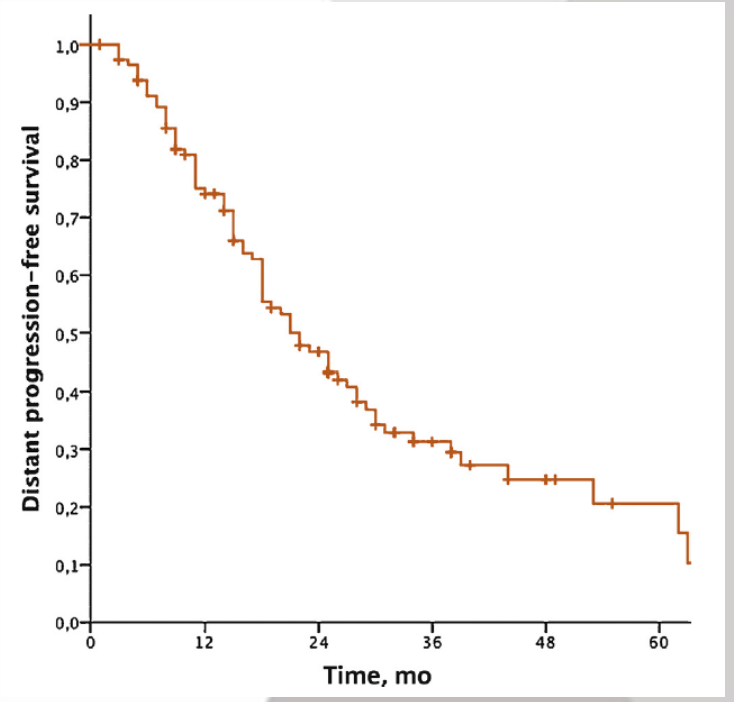


What are the data supporting ablative therapy in OM Pca?

- **Initial Milano experience – Jereczek-Fossa et al, IJROBP 2011**
- 2007-2009, 34 pts/38 lesions (15 local recurrence [P], 4 anastomosis recurrence [A], 16 single lymph node recurrence [LN], 3 patients single metastasis [M]).
- 11C-Choline PET/CT
- Median FU 16.9 months
- 30-month progression-free survival: 42.6%.
- Progression in 2 out of 3 M pts

What are the data supporting ablative therapy in OM Pca? Multicenter retrospective study

- 119 patients – 163 metastases (nodal in 60% and bone metastases in 36%)
- Median FU: 3 yrs
- DPFS: median 21 months (polymetastatic progression in 37 pts)
- LPFS higher in case of lower SBRT dose (79% if BED≤100Gy vs 99% if BED>100 Gy)
- Improvement (NS) in DPFS with the adjunction of concomitant ADT
- No distinction between nodal and bone metastases regarding DPFS



Ost et al, Eur Urol 2016

What are the data supporting ablative therapy in OM Pca? The STOMP trial

- Randomized phase II study
- Asymptomatic PCa
- Biochemical recurrence after primary PCa treatment
- Three or fewer extracranial metastatic lesions on choline PET/CT
- Non castrated
- Randomly assigned (1:1) to either surveillance or MDT of all detected lesions (surgery or stereotactic body radiotherapy).

Time between PCa diagnosis and inclusion, years		
Mean (range)	6.3 (0.5-22.9)	5.9 (0.6-14.2)
Median (IQR)	4.9 (3.3-8.0)	5.3 (3.5-8.3)
PSA at inclusion, ng/mL		
Mean (range)	6.9 (0.3-31.0)	9 (0.7-44.5)
Median (IQR)	3.8 (0.8-9.6)	5.3 (2.8-12)
PSA-DT at inclusion		
≤ 3 months	10 (32.3)	10 (32.3)
> 3 months	21 (67.7)	21 (67.7)
No. of metastases		
1	9 (29.0)	18 (58.1)
2	10 (32.3)	6 (19.3)
3	12 (38.7)	7 (22.6)
Location of metastases		
Nodal	17 (54.8)	17 (54.8)
N1	8 (25.8)	13 (41.9)
M1a	5 (16.2)	4 (12.9)
Combination of N1 and M1a	4 (12.9)	0 (0.0)
Non-nodal	14 (45.2)	14 (45.2)
M1b	11 (35.5)	13 (41.9)
Combination of N1/M1a and M1b	3 (9.7)	0 (0.0)
M1c	0 (0.0)	1 (3.3)

Ost et al, JCO 2017

What are the data supporting ablative therapy in OM Pca? The STOMP trial

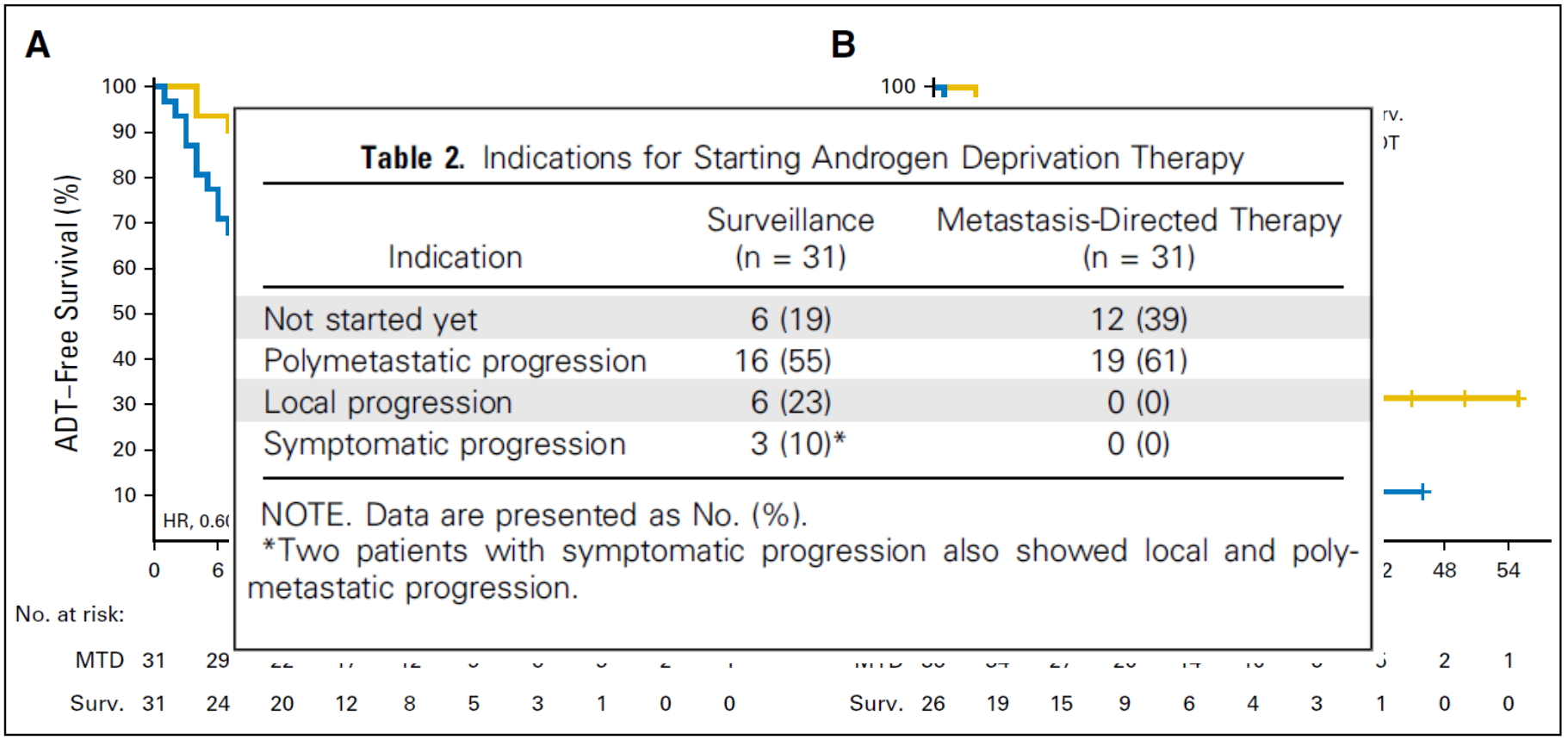


Table 2. Indications for Starting Androgen Deprivation Therapy

Indication	Surveillance (n = 31)	Metastasis-Directed Therapy (n = 31)
Not started yet	6 (19)	12 (39)
Polymetastatic progression	16 (55)	19 (61)
Local progression	6 (23)	0 (0)
Symptomatic progression	3 (10)*	0 (0)

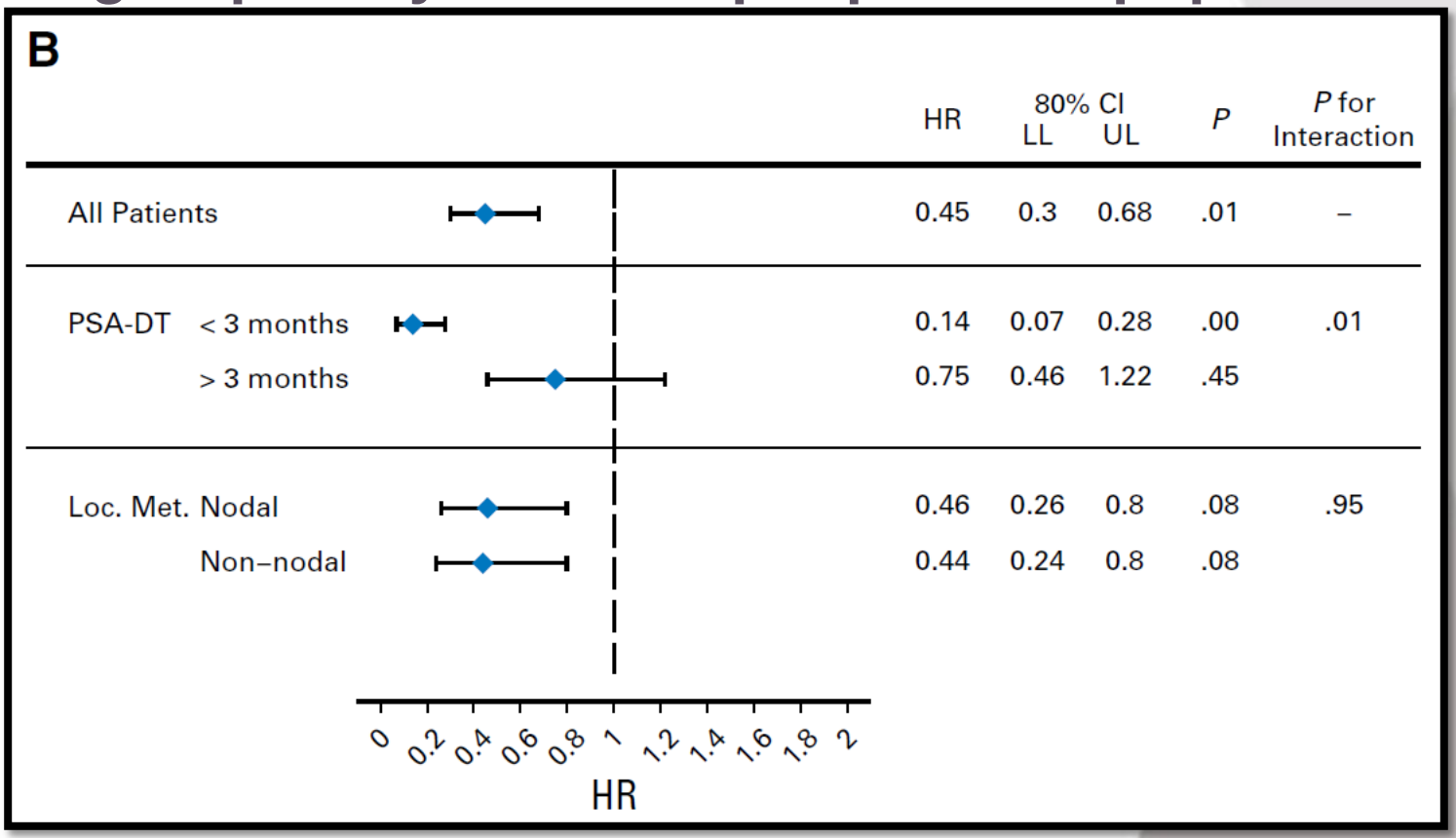
NOTE. Data are presented as No. (%).
*Two patients with symptomatic progression also showed local and polymetastatic progression.

including 4 in the 6 surgically treated patients

Ost et al, JCO 2017

What are the data supporting ablative therapy in OM Pca? The STOMP trial

- Subgroup analysis in the per protocol population

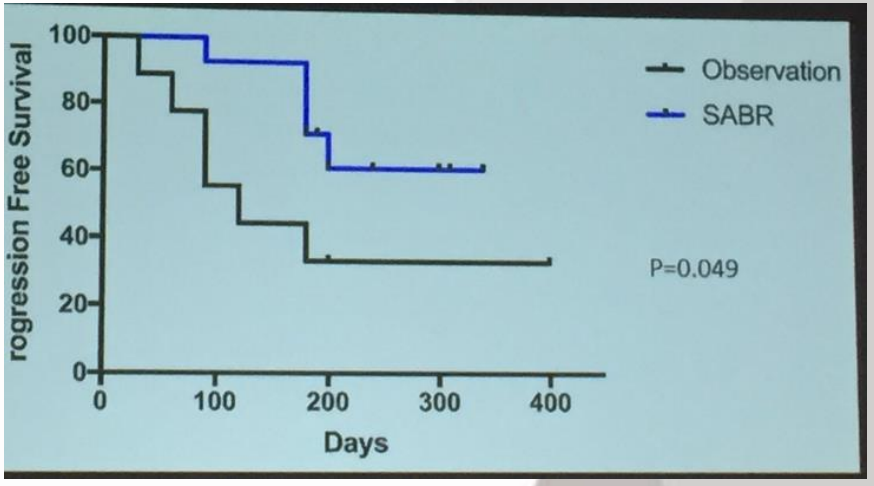


Ost et al, JCO 2017

Additional evidence – the ORIOLE trial

- **Design:**
  - 2:1 randomization to SABR or observation (minimization by primary intervention, prior hormonal therapy, and PSA doubling time)
  - Sample size 54 pts; FU 180 days
  - Primary endpoint: proportion of progressive pts within 180 days (PCWG2 + RECIST + start of ADT + death)

Radwan at al, BMC Cancer, 2017



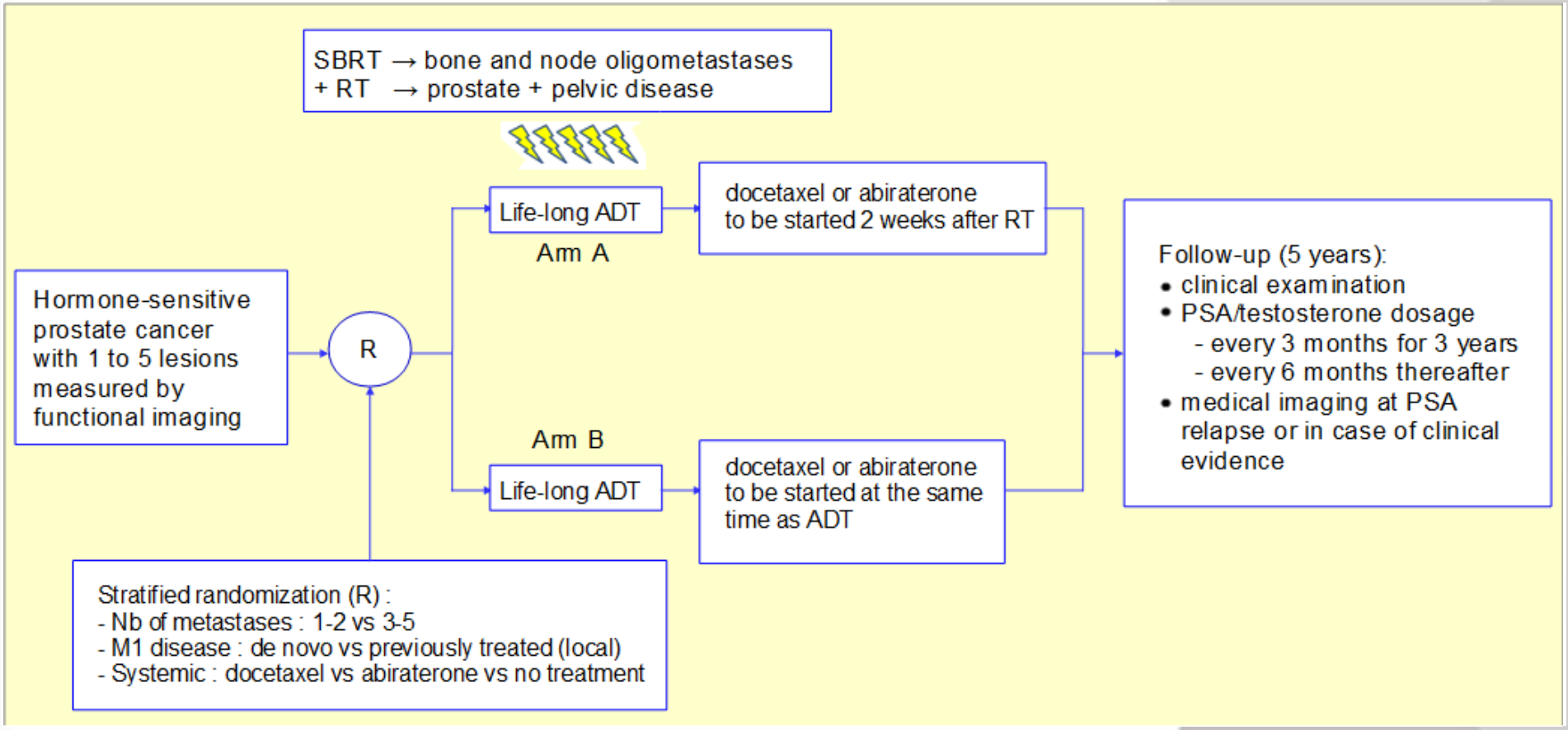
P=0.049!

Tran et al, ASTRO 2017

PRESTO – Prostate-cancer treatment using Stereotactic Radiotherapy for Oligometastases in Hormone-naive patients - a GETUG-AFU Phase III randomized controlled trial

- **Inclusion criteria**
  - Histologically proven adenocarcinoma of the prostate
  - Defined as M1 based on the presence of bone metastasis
  - Diagnostic workup including functional imaging (Choline-PET/CT, PSMA PET/CT or whole body MRI) done before the start of hormonal therapy;
  - With up to 5 asymptomatic or paucisymptomatic metastatic sites including at least one bone lesion.
  - Patients with a previous prostatectomy or radiotherapy to the prostate and/or pelvic lymph nodes are eligible provided they have no active disease within the irradiated areas, based on functional imaging findings

PRESTO – trial schema



Sample size: 350 pts, based on HR of 0.6 (expected 3-year castration resistance free survival rate: 50% vs. 66%)

PRESTO – Endpoints

- **PRIMARY ENDPOINT: Castration resistant prostate cancer free survival (PCWG3)**
- **SECONDARY ENDPOINTS:**
  - Overall Survival,
  - Prostate Cancer Specific Survival
  - Time to castration resistance
  - Time to symptomatic skeletal event, define;
  - Time to symptomatic skeletal event at the treated metastatic bone sites,;
  - Proportion of living patients using intermittent androgen deprivation therapy Time to use of systemic chemotherapy or second line hormonal therapy
  - Time to use of an antalgic palliative bone treatment (interventional radiology or radiotherapy;
  - Toxicity of ablative radiotherapy;
  - Quality of life (EPIC, BPI)
  - Cost efficacy

Summary

- **Oligometastases exist – I'met them!**
- **Management highly controversial. Great opportunity for RCTs!**
- **BUT:**
  - Impact of staging imaging tools
  - Underlying biology not well understood
  - Pt selection key – importance of ancillary studies to define predictive markers of response
- **Hopefully PRESTO opening at Fall 2018**

Thanks. Any questions?

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