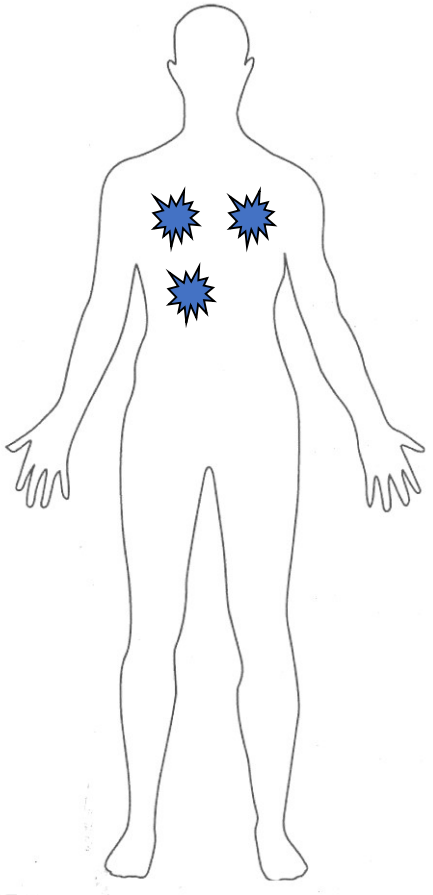
Ruolo della Radioterapia nel paziente oligometastatico ed oligoprogressivo

Rolando M. D'Angelillo
Università degli studi di Roma, Tor Vergata

Definition of Oligometastatic PCa

Hellman and Weichselbaum (1995).. *"there is a subgroup of patients with an intermediate phase of metastatic disease, that presents a potential for disease control with the ablation of the few metastases"*



Ολιγοσ: poche lesioni secondarie

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Hellman S, Weichselbaum RR. Oligometastases. J Clin Oncol. 1995 Jan;13(1):8-10

Definition of Oligometastatic PCa

Is oligometastatic disease, just an issue of number?

Therefore, how many mets?

Does site matter?

What about time of occurrence?

How to detect mets?

What about tumor biology?

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Definition of Oligometastatic PCa

Ολιγοσ: … poco…

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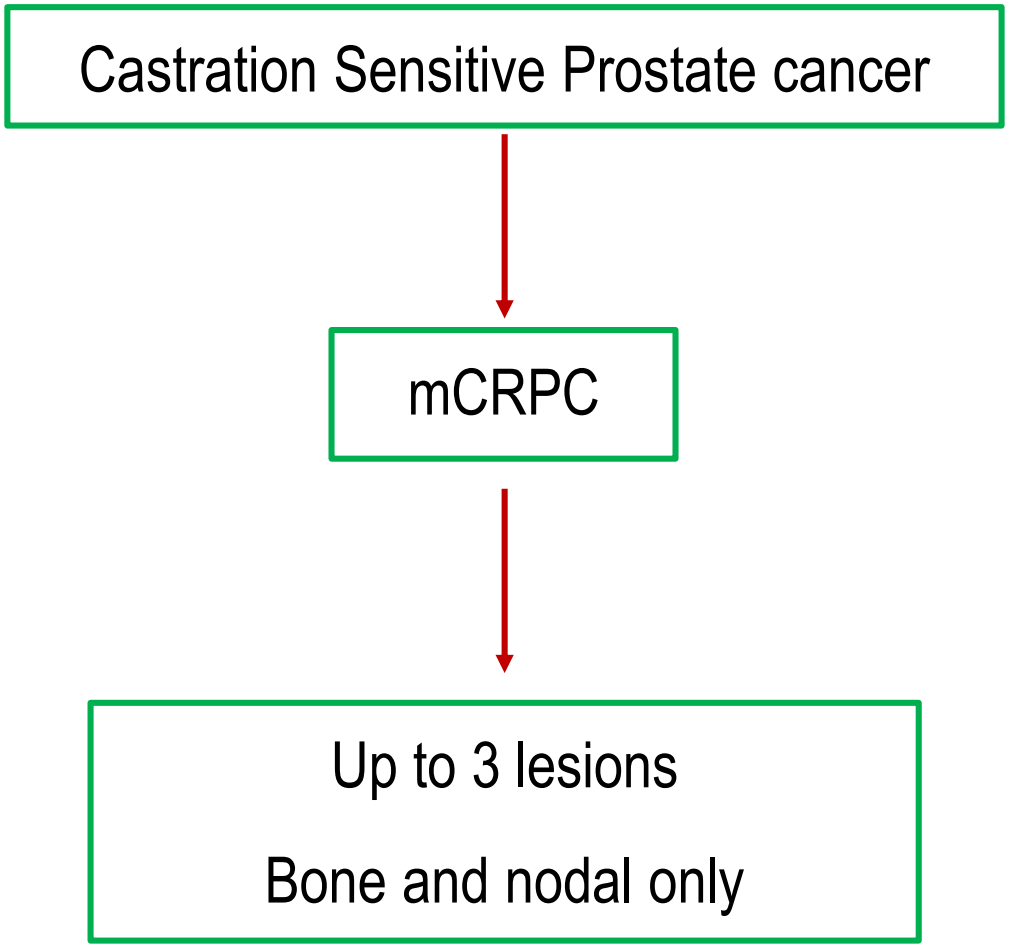
RT in Oligom+ CRPC (first occurence)



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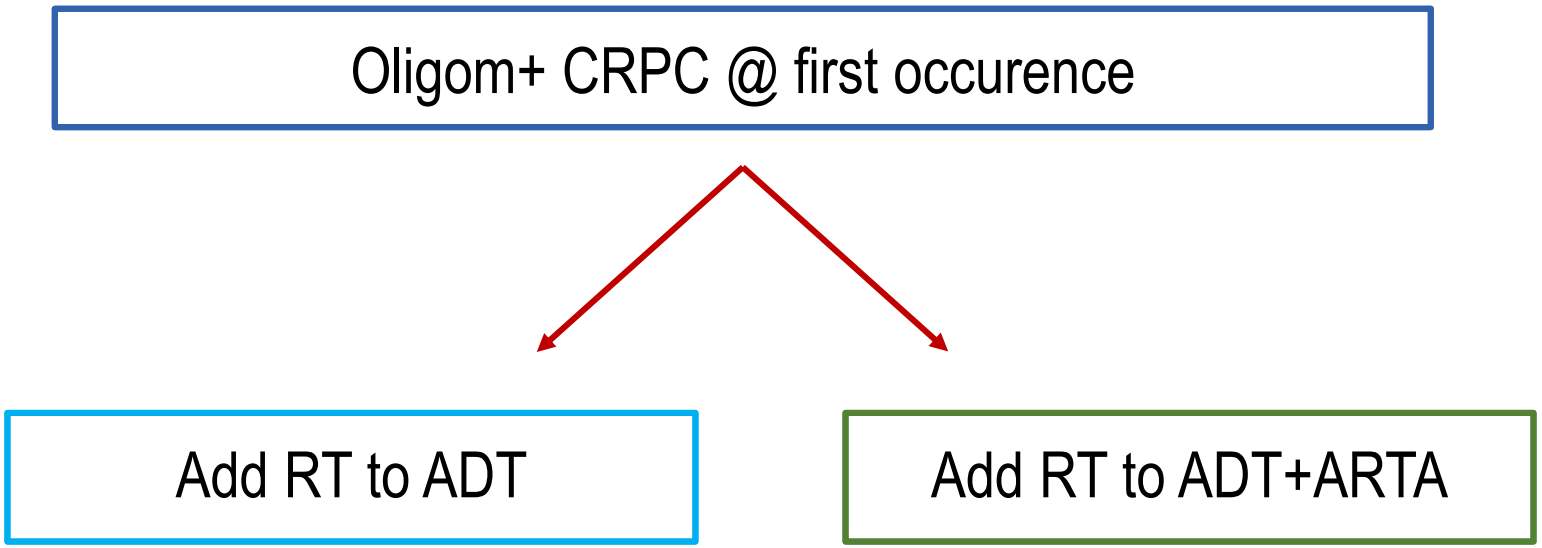
APCC 2015, Ann Oncology 2015;26:1589-604
APCC 2017, European Urologyhttp://dx.doi.org/10.1016/j.eururo.2017.06.002
AIRO position paper, Crit Rev Oncol Hematol,, 2019;138:24-28

Sc RT in Oligom+ CRPC (first occurence)



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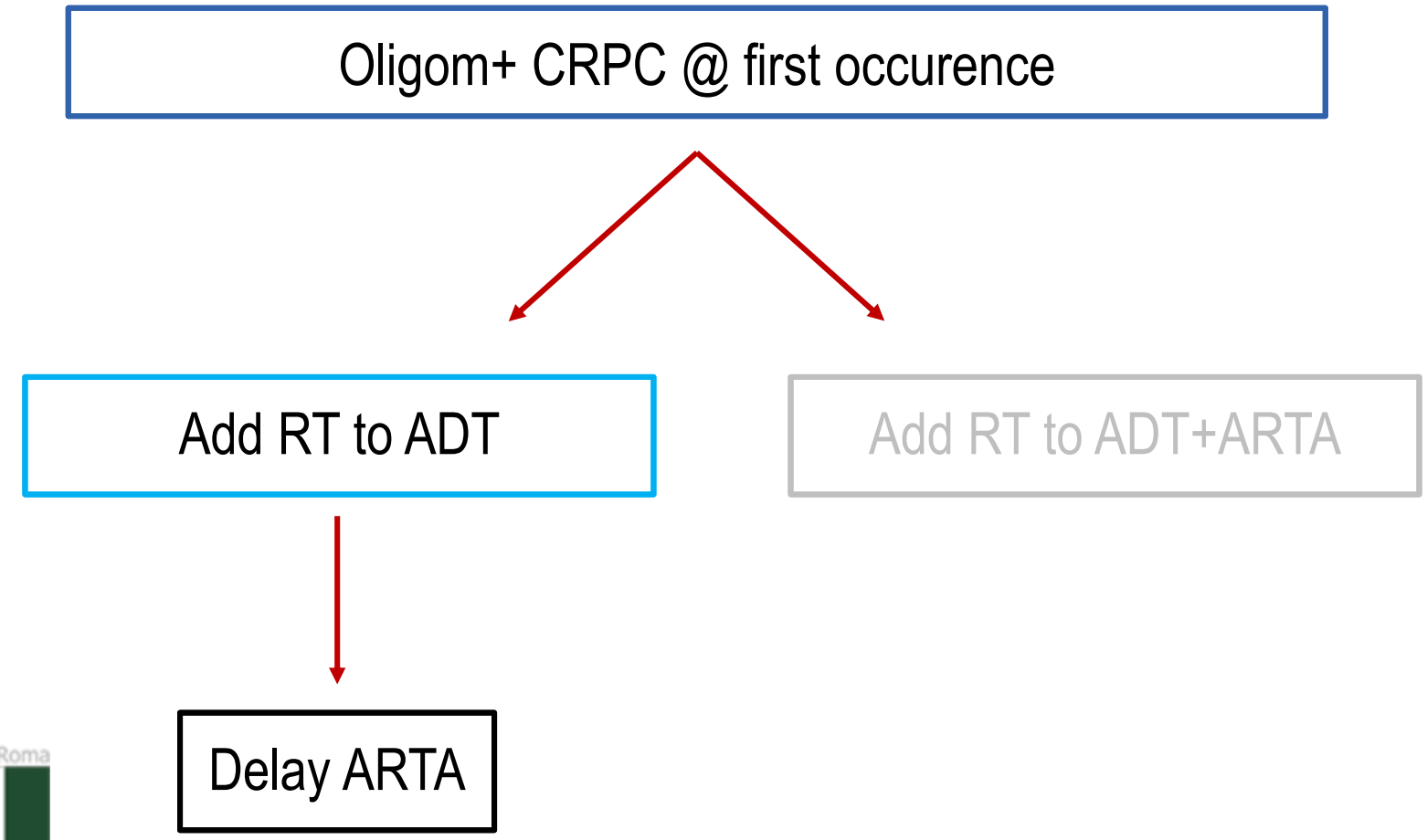

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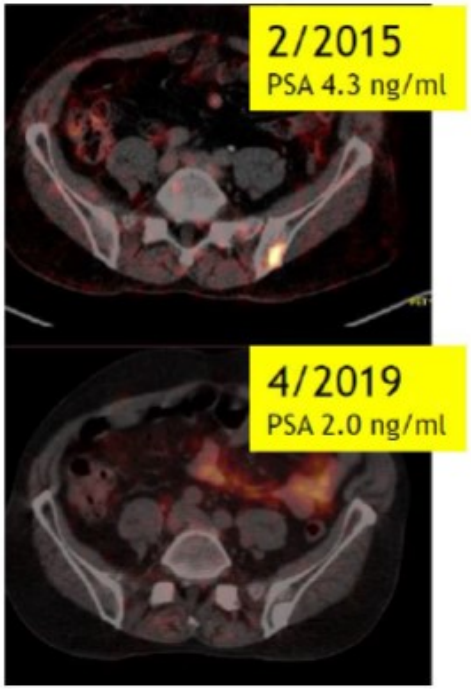
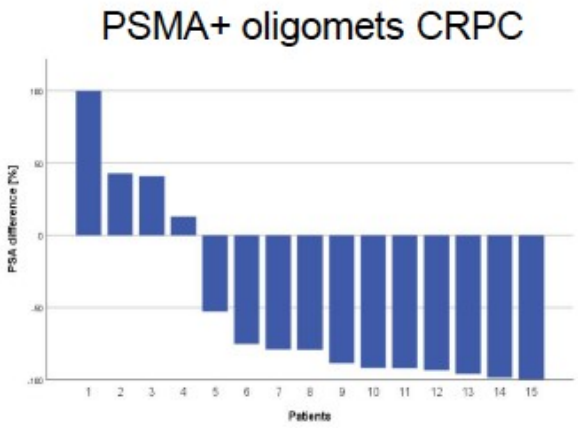
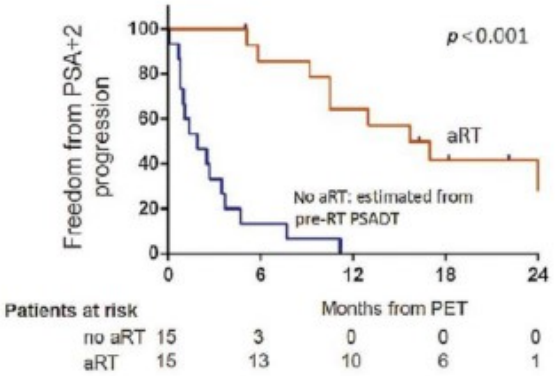
RT in Oligom+ CRPC (first occurence)





PSA-response (%) in 11/15 pts. after local ablative RTx (aRT)



Estimated delay of PSA-progression of 3.3 to 15.6 mo.

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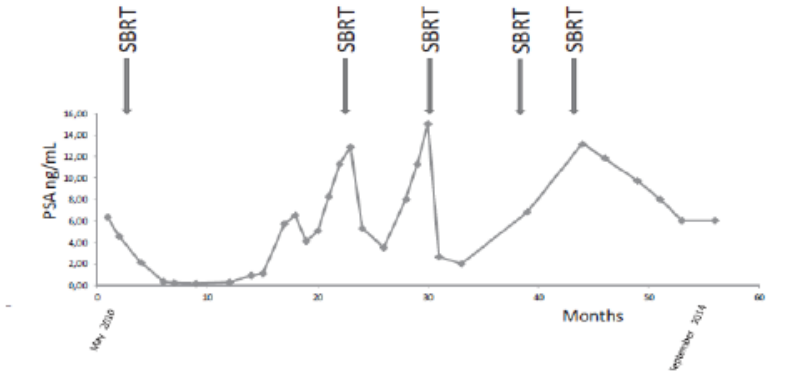
RT in Oligom+ CRPC (first occurence)

What role does stereotactic ablative radiotherapy have in advanced castrate-resistant prostate cancer?

Ryan Phillips[1], Piet Ost[2] & Phuoc T Tran*[1,3]



Oncol Res Treat 2016;39:217–220

«OligometCRPC in the setting of 2nd line hormonal agents can also be converted back to a responsive state…
SBRT may be a valuable addition to the armamentarium of management of mCRCP»

Future Oncol. (2017) 13(24), 2121–2124

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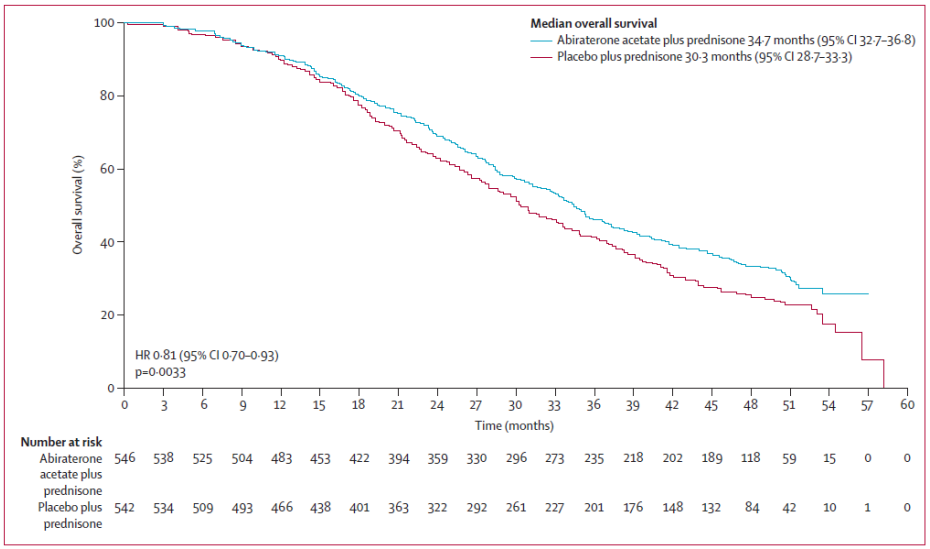
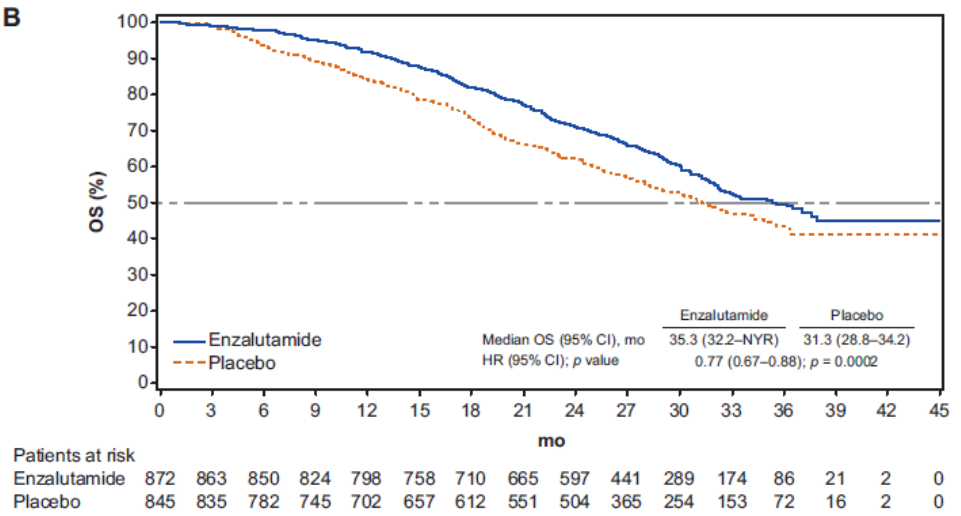
RT in Oligom+ CRPC (first occurence)

Available systemic treatment: CT or ARTA

Androgen Receptor Target Agent (ARTA)





Abiraterone Acetate (AAP)

COU-AA-302, Lancet Oncol 2015;16:152-60.

Enzalutamide (Enza)

Prevail, Eur Urol 2017;71:151-4.

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RT in Oligom+ CRPC (first occurence)

ADT+ additional tx vs. ADT + Ablative RT

Results

ADT + ARTA

 # pts: 2805

Efficacy over placebo with:

OS: 35 mo

rPFS: 16-20 mo

Ryan CJ et al, Lancet Oncol 2015 Feb;16(2):152-60
Beer TM et al, Eur Urol 2017 Feb;71(2):151-54.

ADT+Ablative RT

#pts: 107

Activity with:

Local control: 95%

dPFS: 11 mo

Muldermans et al. Int J Radiat Oncol Biol Phys 2016 Jun 1;95(2):696-702; Triggiani L et al BJC 2017,1-6 doi:10.1038

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RT in Oligom+ CRPC (first occurence)

ADT+ additional tx vs. ADT + Ablative RT

Side effects

ADT + ARTA

Type	All Grade	G3+
Fatigue	36-40%	2%
Hypertension	14-22%	7-14%
Cardiac event	12-22%	3-7%
Any to discontinuation	6-13%	
Any G3-4	48-54%	
Any G5	4-5%	

Ryan CJ et al, Lancet Oncol 2015 Feb;16(2):152-60.
Beer TM et al, Eur Urol. 2017 Feb;71(2):151-54.

ADT+Ablative RT

Type	Grade 1-2	G3
Fatigue	0.7%	---
Pain Flair	12%	---
GI	5%	---
GU	3%	---
Ileus	---	11%
Lymphocele	---	9%

Muldermans et al. Int J Radiat Oncol Biol Phys 2016 Jun 1;95(2):696-702.; Triggiani L et al BJC 2017,1-6 doi:10.1038; Ost P, European Urology 2015;67:852-63.

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RT in Oligom+ CRPC (first occurence)

Oligoprogressive CRPC @ first occurence

↓

Add RT to ADT

↓

Delay ARTA → Which pt could benefit?

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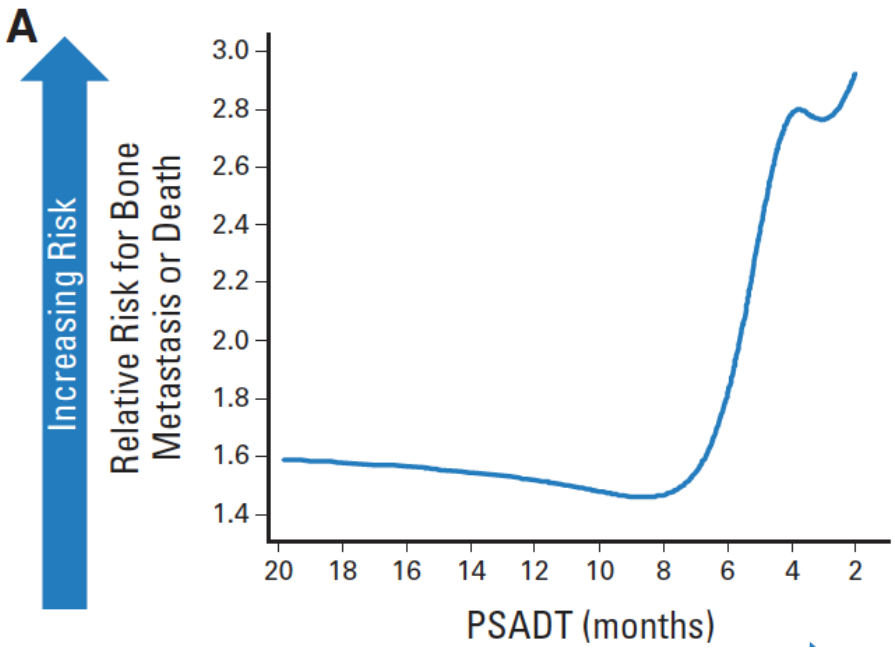
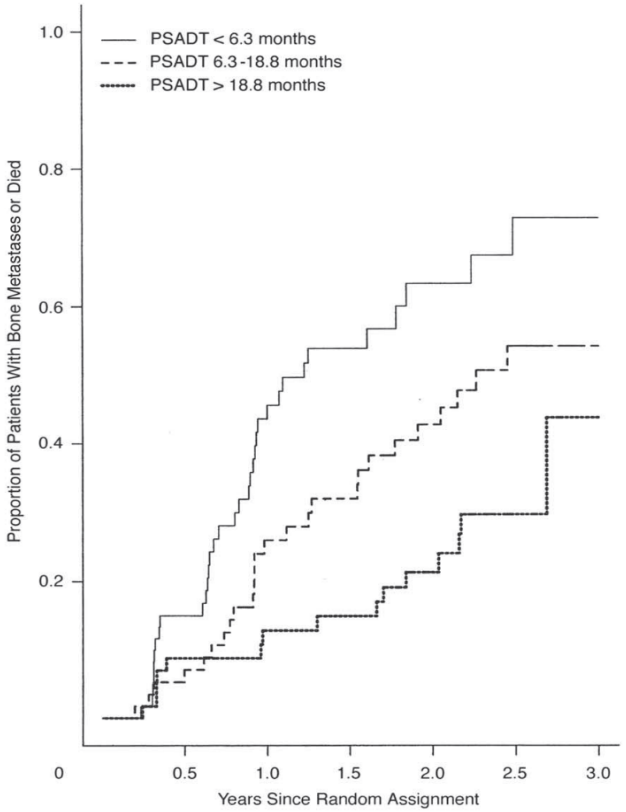
RT in Oligom+ CRPC (first occurence)

Which patient could benefit adding RT to ADT only?

PSA-DT <6 mos & new bone mets





Smith MR et al. J Clin Oncol 2013;31:3800-06.
Smith MR et al. J Clin Oncol 2005;23:2918-25.

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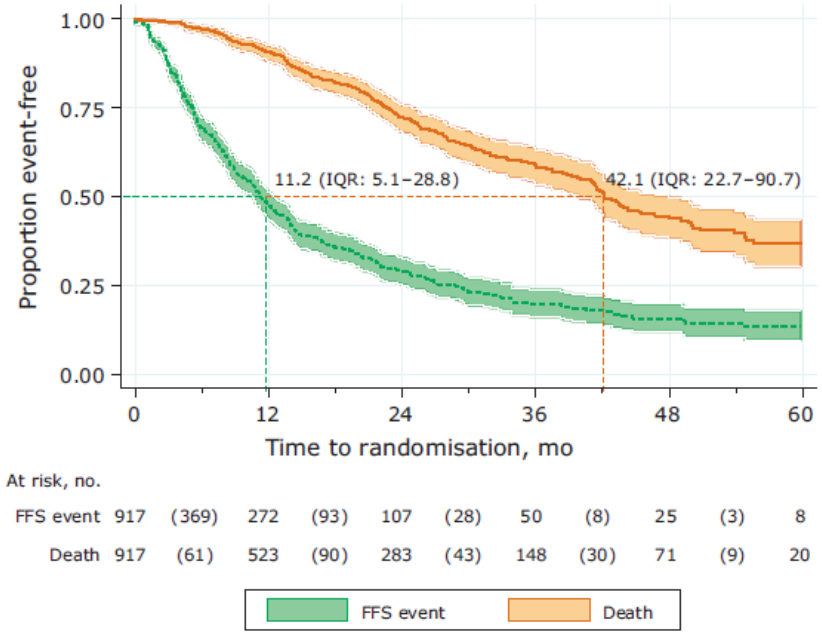
RT in Oligom+ CRPC (first occurence)

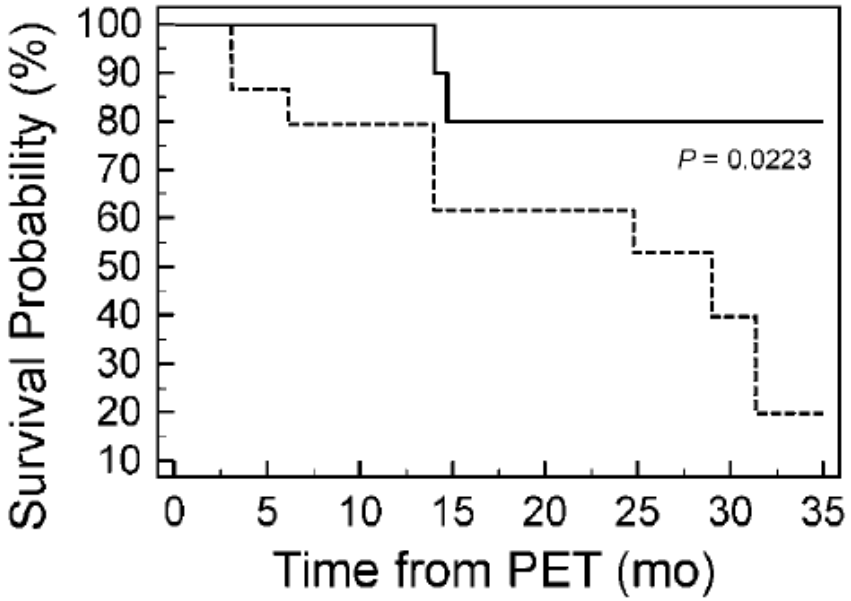
Which patient could benefit adding RT to ADT only?

Time from CSPC to CRPC



James ND et al. Eur Urol 2015;67:1028-38.

M+ burden @PET



Kwee SA et al. J Nucl Med 2014;55:905-10.

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RT in Oligom+ CRPC (first occurence)


Critical Reviews in Oncology / Hematology 138 (2019) 24–28

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In an asymptomatic or minimally symptomatic mCRPC patient with a PSA doubling time > 6 months, time to castration-resistant phenotype >12 months, and oligometastases up to three nodal or bone lesions detected by metabolic imaging, RT with radical intent to metastatic sites could be offered as alternative to ARTA to delay systemic treatment

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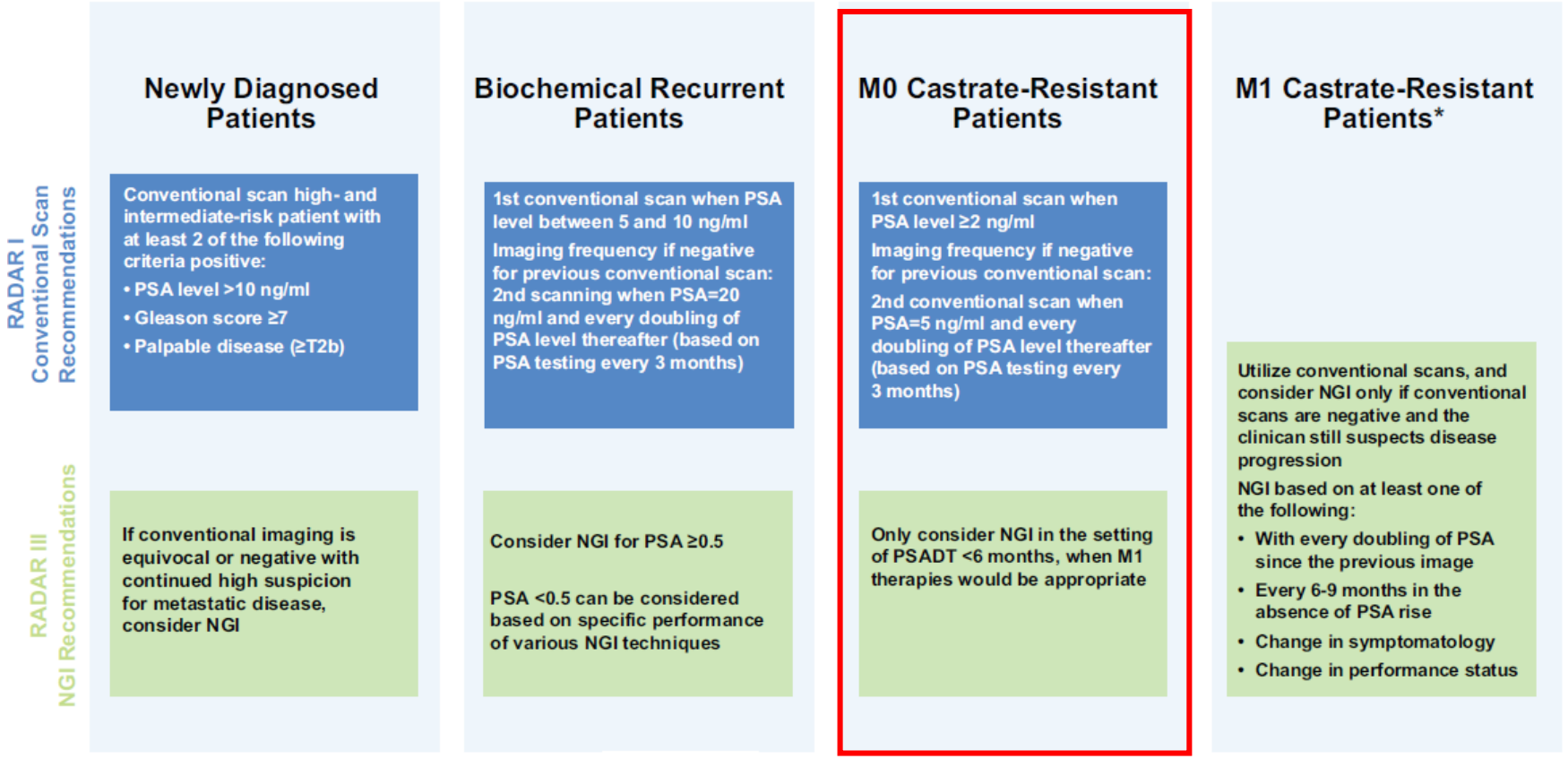
AIRO position paper, Crit Rev Oncol Hematol,, 2019;138:24-28

Next Generation Imaging



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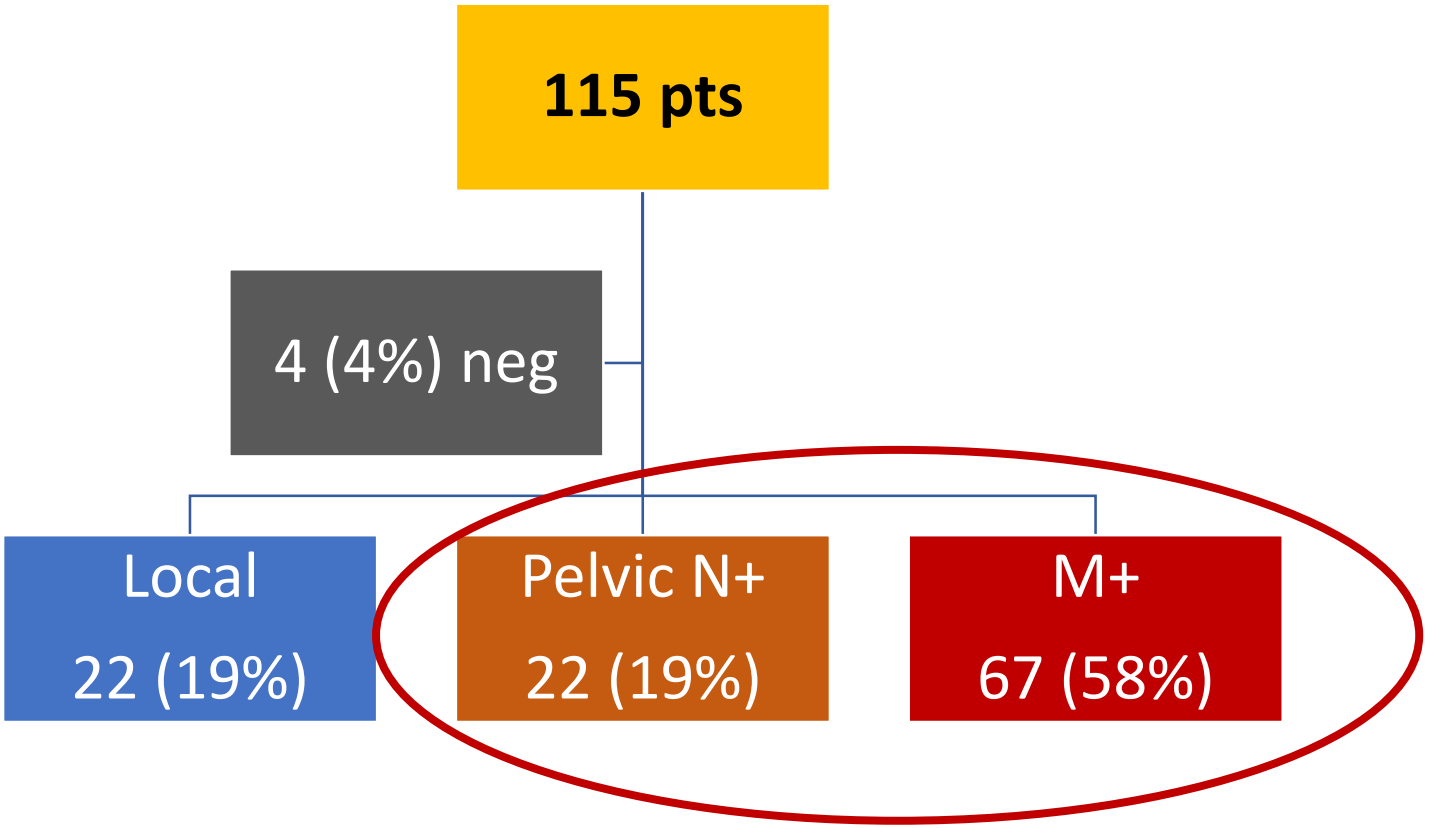
Crawford ED, J Urol DOI: 10.1016/j.juro.2018.05.164

RT in Oligom+ CRPC (first occurence)

NGI: PSMA PET-CT

115 M0 CRPC pts with PSA> 2 ng/ml and PSA-DT< 10 months

PSA DT < 6mos: 85 (74%) PSA-DT > 6mos: 30 (26%)



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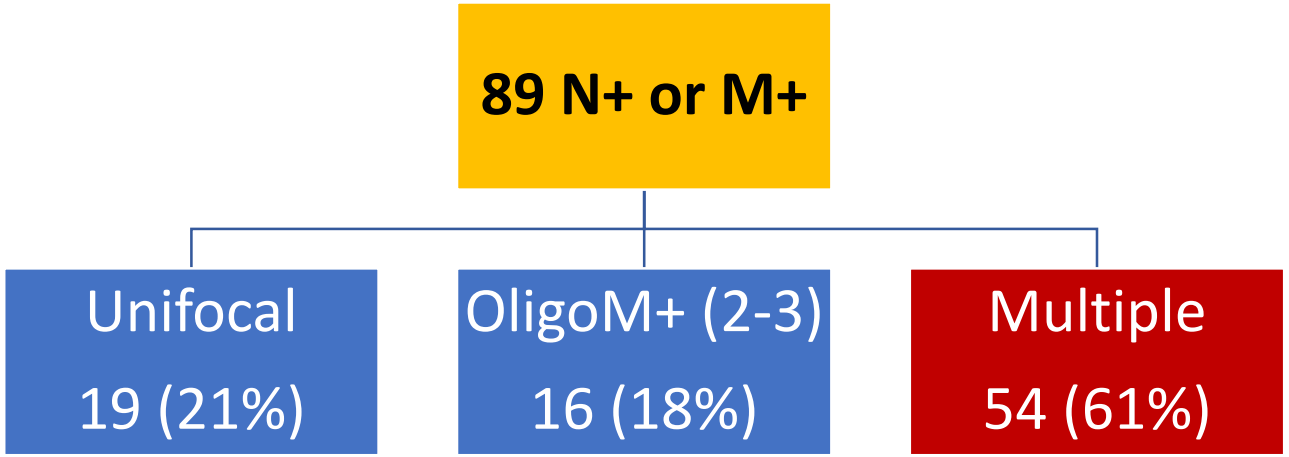
Fendler WP, Clin Can Res DOI: 10.1158/1078-0432.CCR-19-1050

RT in Oligom+ CRPC (first occurence)

NGI: PSMA PET-CT



Potentially suitable for Ablative/Radical RT: 57/115 (49.5%)

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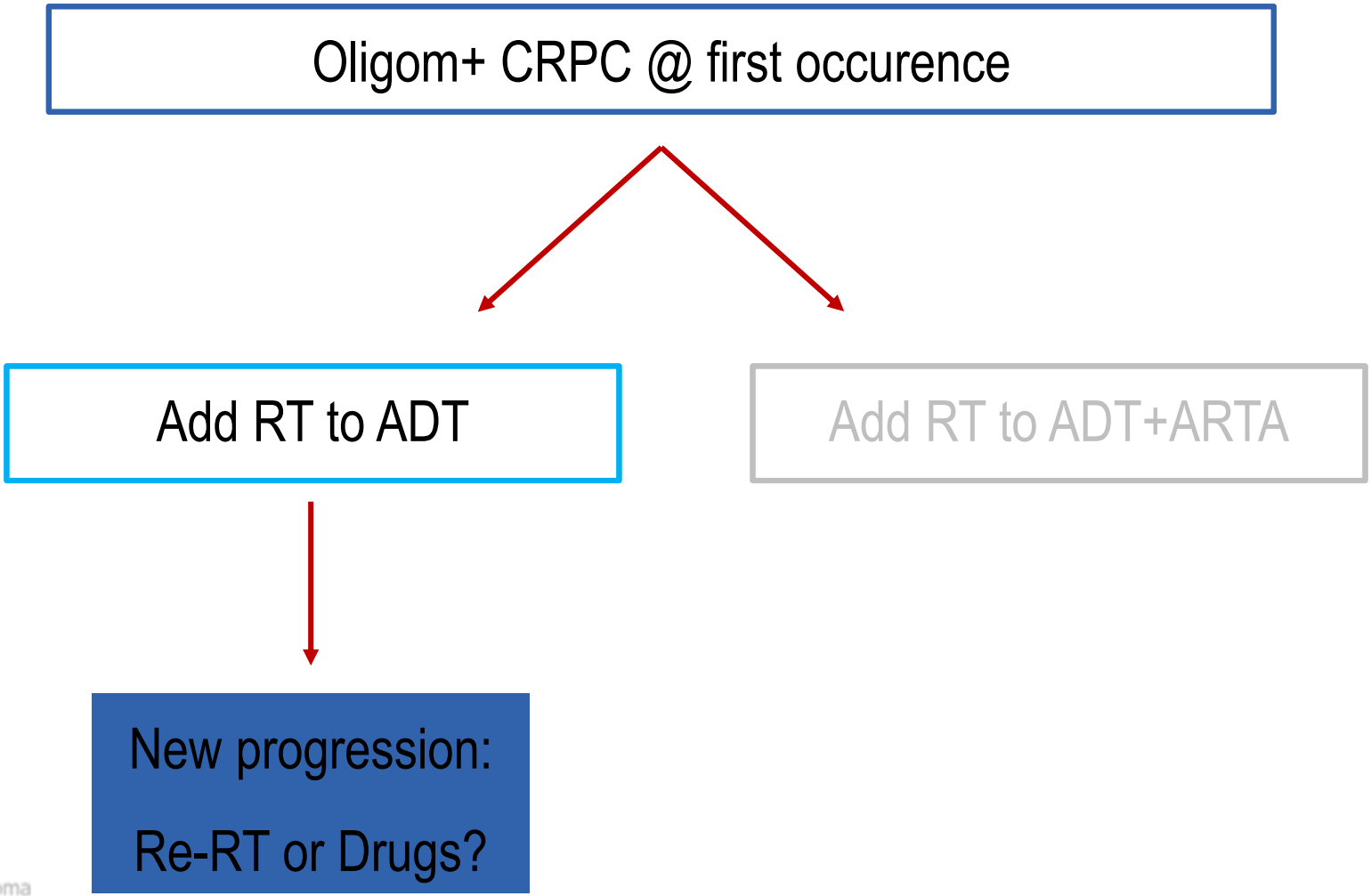
Fendler WP, Clin Can Res DOI: 10.1158/1078-0432.CCR-19-1050

RT in Oligom+ CRPC (first occurence)



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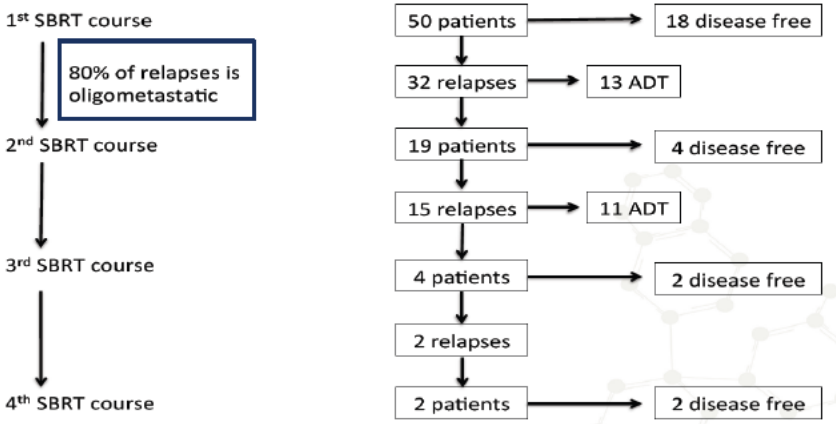
RT in Oligom+ CRPC (first occurence)

Progression is not the end of the story…



Decaestecker K. *et al*. Radiat Oncol 2014
Murphy DG *et al*. Eur Urol 2017

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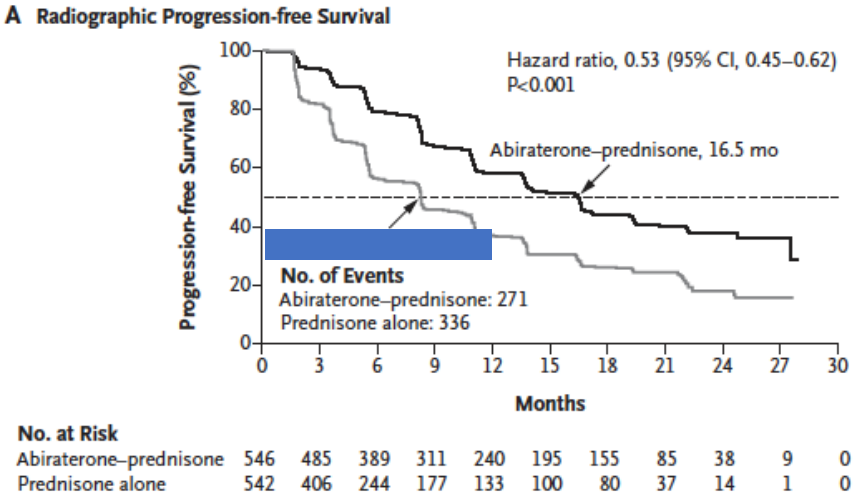
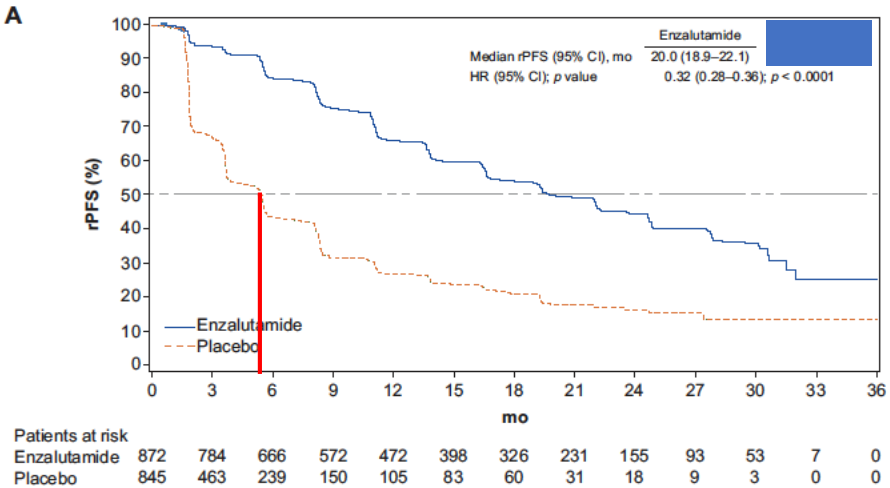
RT in Oligom+ CRPC (first occurence)

CT and Bone scan positive





At least six months or more between each treatment if CT and Bone Scan positive

Ryan CJ et al, DOI: 10.1056/NEJMoa1209096.
Beer TM et al, DOI: 10.1016/j.eururo.2016.07.032

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RT in Oligom+ CRPC (first occurence)

CT and Bone scan negative, PET-CT positive

	SPARTAN	PROSPER	ARAMIS
MFS – Placebo	16.2 mos	14.7 mos	18.4 mos
PSA progression - Placebo	3.7 mos	3.9 mos	7.3 mos

More than one year between each treatment

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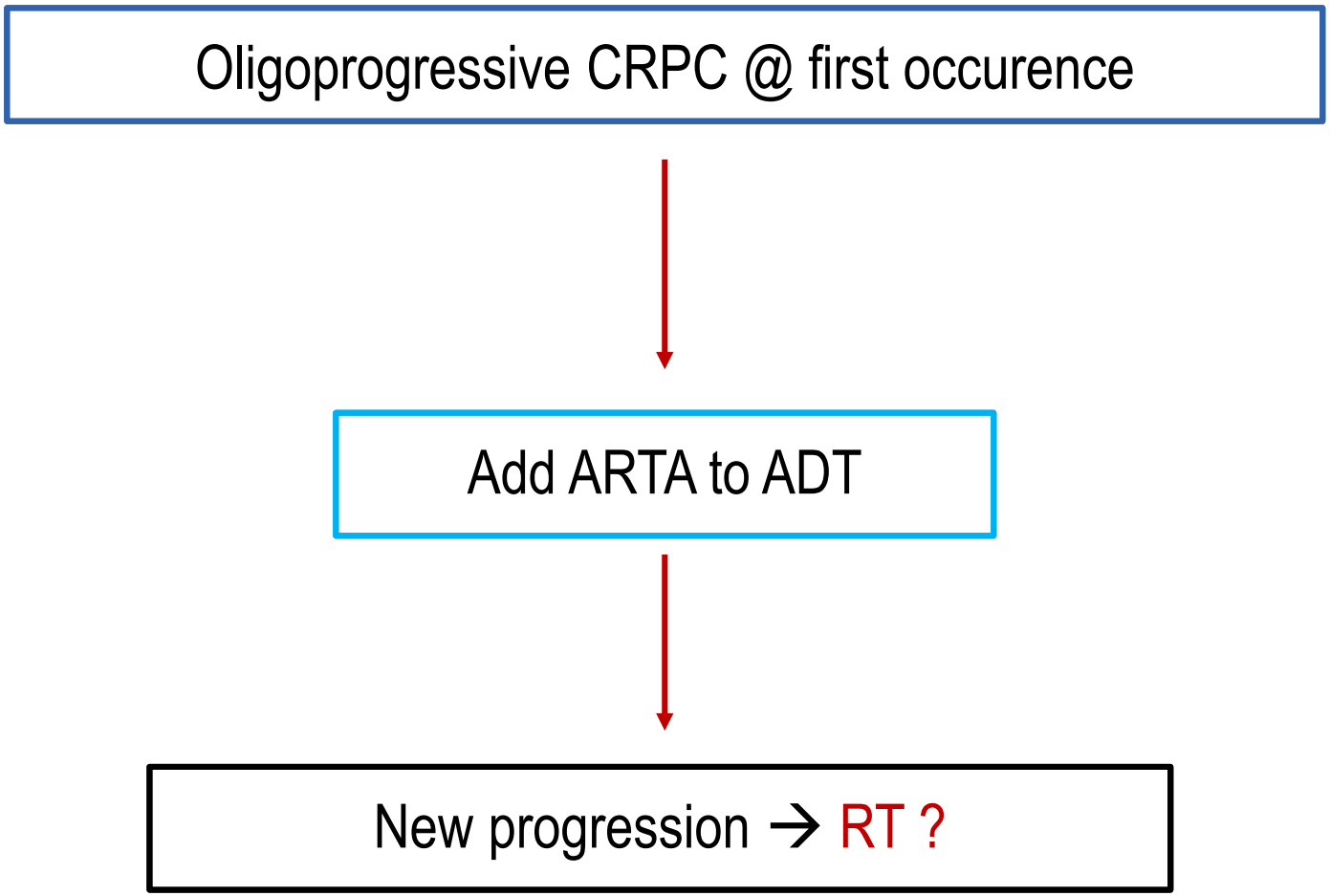
RT in Oligoprogressive CRPC



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RT in Oligoprogressive CRPC

VOLUME 34 · NUMBER 12 · APRIL 20, 2016

JOURNAL OF CLINICAL ONCOLOGY

SPECIAL ARTICLE

Trial Design and Objectives for Castration-Resistant Prostate Cancer: Updated Recommendations From the Prostate Cancer Clinical Trials Working Group 3

RECOMMENDATION FROM THE PROSTATE CANCER CLINICAL WORKING GROUP 3 (2016):

In cases in which multiple sites of disease continue to respond but one to two sites grow, focal therapy such as radiation or surgery could be administered to the resistant site(s) and systemic therapy continued.

Scher, JCO, 2016

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Adding RT to ADT + AA

COU-AA-301 TRIAL

Feasibility

More than 60% of patients received RT to bone

No new safety signals were identified with 20.2 months median follow up

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Logothetis et al, Lancet Oncol 2012 Dec;13(12):1210-7.
Fizazi et al, Lancet Oncol 2012 Oct;13(10):983-92.

RT in Oligoprogressive CRPC

Study	Design	N. pts	Outcome	Adverse events
Tabata, 2012	Retrospective	35	OS @ 3 yrs: 77.2% PFS @1yr: 64.8%	N.R
Ahmed, 2013	Retrospective	17	LC @6 months:100% bPFS @6 months: 71%	2 G2 Events
Muldermans, 2016	Retrospective	66	MC @2 yrs: 82% bPFS @2 yrs:54% dPFS @2 yrs:45% OS @2 yrs:83	6 G1 Events 2 G2 Events
Triggiani, 2017	Retrospective	41	dPFS@ 1 yr: 43.2% dPFS@ 2 yrs 21.6%	1 G1 Event

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RT in Oligoprogressive CRPC

ANTICANCER RESEARCH *37*: 3717-3722 (2017)
doi:10.21873/anticanres.11744

Combining Abiraterone and Radiotherapy in Prostate Cancer Patients Who Progressed During Abiraterone Therapy

BEATRICE DETTI[1], ROLANDO M. D'ANGELILLO[2], GIANLUCA INGROSSO[3], EMANUELA OLMETTO[1], GIULIO FRANCOLINI[1], LUCA TRIGGIANI[4], ALESSIO BRUNI[5],

- 32 consecutive patients affected by metastatic castration-resistant prostate cancer (mCRPC) treated with abiraterone acetate
- Median progression-free survival (PFS) was 12.6 months from the initiation of abiraterone treatment.
- From RT administration, PFS was 9.6 months
- Median overall survival (OS) since abiraterone initiation was 18.9 months

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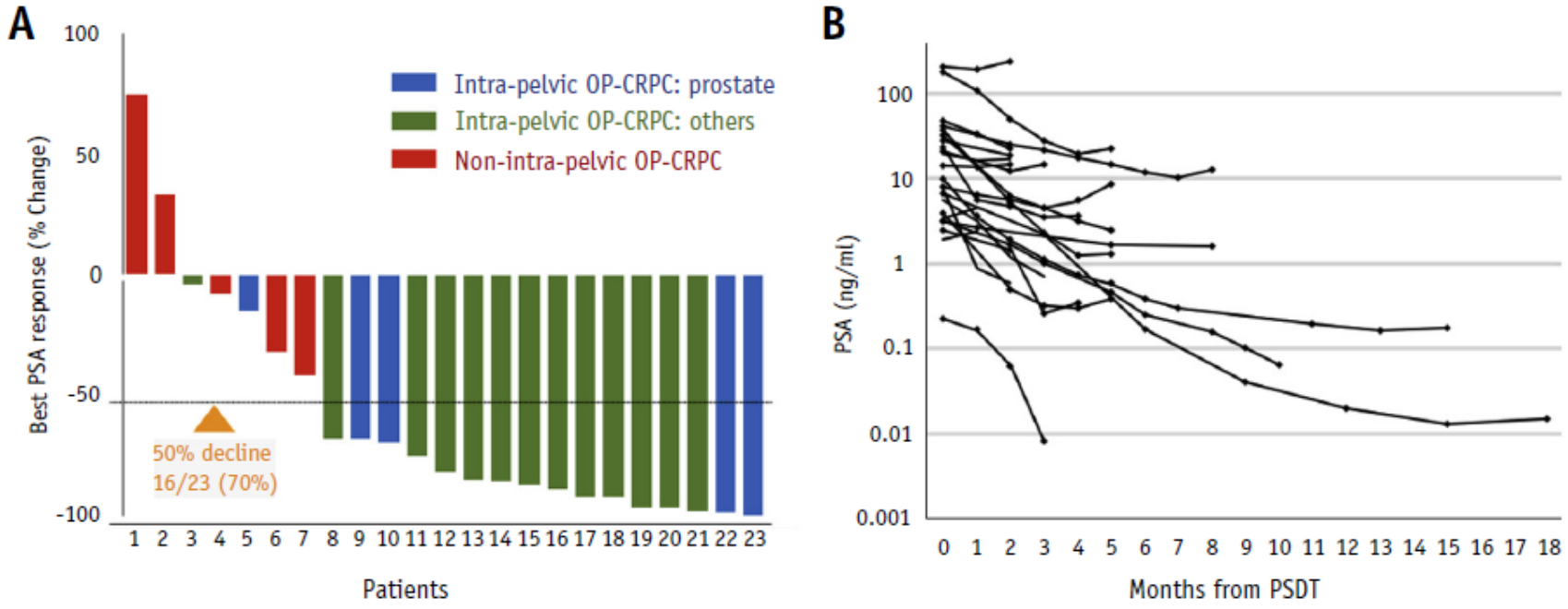
RT in Oligoprogressive CRPC

Treatment of Oligoprogressive mCRPC

23 Oligo-Progressive CRPC pts treated with radical RT on site of progressive disease

18 intrapelvic and 5 extra-pelvic disease



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Yoshida S, Red journal: 10.1016/j.ijrobp.2019.06.011

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AIRO position paper, Crit Rev Oncol Hematol,, 2019;138:24-28

RT in Oligometastatic and Oligoprogressive CRPC

Conclusions

Consider RT as alternative to drugs in selected CRPC patients, and remember that at least 6-12 months should be awaited from first to second RT

Do not omit local treatment in oligoprogressive disease

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