UCSF Helen Diller Family Comprehensive Cancer Center

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Treatment of oligometastatic and oligoprogressive CRPC

Eric J. Small, MD
University of California, San Francisco, CA, USA

UCSF Helen Diller Family Comprehensive Cancer Center

Disclosures – EJ Small

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Definitions: Oligometastatic CRPC

Oligometastatic CRPC

Limited number of metastases in a patient who has ADT-refractory PCa

Oligoprogressive CRPC

CRPC disease progression which is manifested as new oligometastases (some would hold in patients with **pre-existing metastases**)

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But, because the identification of pre-existing metastases is dependent on imaging modality, timing, and frequency……

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Definitions: Oligometastatic CRPC

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Limited number of metastases in a patient who has ADT-refractory Pca

~~**Oligoprogressive CRPC**~~

~~CRPC disease progression which is manifested as new oligometastases (some would hold in patients with **pre-existing metastases**)~~

Synchronous Oligometastatic CRPC

Metastases are synchronous with the emergence of ADT resistance

Metachronous Oligometastatic CRPC

(New) metastases follow the clinical emergence of ADT resistance

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Oligomet CRPC: Many unanswered questions

Questions Shared with (hormone naïve) prostate cancer

- What is the cutpoint between oligomet and polymet?
- Optimal imaging technology to identify oligomets?
- Optimal timing and frequency of imaging?
- Does the modality of oligomet ablation matter?

Questions with unique considerations in **CRPC** Disease State

1. Does it matter if oligomets are synchronous or metachronous?
2. What is the role of changing/adding systemic therapy?
3. What are appropriate endpoints to measure efficacy?

1. Does it matter if oligomets are synchronous or metachronous?

Oligomets Synchronous with CRPC (oligomets as first manifestation of CRPC)

- More systemic therapeutic options
- More radiosensitive than patients with later dz?
- Ablation of early CRPC clone(s) that have developed metastatic potential may delay the progression to a more subclonal cancer

Oligomets Metachronous (come after) CRPC

- Fewer systemic therapeutic options if CRPC already being treated
- Is radiobiology different than in patients whose CRPC has just emerged?
- Likely that a subclonal cancer has already been established, and ablation of metastases won't affect clonal evolution

2. What is the role of systemic therapy?

73 year old man

8 yrs ago: PSA 12, GS 4 + 3, cT3b, N0, M0

RP, adjuvant XRT

4 years ago: PSA recurrence

3 years ago treated with ADT

1 year ago PSA started to climb

PSA now 4.6, Testosterone 18
PSADT = 6.8 months

Negative Tc Bone Scan
Negative CT Abd/Pelvis

2. What is the role of systemic therapy?

Diagnosis: nmCRPC

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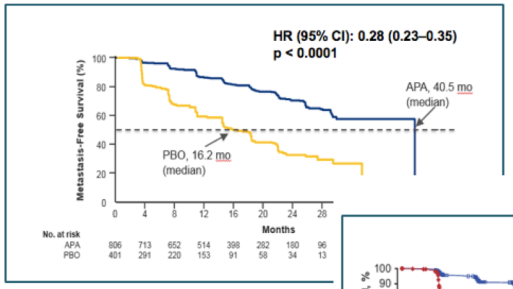
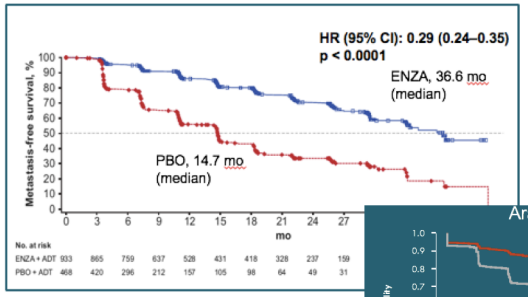
Diagnosis: nmCRPC
Treatment:
apalutamide, enzalutamide, or darolutamide

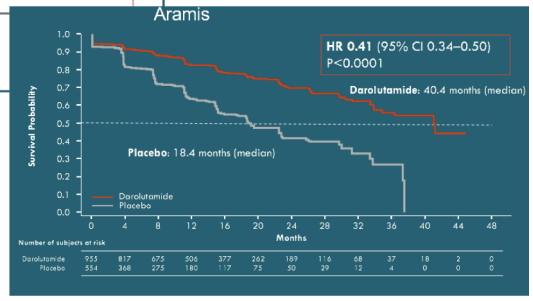
The "SPA" treatment
Spartan, **P**rosper, **A**ramis

SPARTAN[1]



PROSPER[2]





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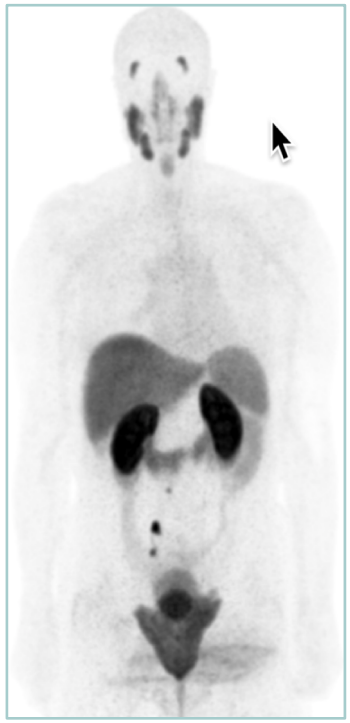
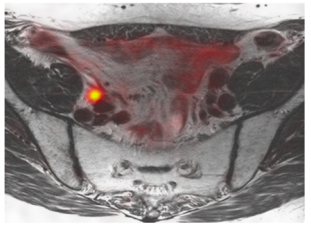
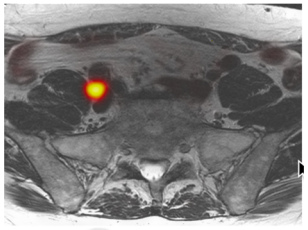
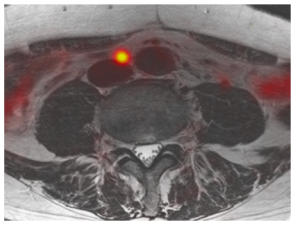
Prior to SPA Therapy a 68Ga-PSMA-11 PET undertaken.









Diagnosis: PSMA PET detected oligometastatic dz

Treatment of “nmCRPC” that isn’t non-metastatic

Higher sensitivity imaging modalities will further reduce the proportion of patients with “non-metatstatic” CRPC.

How likely is PSMA PET to reveal metastases in nmCRPC SPA-like patients?

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Retrospective study of "SPA-like" nmCRPC patients who had previously undergone PSMA PET

Eligibility

Histologically confirmed PCa; N = 200

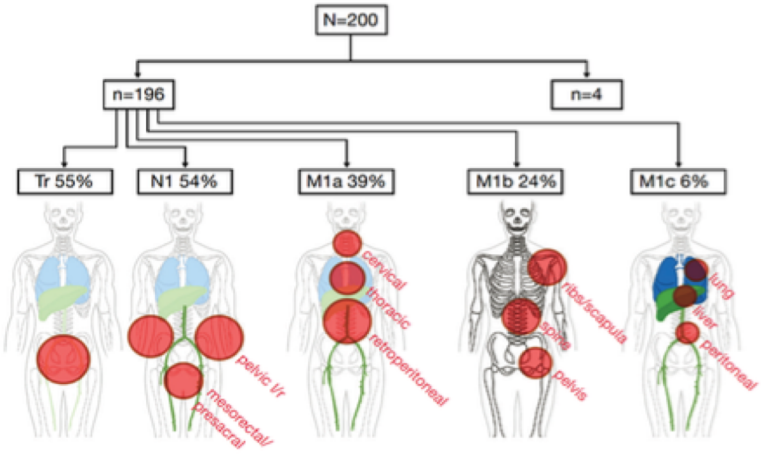
CRPC

PSA > 2

PSADT </= 10 mos or GS 8,9,10

No pelvic node > 2 cm

No known extrapelvic mets



Results

PSMA PET detected disease in 98% of pts

24% of pts had loco-regional (Tr)

20% of pts had (any) N1 disease

54% of pts had (any) M1 disease

Pts with single metastasis:	15%
Pts with 2-3 metastases:	14%
Pts with oligometastatic dz:	**29%**

Fendler et al. In press, Clin Can Res

Treatment of nmCRPC that isn't non-metastatic

Level 1 evidence supports the use of a next generation AR Inhibitor in nmCRPC men who are very likely to have oligometastatic disease on functional imaging.

Role of ablative RT of oligomets without systemic therapy: very limited data

Combined aRT and a SPA regimen certainly reasonable, but not yet studied.

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What is the utility of local ablative radiotherapy (without systemic therapy) to control oligomet CRPC?

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

European Association of Urology

Brief Correspondence

Can Local Ablative Radiotherapy Revert Castration-resistant Prostate Cancer to an Earlier Stage of Disease?

Fabian Lohaus [a,b,c], *Klaus Zöphel* [c,e], *Steffen Löck* [b,c,a], *Manfred Wirth* [g,h], *Jörg Kotzerke* [c,e], *Mechthild Krause* [a,b,c,f,h], *Michael Baumann* [a,b,d,f,h], *Esther G.C. Troost* [a,b,c,f,h], *Tobias Hölscher* [a,b,*]

(Dresden) Nov 2018

Methods

Retrospective Study

Patient eligibility (n = 15)

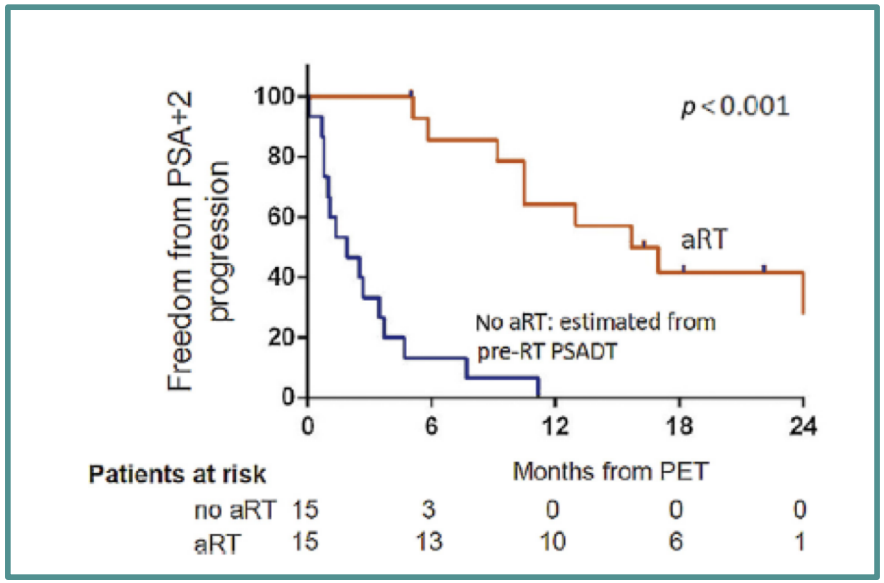
- Prior definitive local rx
- CRPC
- PSMA PET +
- Asymptomatic mets
- Oligomet(s) treated with ablative RT
- At least 2 PSA values post aRT

Methods

Point of PSA Progression determined for each pt: PSA nadir + 2 ng/ml

The individual time to PSA Progression without aRT was estimated for all pts by their individually calculated PSA doubling time (PSADT) before aRT.

Results



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World Journal of Urology
pp 1–7 | Cite as

Metastasis-directed stereotactic radiotherapy for oligoprogressive castration-resistant prostate cancer: a multicenter study

Authors | Authors and affiliations

Luca Triggiani, Rosario Mazzola, Stefano Maria Magrini, Gianluca Ingrosso, Paolo Borghetti, Fabio Trippa, Andrea Lancia, Beatrice Detti, Giulio Francolini, Fabio Matrone, Roberto Bortolus, Giuseppe Fanetti, Ernesto Maranzano, Francesco Pasqualetti, Fabiola Paiar, Marco Lorenzo Bonù, Alessandro Magli, Alessio Bruni, Ercole Mazzeo, Ciro Franzese, Marta Scorsetti, Filippo Alongi, Barbara Alicja Jereczek-Fossa, Piet Ost, Michela Buglione, show less

Original Article
First Online: 11 March 2019

Study Design

Retrospective Study; 11 centers

86 pts with 117 lesions

Oligoprogressive during ADT (synchronous)

Choline PET CT or CT + Bone Scan

Controlled Primary Tumor

Results

Median (Next) metastasis free survival: 12.3 months

1 year (next) metastasis free survival rate: 52.3%; 1 yr systemic rx free os = 71%

2 year (next) metastasis freee survival rate: 33.7%

Median systemic-therapy free OS: 21.8 months

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International Journal of Radiation Oncology biology • physics
Official Journal of the American Society for Radiation Oncology ASTRO

Article in Press (June, 2019)

Progressive Site-Directed Therapy for Castration-Resistant Prostate Cancer: Localization of the Progressive Site as a Prognostic Factor

Soichiro Yoshida, MD, PhD[*,†,‡], Taro Takahara, MD, PhD[†,‡], Yuki Arita, MD[‡,§], Chikako Ishii, MD, PhD[‡], Yusuke Uchida, MD[*], Keiko Nakagawa, MD, PhD[‖], Kazuma Toda, MD, PhD[‖], Tsuyoshi Sakamoto, BHS[¶], Toshiki Kijima, MD, PhD[*], Minato Yokoyama, MD, PhD[*], Junichiro Ishioka, MD, PhD[*], Yoh Matsuoka, MD, PhD[*], Kazutaka Saito, MD, PhD[*], Ryoichi Yoshimura, MD, PhD[‖], Yasuhisa Fujii, MD, PhD[*]

Study Design

Retrospective Study
23 pts with CRPC, who developed subsequent oligomets (metachronous)
Whole body dw MRI at time of planned new systemic therapy
No change in systemic therapy (recommended)

Results

7/23 pts had radiation to prostate or pelvic nodes
15/23 pts had radiation to bone (1pt both)

	All Patients	Intra-pelvic mets	Extra-pelvic mets
>50% decline in PSA	70%	89%	0%
Time to PSA PD	8.7 mos	10.1 mos	4.8 mos

Conclusions

Ablative RT of both synchronous and metachronous oligometastatic CRPC is feasible, and safe.

Data are provocative, but very premature

No prospective, comparative data to suggest that aRT is beneficial.

No prospective data to compare ablativeRT (or surgery) in synchronous vs metachronous mets

No prospective data to define the role of adding aRT to systemic therapy

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Diagnosis: nmCRPC

Treated with Apalutamide.
PSA declines to undetectable, but after 3 years starts to progress.

Re-imaging reveals 2-3 new lesions in bone

Oligo-recurrent nmCRPC while on appropriate therapy

- No data yet to suggest that biology is different from poly-metastatic CRPC.
- Utility of secondary ASI not well tested, but likely limited
- Established systemic therapy options include chemotherapy, SipT, radium
- Risk/benefit ratio of chemotherapy vs aRT may favor aRT, but there are no data.

Questions with unique considerations in CRPC Disease State

1. **Does it matter if oligomets are synchronous or metachronous?**

   A: Probably, but unproven

2. **What is the role of changing/adding systemic therapy?**

   A: Other than “SPA” therapy for nmCRPC, unknown, but likely important.

3. **What are appropriate endpoints to measure efficacy?**

   A: Unknown. PSA Decline a reasonable screen.

   ?MFS

Thank you!

Questions?
Meet me here later this afternoon to discuss.