ONKOLOGICKÁ KLINIKA
FAKULTNÍ NEMOCNICE OLOMOUC

Department of Clinical and Molecular Pathology

Cell-free DNA for prostate cancer progression monitoring

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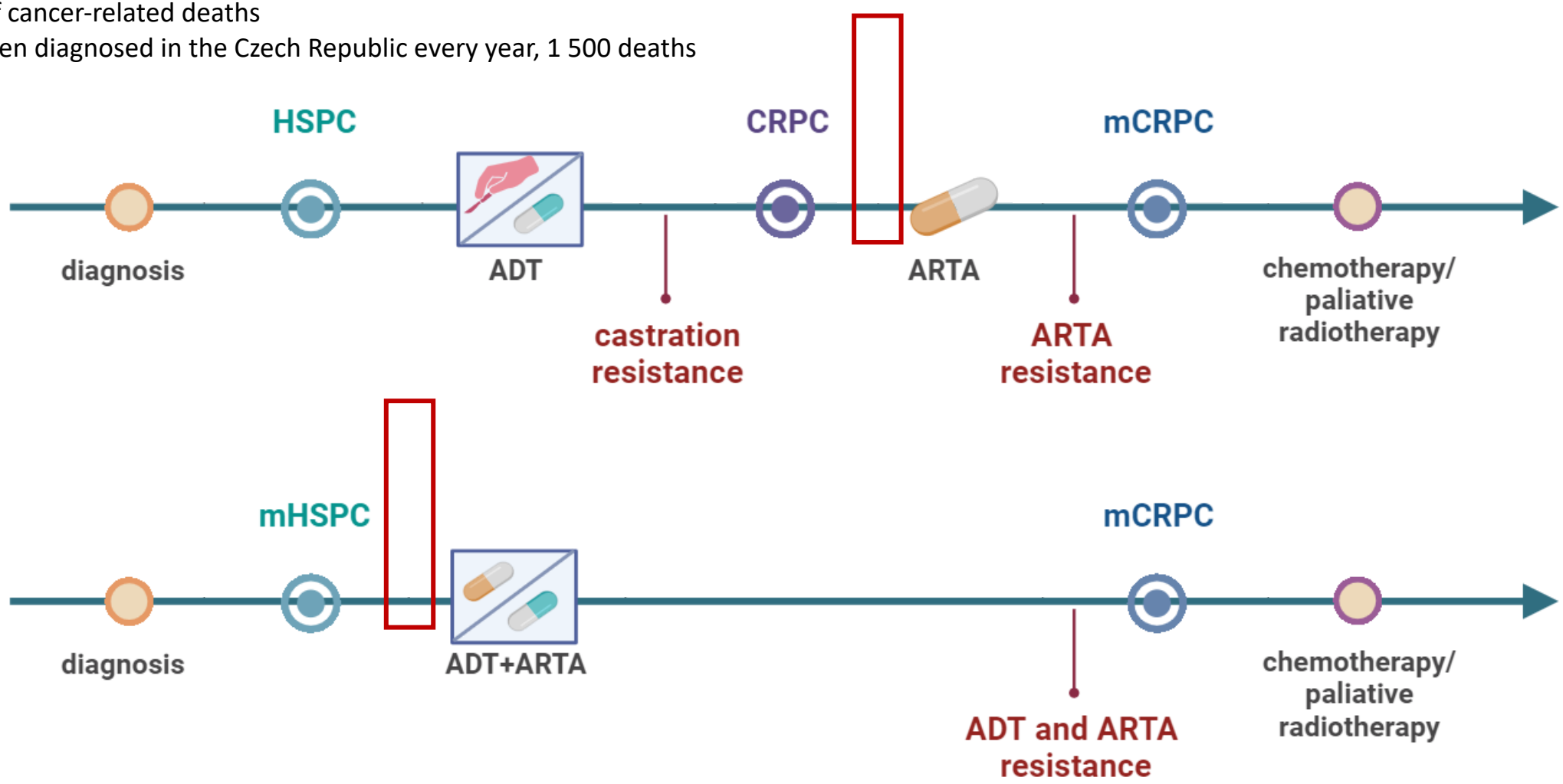
Liquid biopsy for monitoring of ARTA failure:

- Current survival of all prostate cancer (PCa) patients is 97% in western world (Siegel et al. 2023). However, due to the high incidence, PCa is the second leading cause of cancer-related deaths
- 8 000 men diagnosed in the Czech Republic every year, 1 500 deaths



Scheme of treatment: hormonal-sensitive PCa (HSPC) treated by androgen deprivation therapy (ADT), after castration resistant PCa (CRPC) occurrence treatment by androgen receptor-targeting therapy (ARTA), treatment failure, development of metastatic castration-resistant PCa (CRPC) and progression
:metastatic hormonal-sensitive PCa (mHSPC) treated by androgen deprivation therapy (ADT) in combination with androgen receptor-targeting therapy (ARTA), treatment failure, development of metastatic castration-resistant PCa (CRPC) and progression.

Liquid biopsy for monitoring of ARTA failure:

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- However, due to the high incidence, PCa is the second leading cause of cancer-related deaths
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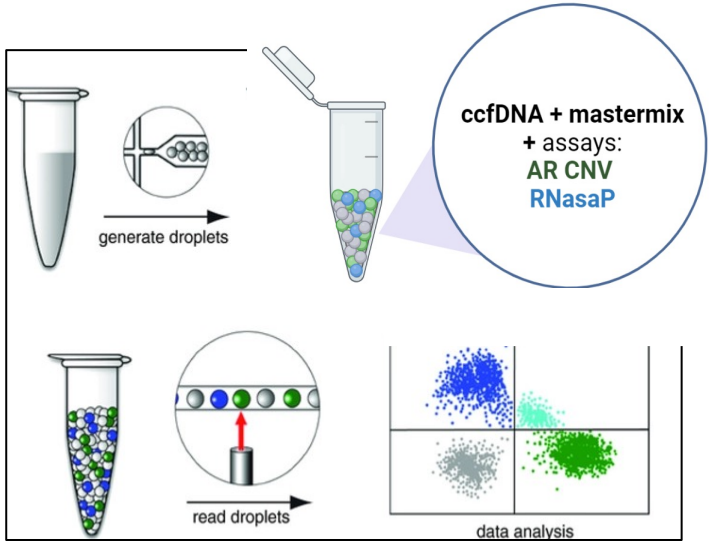
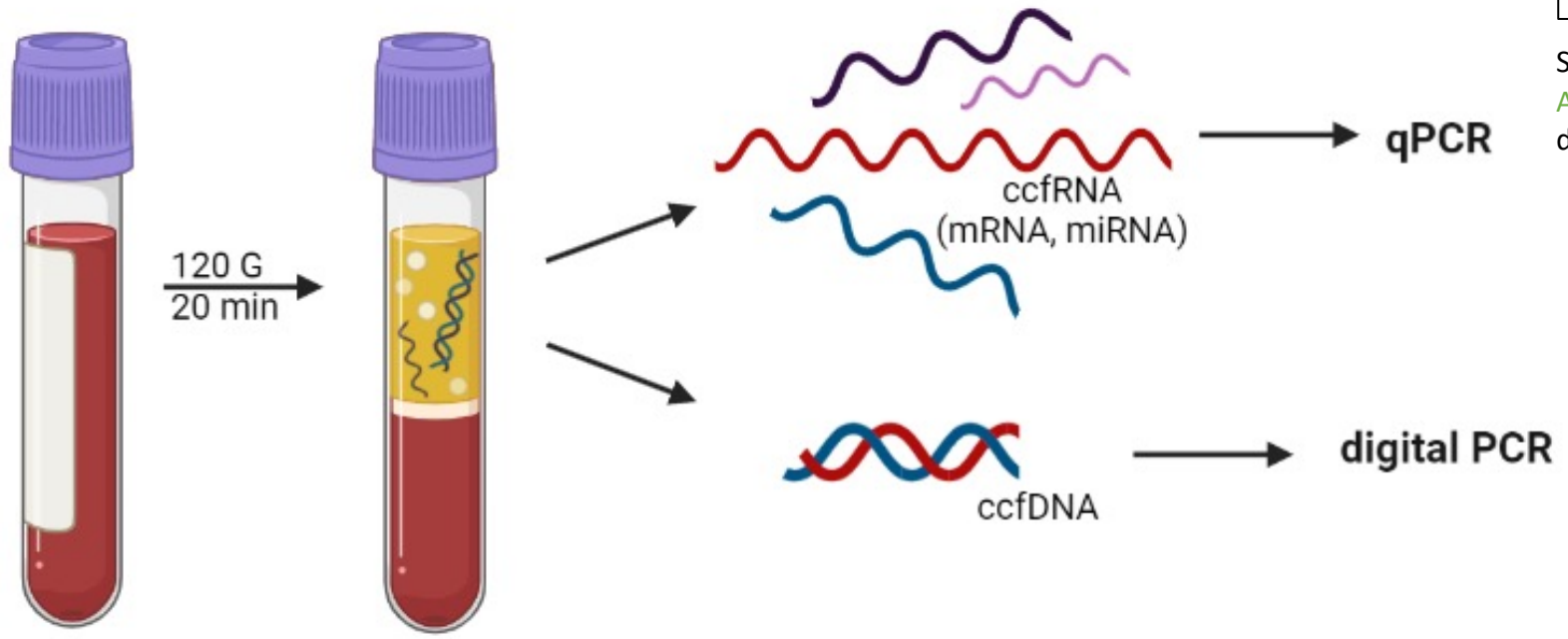


Suitable method for CNV analysis (compatriotism of AR gene positive droplets to RNAsaP positive droplets)



Scheme of the LB samples processing: blood sample, plasma separation (120g, 20 min); ccfDNA/RNA isolation; real-time PCR or digital PCR.

Literature about CNV of AR gene and digital PCR

Journal of *Clinical Medicine*

Article

Biomarkers of Castrate Resistance in Prostate Cancer: Androgen Receptor Amplification and T877A Mutation Detection by Multiplex Droplet Digital PCR

Francis P. Young [1,2], Therese M. Becker [1,2,3], Mohammed Nimir [1,2], Thomas Opperman [1,2], Wei Chua [3,4], Bavanthi Balakrishnar [4], Paul de Souza [2,3] and Yafeng Ma [1,2,*]

International Journal of *Molecular Sciences*

Article

Droplet Digital PCR Based Androgen Receptor Variant 7 (AR-V7) Detection from Prostate Cancer Patient Blood Biopsies

Yafeng Ma [1], Alison Luk [1], Francis P. Young [1,2], David Lynch [1,3], Wei Chua [4], Bavanthi Balakrishnar [4], Paul de Souza [1,2,3,4] and Therese M. Becker [1,2,3,*]

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Plasma *AR* and abiraterone-resistant prostate cancer

Alessandro Romanel[#1], Delila Gasi Tandefelt[#2], Vincenza Conteduca[2,3], Anuradha Jayaram[2,4], Nicola Casiraghi[1], Daniel Wetterskog[2], Samanta Salvi[3], Dino Amadori[3], Zafeiris Zafeiriou[2,4], Pasquale Rescigno[2,4], Diletta Bianchini[2,4], Giorgia Gurioli[3], Valentina Casadio[3], Suzanne Carreira[2], Jane Goodall[2], Anna Wingate[2,4], Roberta Ferraldeschi[2,4], Nina Tunariu[2,4], Penny Flohr[2], Ugo De Giorgi[3], Johann S de Bono[2,4], Francesca Demichelis[1,5,6,8], and Gerhardt Attard[2,4,8]

Prognostic association of plasma cell-free DNA-based androgen receptor amplification and circulating tumor cells in pre-chemotherapy metastatic castration-resistant prostate cancer patients

Manish Kohli[1] · Jian Li[2,3] · Meijun Du[3] · David W Hillman[4] · Scott M. Dehm[5,6] · Winston Tan[7] · Rachel Carlson[4] · Michael B. Campion[8] · Liguo Wang[4] · Liewei Wang[9] · Huijuan Zhang[3,10] · Peng Zhang[3] · Deepak Kilari[11] · Chiang-Ching Huang[12] · Liang Wang[3]

SCIENTIFIC REPORTS

OPEN

Plasma androgen receptor and serum chromogranin A in advanced prostate cancer

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Vincenza Conteduca[1,2], Emanuela Scarpi[3], Samanta Salvi[4], Valentina Casadio[4], Cristian Lolli[1], Giorgia Gurioli[4], Giuseppe Schepisi[1], Daniel Wetterskog[2], Alberto Farolfi[1], Cecilia Menna[1], Delia De Lisi[5], Salvatore Luca Burgio[1], Himisha Beltran[6], Gerhardt Attard[2,7] & Ugo De Giorgi[1]

Clinical Chemistry 0:0
1–10 (2020)

Other Areas of Clinical Chemistry

Prognostic Value of Novel Liquid Biomarkers in Patients with Metastatic Castration-Resistant Prostate Cancer Treated with Enzalutamide: A Prospective Observational Study

Guillemette E. Benoist,[a] Inge M. van Oort,[b] Emmy Boerrigter,[a] Gerald W. Verhaegh,[b] Onno van Hooij,[b] Levi Groen,[b] Frank Smit,[c] Pieter de Mol,[d] Paul Hamberg,[e] Vincent O. Dezentjé,[f] Niven Mehra,[g] Winald Gerritsen,[g] Diederik M. Somford,[h] Nielka P.H. van Erp,[a] and Jack A. Schalken[b,*]

biomedicines

Article

The Percentage of Free PSA and Urinary Markers Distinguish Prostate Cancer from Benign Hyperplasia and Contribute to a More Accurate Indication for Prostate Biopsy

Zlata Huskova [1], Jana Knillova [1], Zdenek Kolar [1], Jana Vrbkova [2], Milan Kral [3,*] and Jan Bouchal [1,*]

Androgen receptor gene status in plasma DNA associates with worse outcome on enzalutamide or abiraterone for castration-resistant prostate cancer: a multi-institution correlative biomarker study

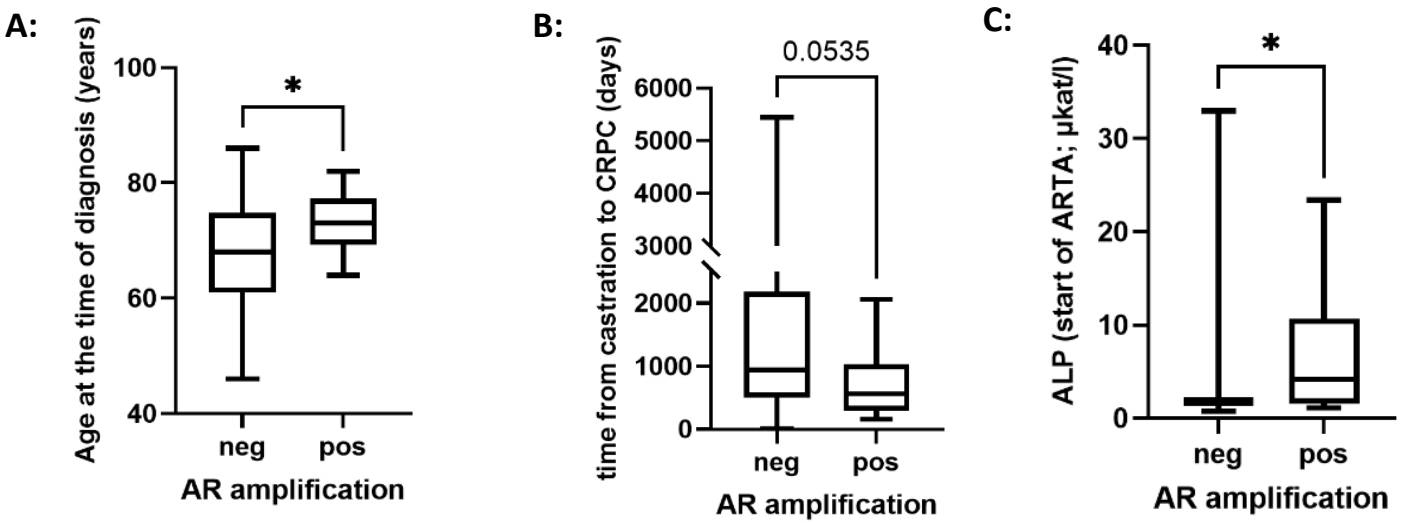
V. Conteduca[1,2†], D. Wetterskog[1†], M. T. A. Sharabiani[3†], E. Grande[4†], M. P. Fernandez-Perez[5], A. Jayaram[1,6], S. Salvi[2], D. Castellano[7], A. Romanel[8], C. Lolli[2], V. Casadio[2], G. Gurioli[2], D. Amadori[2], A. Font[9], S. Vazquez-Estevez[10], A. González del Alba[11], B. Mellado[12], O. Fernandez-Calvo[13], M. J. Méndez-Vidal[14], M. A. Climent[15], I. Duran[16], E. Gallardo[17], A. Rodriguez[18], C. Santander[19], M. I. Sáez[20], J. Puente[21], D. Gasi Tandefelt[1], A. Wingate[1], D. Dearnaley[6,22], PREMIERE Collaborators[5], Spanish Oncology Genitourinary Group, F. Demichelis[8,23], U. De Giorgi[2‡], E. Gonzalez-Billalabeitia[5,24*‡] & G. Attard[1,6*‡]

Testosterone levels and androgen receptor copy number variations in castration-resistant prostate cancer treated with abiraterone or enzalutamide

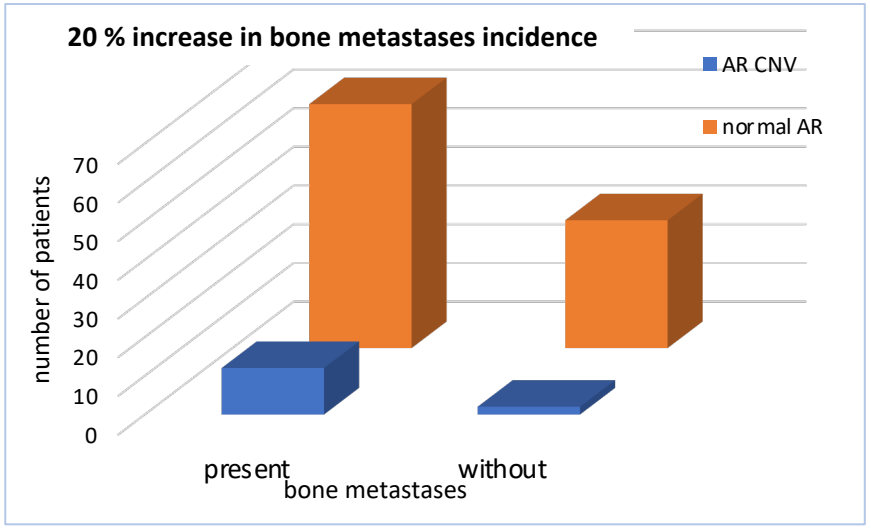
Cristian Lolli, Delia De Lisi, Vincenza Conteduca, Giorgia Gurioli, Emanuela Scarpi, Giuseppe Schepisi, Giorgia Ravaglia, Cecilia Menna, Alberto Farolfi, Amelia Altavilla ... See all authors

Amplification of AR associates with clinical parameters

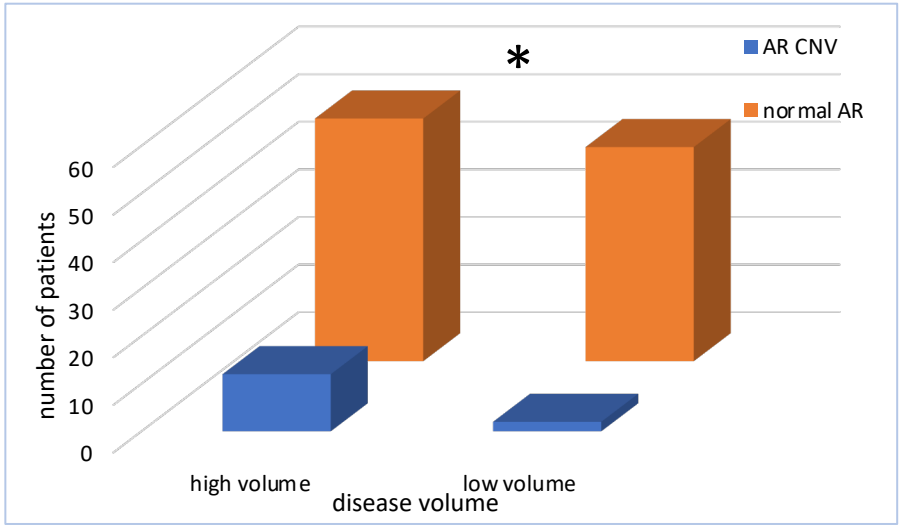
15.4 % of 110 patients (42 mHSPC and 68 mCRPC) **had AR gene amplification** in baseline LB samples (taken before ARTA started)



Statistical analysis (Mann-Whitney test) of patients with amplification of AR gene (pos) or without AR gene amplification (neg) from baseline plasma samples with the clinical characteristics of the patients **A:** Patients with CNV of AR were significantly older at the time of diagnosis (p=0.0122) than patients without AR CNV. **B:** Patients with CNV of AR had a quicker occurrence of CRPC compared to CNV negative patients (p=0.0535). C: Patients positive for CNV of AR had elevated levels of ALP (p=0.0185) Box plots represent the median, 25, 75 percentiles and the range of values. The p-value <0.05 is indicated by *.

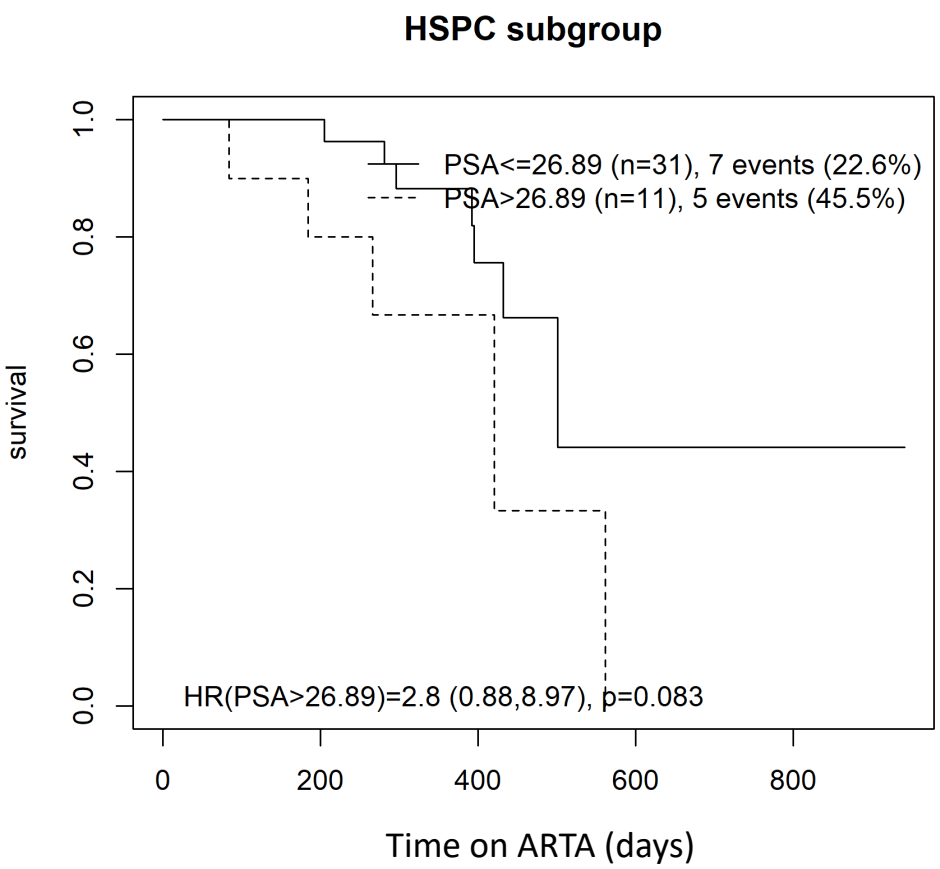


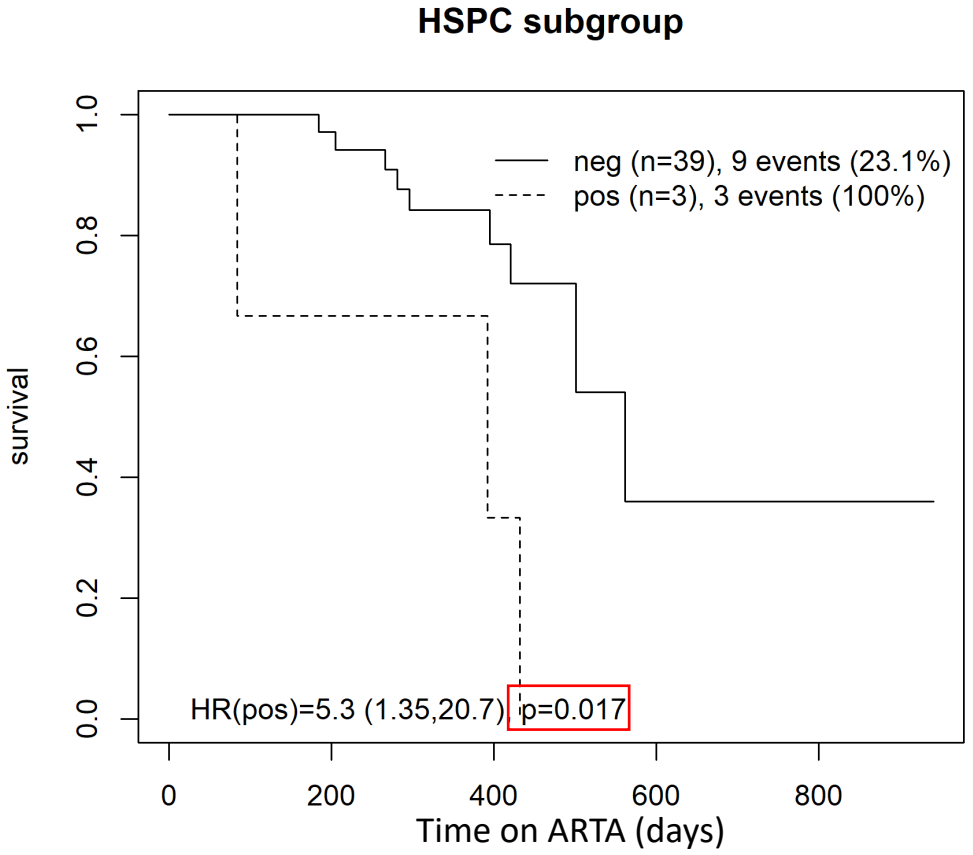
86 % (12 of 14) patients with CNV of AR had bone metastases compared to 66 % of patients without CNV of AR (p=0.0757).



Patients with AR gene amplification had **more often high-volume disease** at the start of ARTA compared to the patients without AR amplification (p=0.0286).

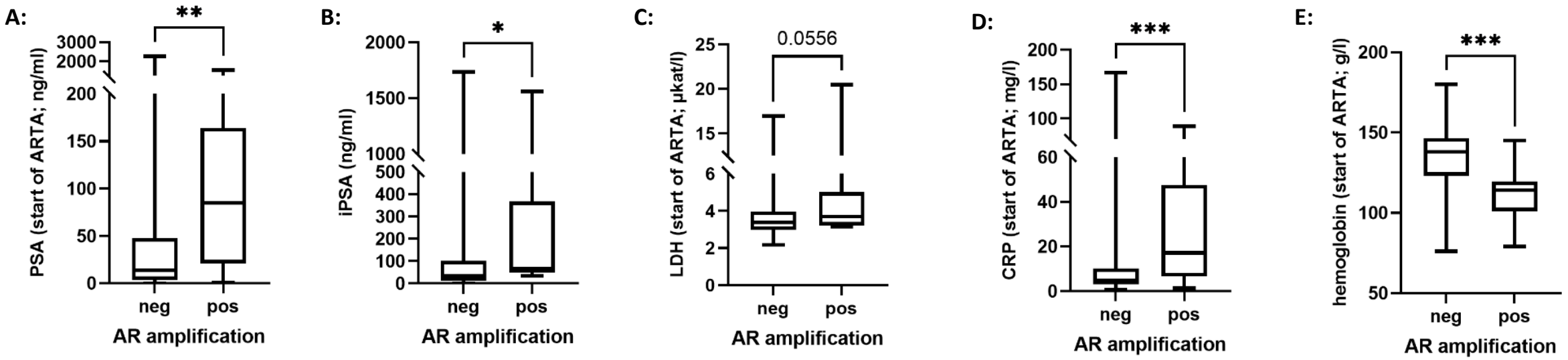
Survival on ARTA based on AR CNV status





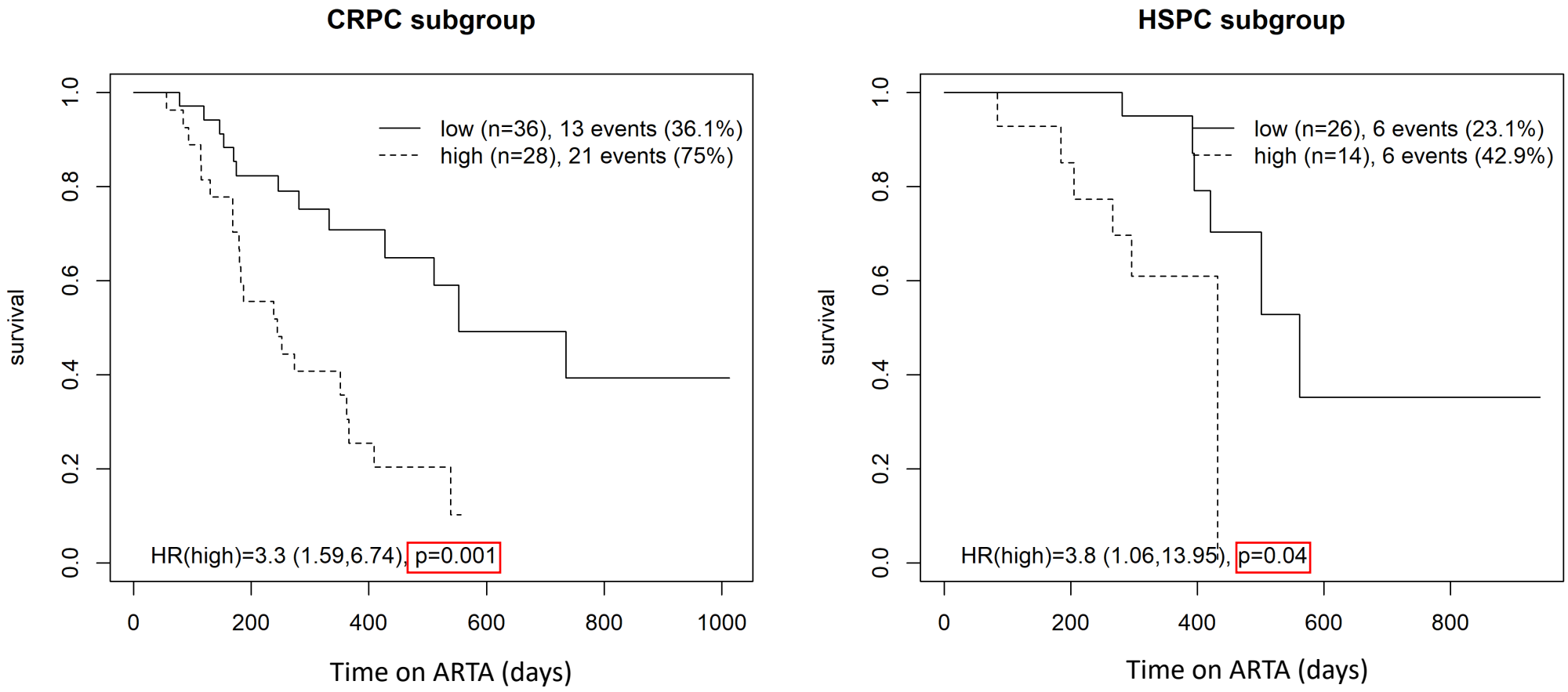
Kaplan-Meier analysis of time on ARTA in HSPC (n=42) and **CRPC** (n=68) **patients positive or negative for amplification of AR gene** (CNV, copy number variation)**.** HSPC patients with amplification of AR gene were treated by ARTA for significantly shorter time (**p=0.017**).

Amplification of AR associates with laboratory results



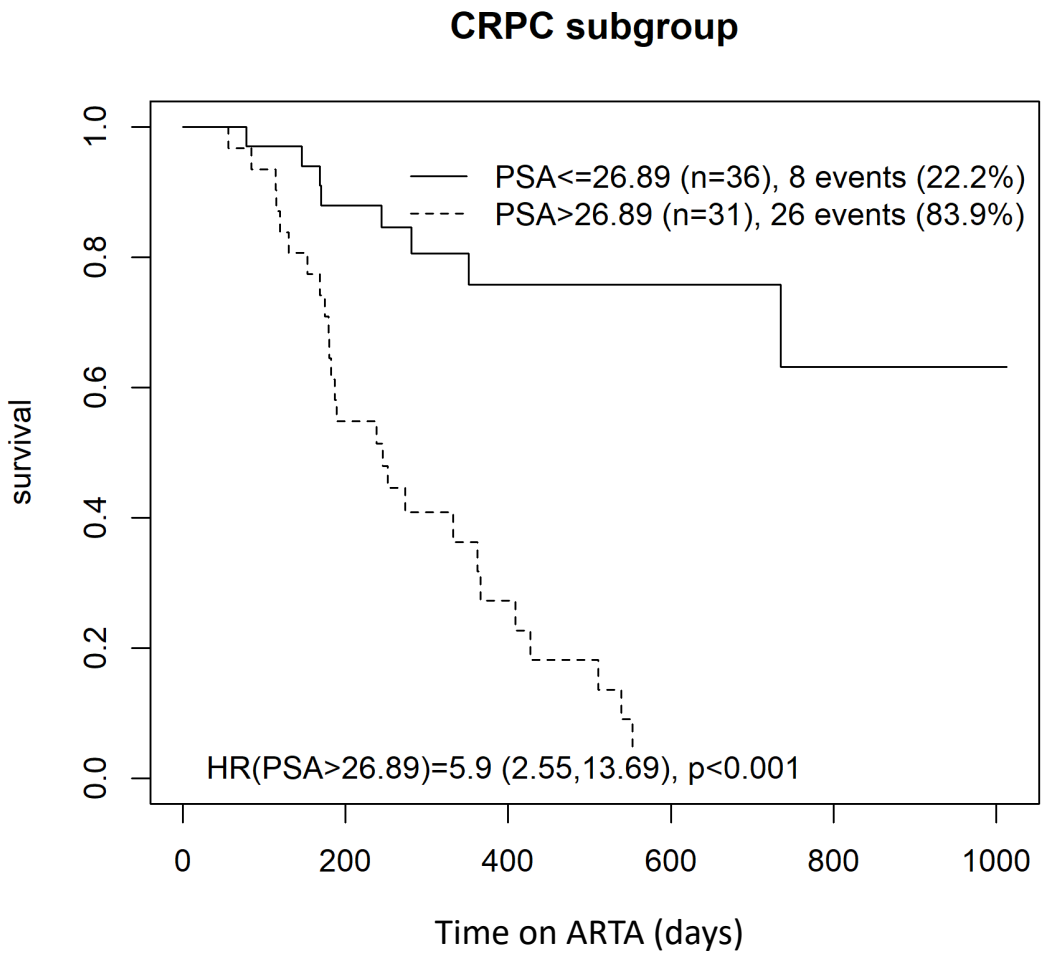
Statistical analysis (Mann-Whitney test) of patients with amplification of AR gene (pos) or without AR gene amplification (neg) from baseline plasma samples with the clinical characteristics of the patients **A:** Patients with amplification of AR had significantly higher PSA levels at the start of ARTA (p=0.0082), **B:** and increased initial PSA (p=0.0116). **C:** elevated levels of LDH (0.0556). **D:** Patients with amplification of AR had also significantly higher CRP levels at the start of ARTA therapy (p=0.0007). **E:** Patients positive for CNV of AR had decreased levels of hemoglobin (p=0.0001). Box plots represent the median, 25, 75 percentiles and the range of values. The p-values <0.05, <0.01, and <0.001 are indicated by *, ** and *** respectively.

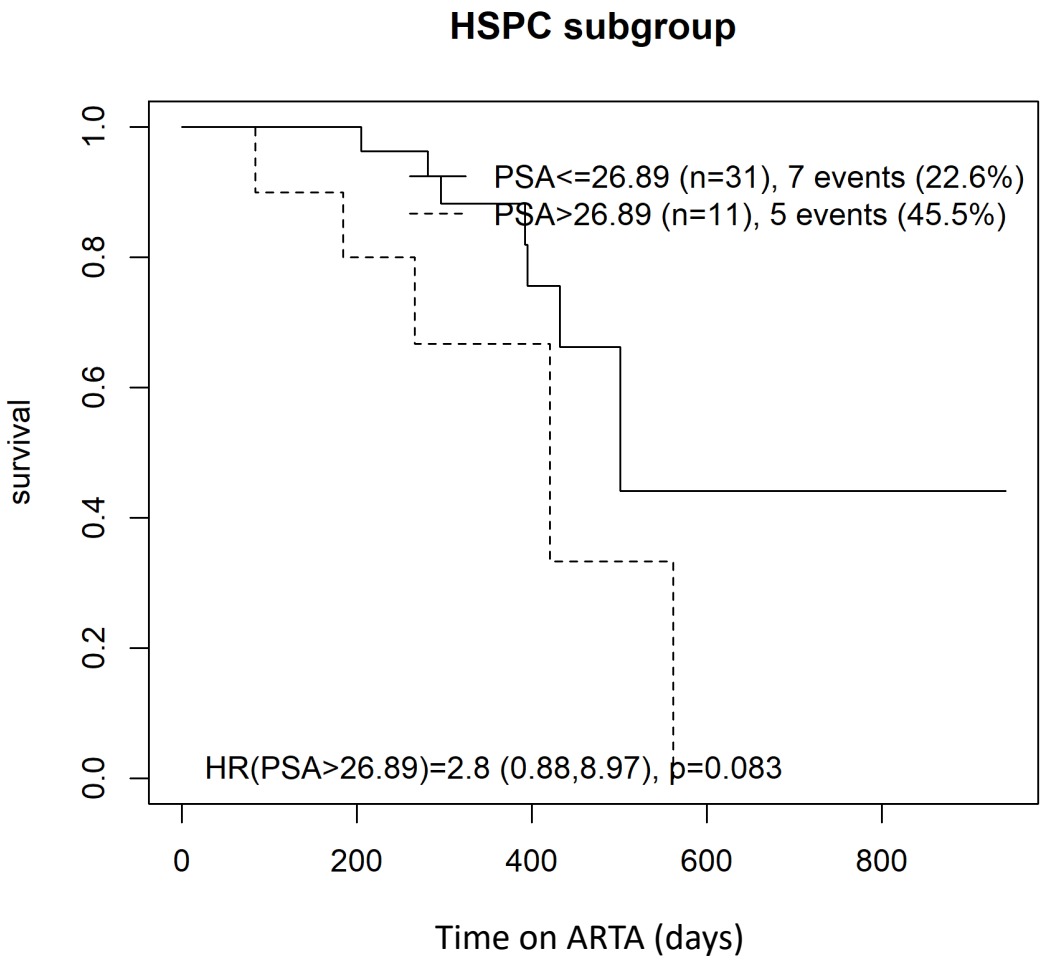
Survival on ARTA based on CRP status



Kaplan-Meier analysis of time on ARTA in HSPC (n=40) **and CRPC** (n=64) **patients with low, high, or extra high levels of C-reactive protein.** CRPC patients with high levels of CRP (at the start of ARTA) were treated by ARTA for significantly shorter time (p=0.001). Also, the HSPC patients with high levels of CRP were treated by ARTA for a significantly shorter time (p=0.04). The low CRP < 4.9, high CRP ≥ 4.9 ng/ml.

Survival on ARTA based on PSA status



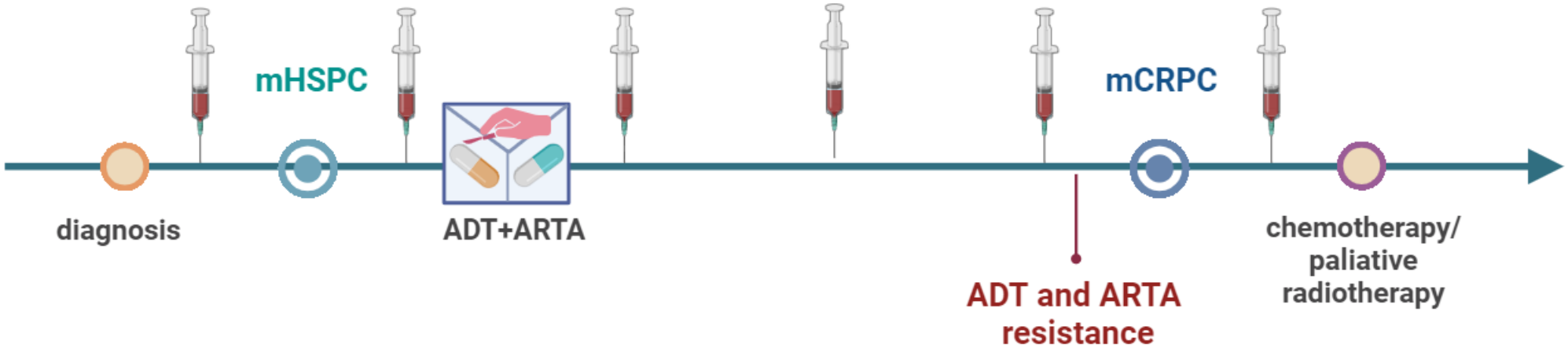


Kaplan-Meier analysis of time on ARTA in HSPC (n=42) and **CRPC** (n=67) patients with **PSA levels** lower or higher then cut-off (26.89 ng/ml) at the start of ARTA. CRPC patients with low levels of PSA were treated by ARTA for significantly longer time.

Conclusion:

- AR amplification positive patients had higher age, shorter time to resistance occurrence, increased levels of PSA, LDH and ALP, and CRP and decreased levels of hemoglobine.
- The amplification of AR gene corelated with shorter survival on ARTA therapy in HSPC patients.
- High levels of CRP corelated with shorter survival on ARTA therapy in both HSPC and CRPC patients.

- Analysis of AR gene amplification could be useful for prediction of ARTA therapy failure and progression monitoring in mHSPC patients.



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Thank you for your attention!

Special thanks:

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