Oli-P and beyond – Endpoints for PSMA based local ablative Radiotherapy

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Conflicts of interest

- none

1. The natural course of disease after BCR
2. Clinical relevant endpoints
3. The Oli-p Study
4. Oli-CR-P Study
5. The future

Natural history of rising PSA

- Time to metastases (no ADT) from BCR : 8 y
- Time to first bone MET (with ADT) with rising PSA: 2,5 y
- Little impact of BCR after RP / RT on survival in unselected patients
- Non-significant OS benefit of ADT at BCR in unselected patients
- Time to symptomatic prog in non-metastatic CRPC: 1,8 y
- No impact of bone directed therapies in nm-CRPC

Predictors of progression:

Gleason score (>/=7)

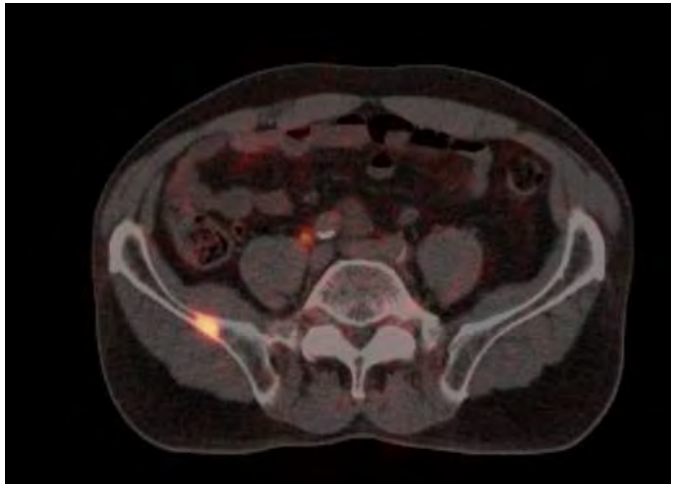
short PSA-doubling time (<12 mon)

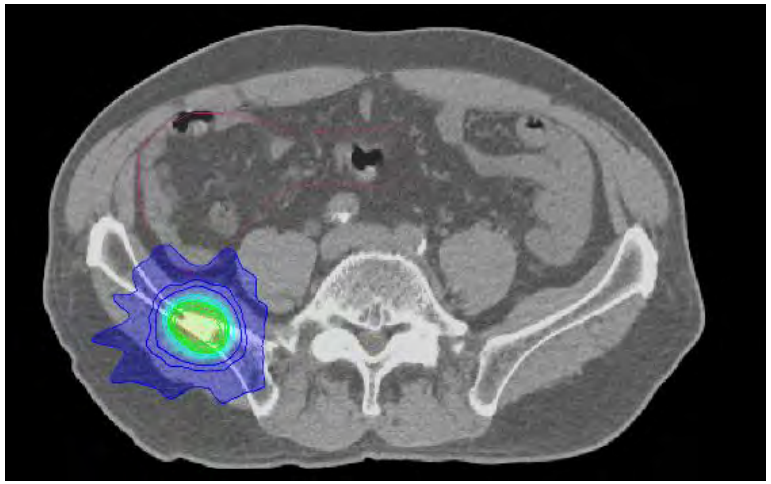
After RT: Short IBF (<18 mon)!

Pound et al. JAMA 1999
Smith et al. JCO 2005
Duchese et al Lancet Oncol 2016
Van den Bergh et al EurUro 2016
Van den Broeck et al EurUro 2018
Aly et al. EurUro 2018

PSMA-PET hybrid imaging

- Opportunity to detect MET at low PSA
- Prospective impact on outcome is lacking
- Broadly available (Germany)
- not generally covered by insurances
- High contrast





Timepoint of local ablative Radiotherapy

Castration sensitive

- Before ADT
- When to start ADT?
- Gain for the patient

Castration resistant

- palliation
- Before broadening of systemic therapy?
- Low volume CRPC?

Duchese et al. LancetOncol 2016
Wei et al. CurOpUro 2017

Timing of ADT

- Randomized Phase III trial immediate vs delayed ADT at BCR
- Intermittent ADT was possible

- ADT at BCR (vs delayed) has no impact 5 y-OS!
- Median time to progression: 1,6 y

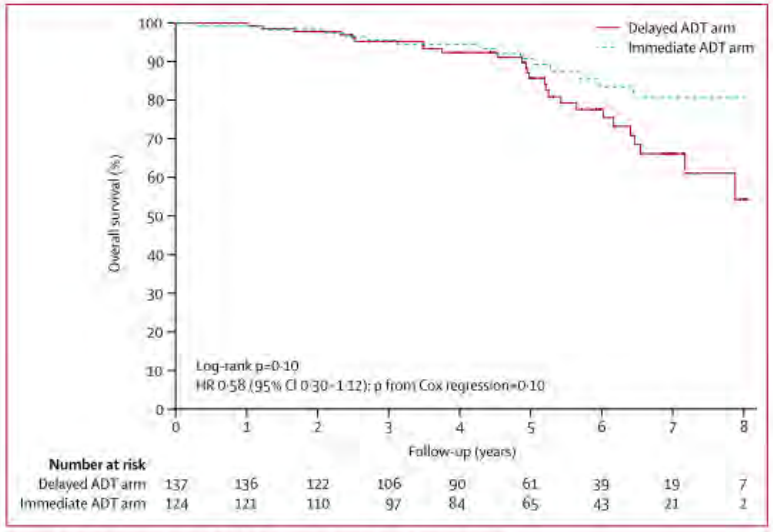


Figure 3: **Overall survival in the PSA-relapse subpopulation (group one)**
PSA=prostate-specific antigen. ADT=androgen-deprivation therapy. HR=hazard ratio.

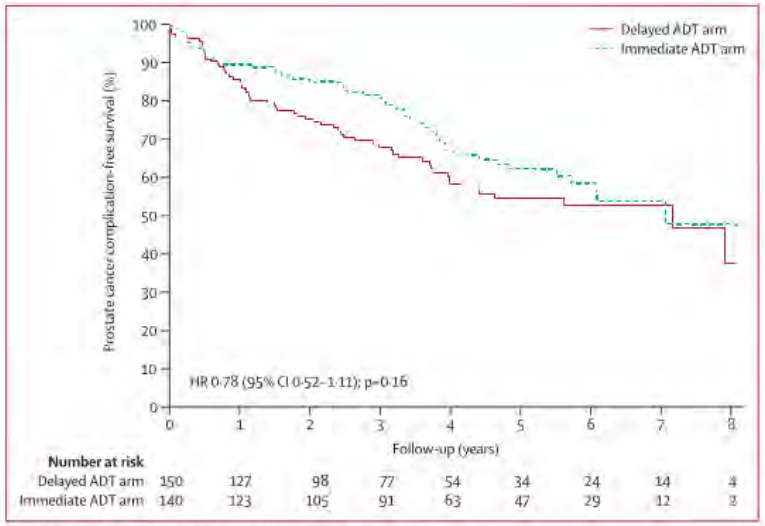


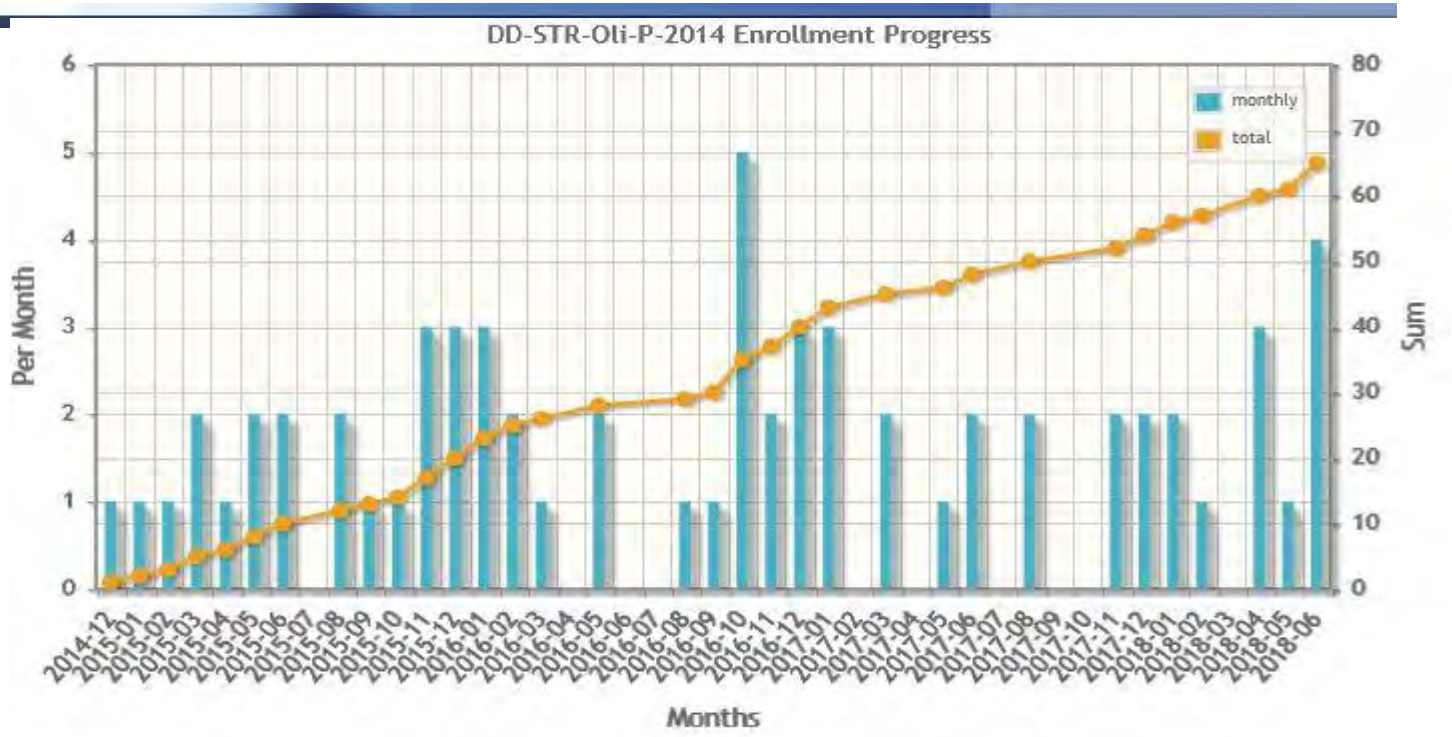
Figure 4: **Time to first prostate cancer complication**
ADT=androgen-deprivation therapy. HR=hazard ratio.

Duchese et al LancetOncol 2016

Endpoints for Oligometastatic disease

- Castration sensitive
  - Time to ADT?
  - Time to PSA-progression
  - **Time to CRPC**
  - Not OS
- Castration resistant disease
  - Time to PSA progression?
  - Time to skeletal events
  - Time to taxan (intensified systemic treatment)?
  - Survival

Oli-P-Study



Patient with Oligo-MET and PSA <10

Clinical decision

Arm A
3*10 Gy

Arm B
25*2 Gy

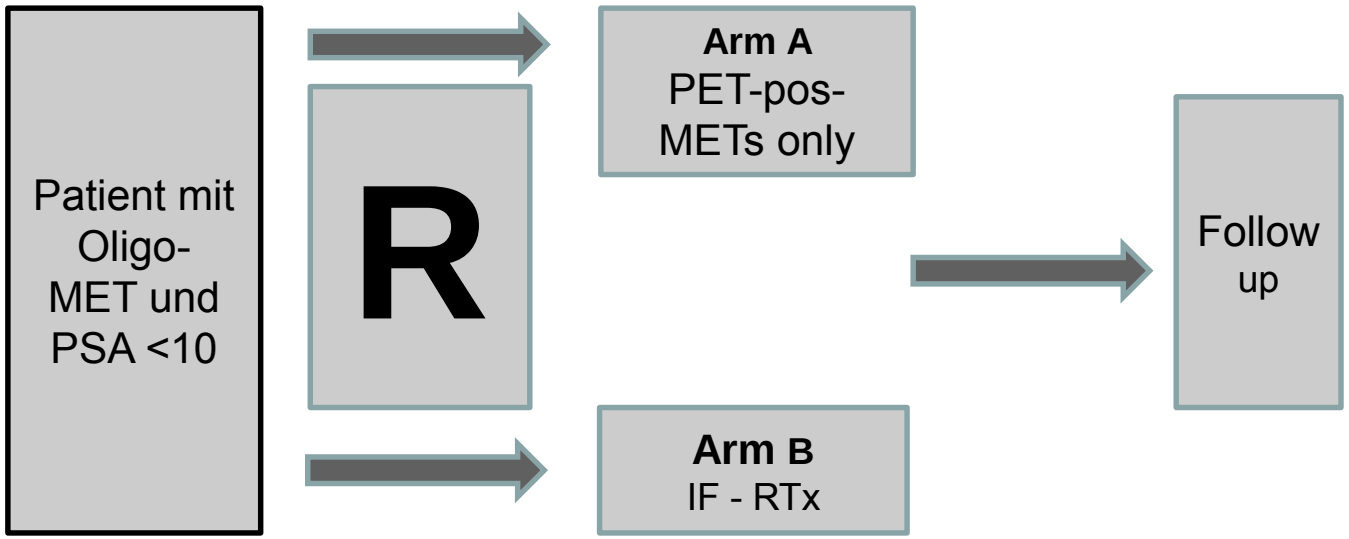
Follow up

Open Questions

- Endpoints – Delay of Androgen Deprivation Therapy?
- Comparisons with immediate ADT?
- Sequential treatment?
- Target volume?
- Nodes: Dose to microscopic areas?
- Bone: include the whole vertebral body?

Oli-P 2 Study (in discussion)

PSMA based staging at PSA Progression
Endpoint PSA-Progression
Patient number based on Oli-P



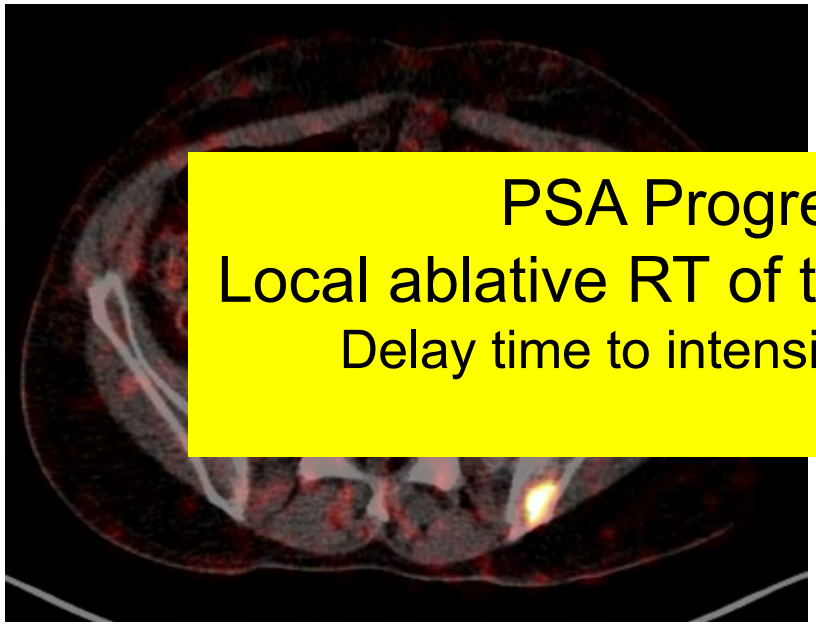
SBRT in oligoprogressive CRPC

- No prospective data on local therapy in CRPC patients
- PSMA at PSA Progression identifies first MET

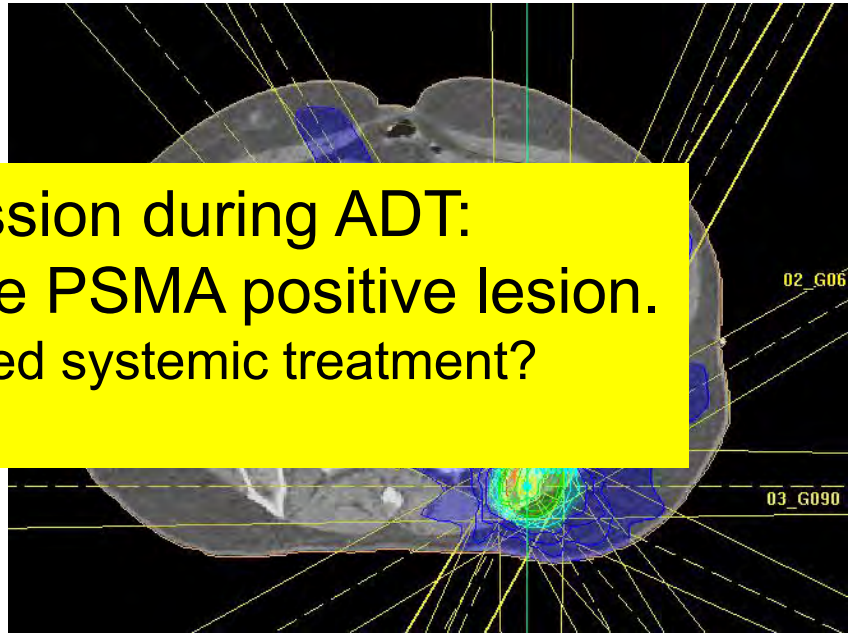
Does this matter?

Local ablative RT in CRPC

16.10.2012	lap. RPE, pLAD: pT2c pN0(0/9) M0 R0; Gleason-Score 3+5=8, PSA=19
2013	**PSA-persistence** at 5,8 ng/ml → ADT
02/2015	**PSA-progression up to** 4,3 ng/ml → PSMA-PET
11.02.2015	solitary bone metastases **os ilium**
05.2015	**SABR**, 3 x 10Gy
12/2015	PSA <0,07



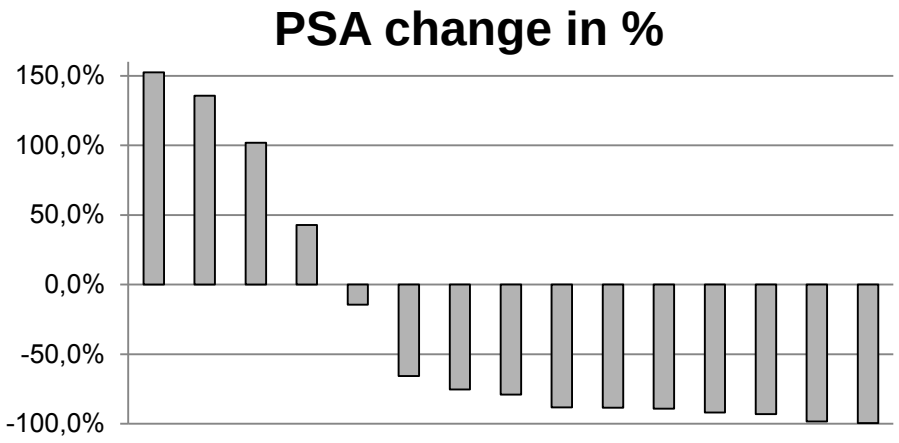
PSMA-PET-CT at PSA 4,3 under ADT

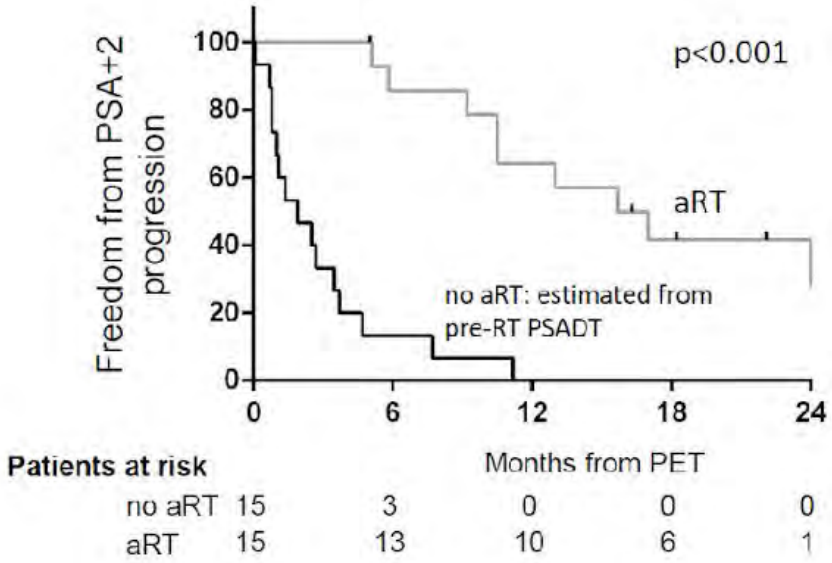


SABR 3 x 10 Gy

PSA Progression during ADT:
Local ablative RT of the PSMA positive lesion.
Delay time to intensified systemic treatment?

PSMA-PET at PSA-Progression under ADT n=15





PSA-Response in 11/15 Patienten

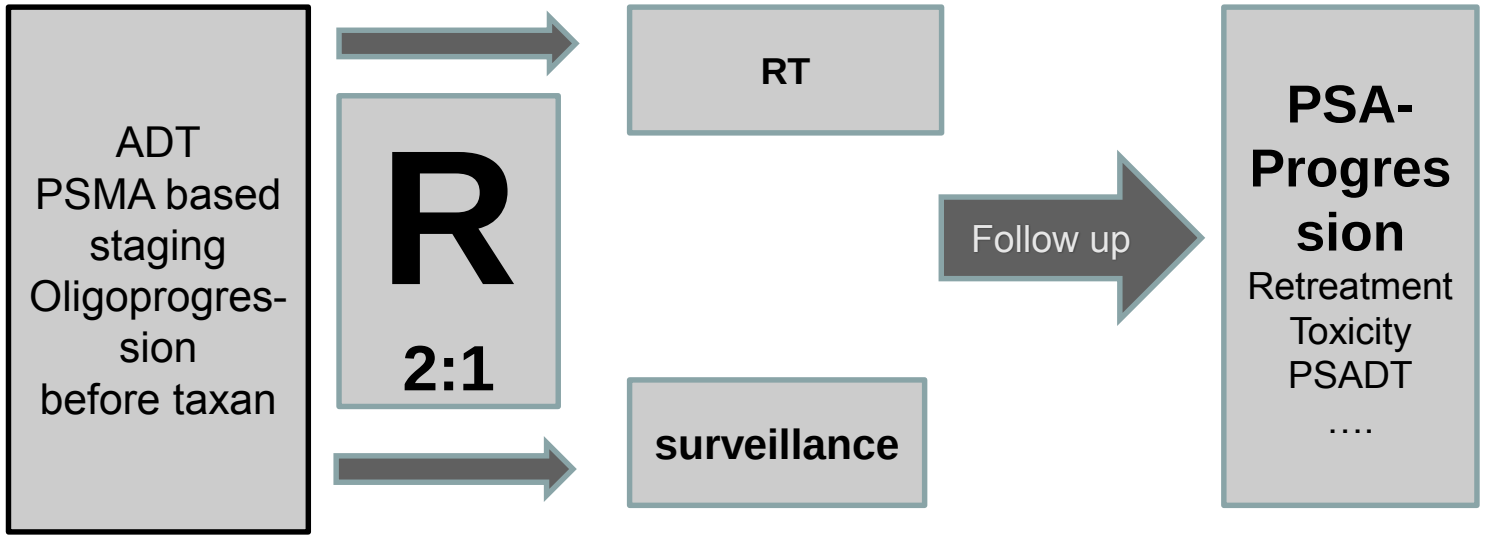
Estimated delay of further PSA Progression from 3,3 to 15,6 months

manuscript accepted EurUrol 2018

Oli-CR-P-Study

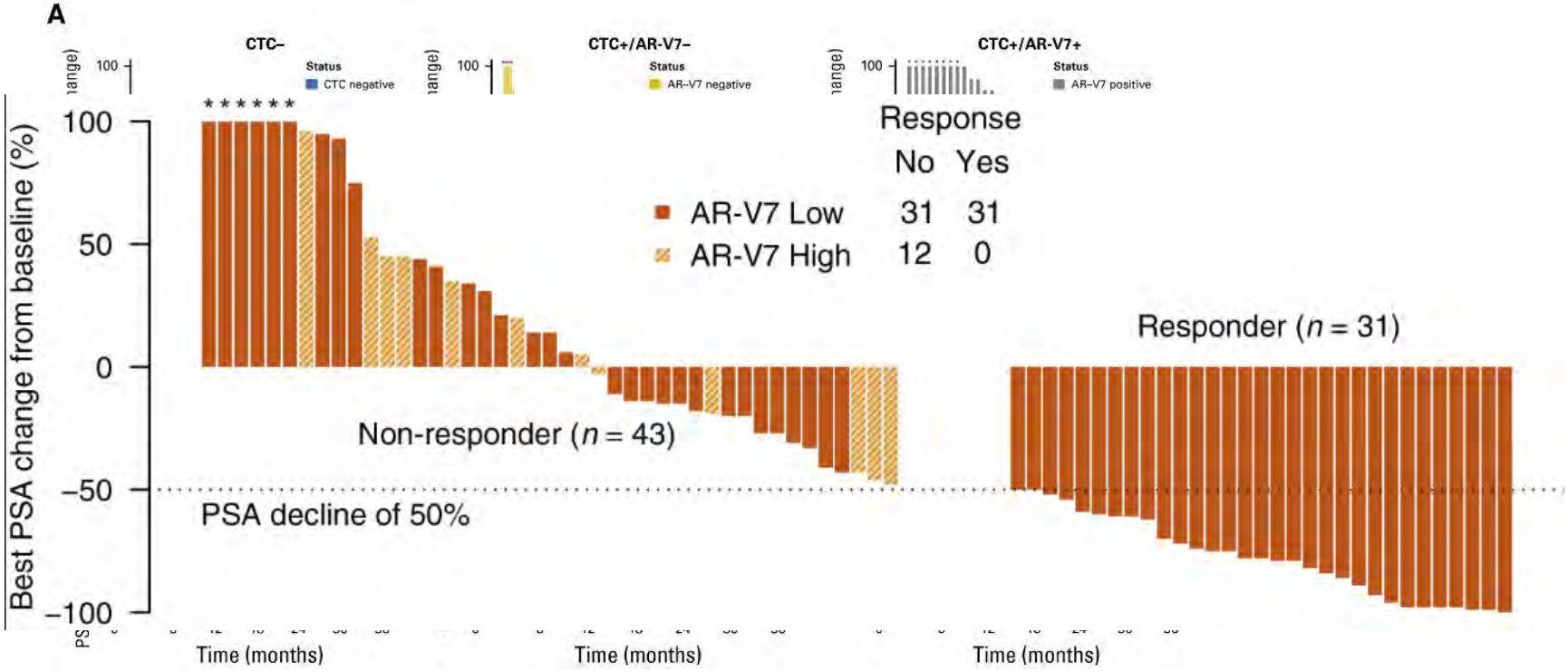
rising PSA under ADT, n=66

RT 2→50 Gy or 3*10 Gy



Blood based Biomarker- CTCs

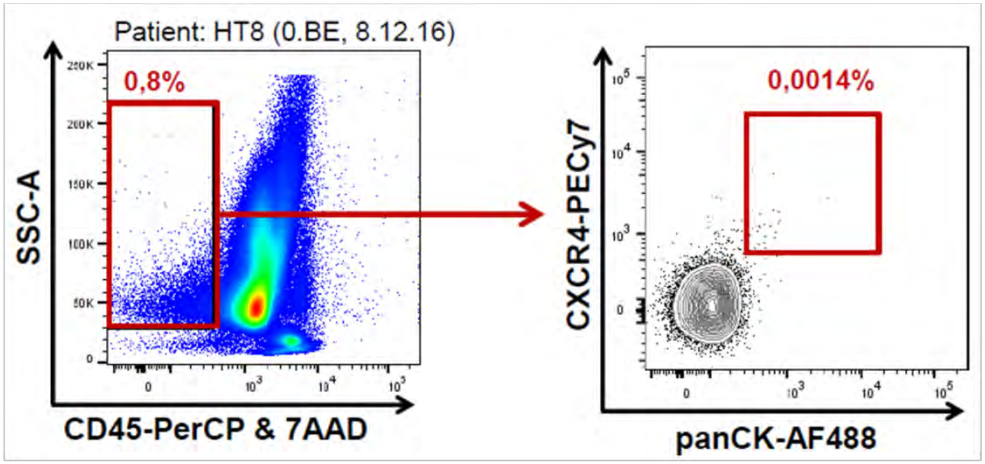
- In metastatic CRPC detection of specific CTCs is prognostic relevant

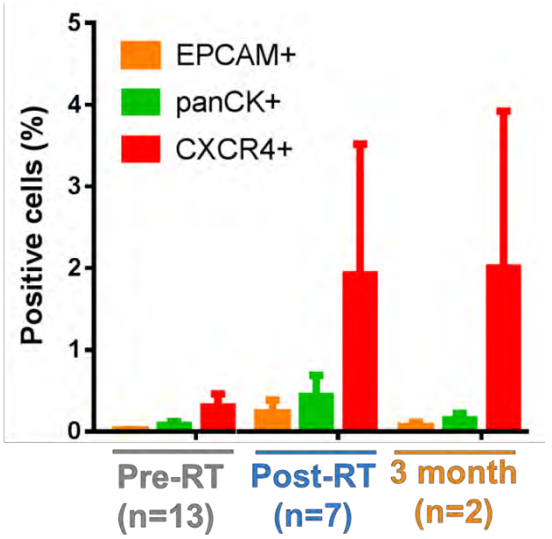


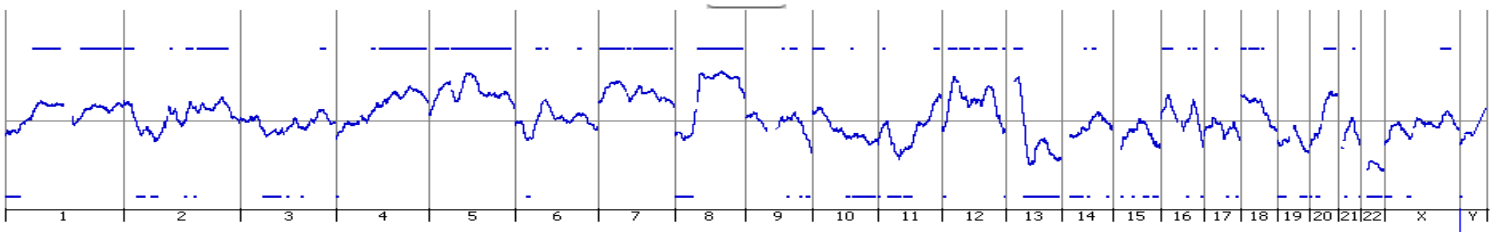
Scheer et al. JAMA 2016
Antonarakis et al. JCO 2017
Seitz et al. EurUro 2017

CTC in Dresden

- In studies blood is collected
- In low volume CRPC, detection is difficult





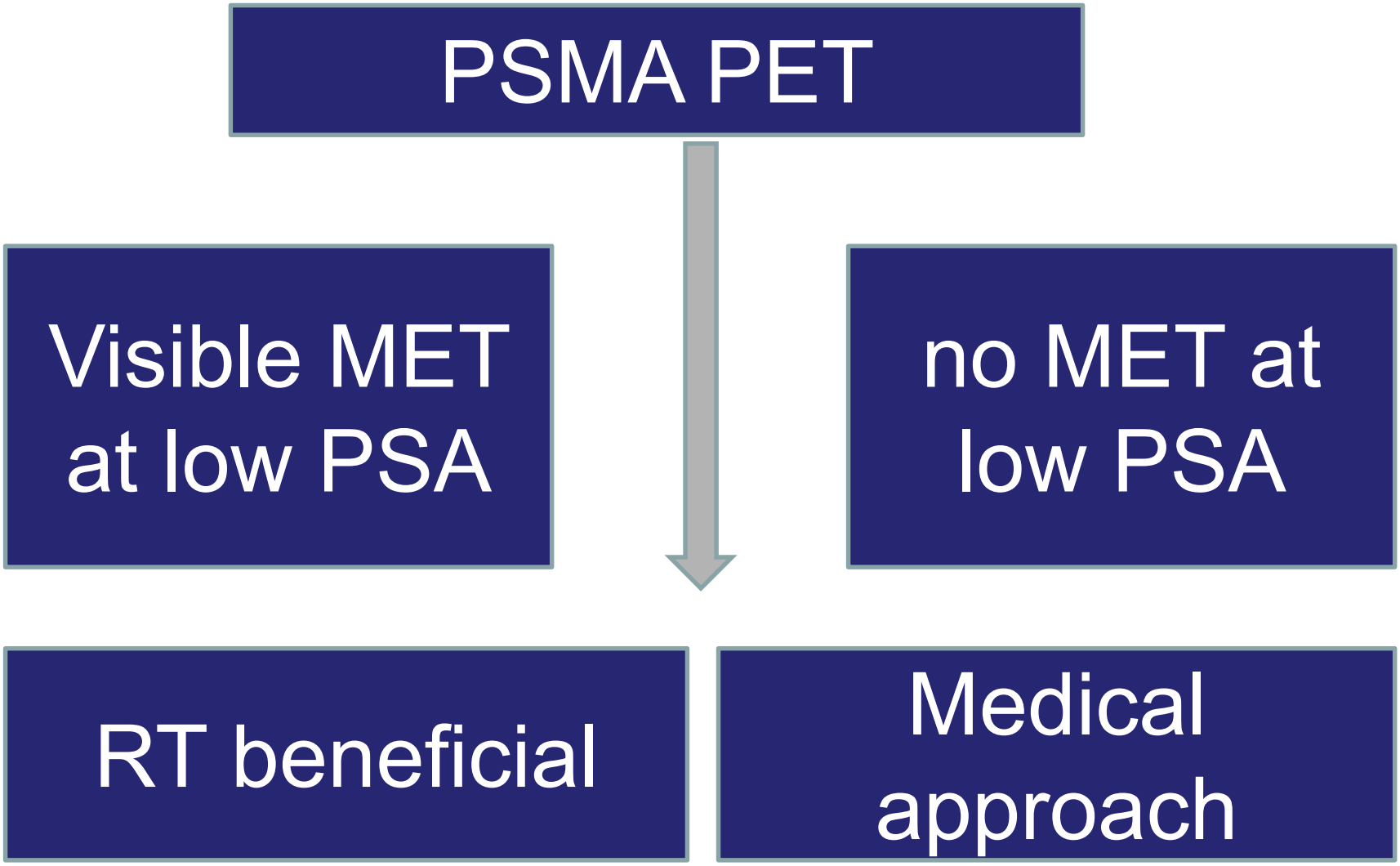


unpublished C. Peitzsch

Natural history of rising PSA
A chance for local ablative RT?

- Castration sensitive
  - La-RT is effective
  - Comparison is lacking
  - ADT +/- RT
  - RT +/- ADT
  - Target volume
  - Treat again?
- CRPC
  - Does local treatment of all visible MET matter?
  - Treat again?
  - Combination to NG-hormonal manipulation?

PSMA as predictive Biomarker?



Summary

- PSMA is effective to guide treatment
- Think about PSMA in high risk patients at PSA Progression
- La-RT is efficant to control local tumor
- It seems that this is no curative treatment
- absolute effect in CRPC seems to be higher than in ADT naive patients
- 2/3 of MET detected by PSMA are Ln → treatment failures
- In high risk patients combine La-RT with ADT?

Thank you for your attention

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