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MEETING SUMMARY

ESMO 2016 – COPENHAGEN, DENMARK
OCTOBER 7TH TO 11TH 2016

PROSTATE CANCER

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PROSTATE CANCER NEWS FROM ESMO 2016

ASS. PROF. TANYA DORFF

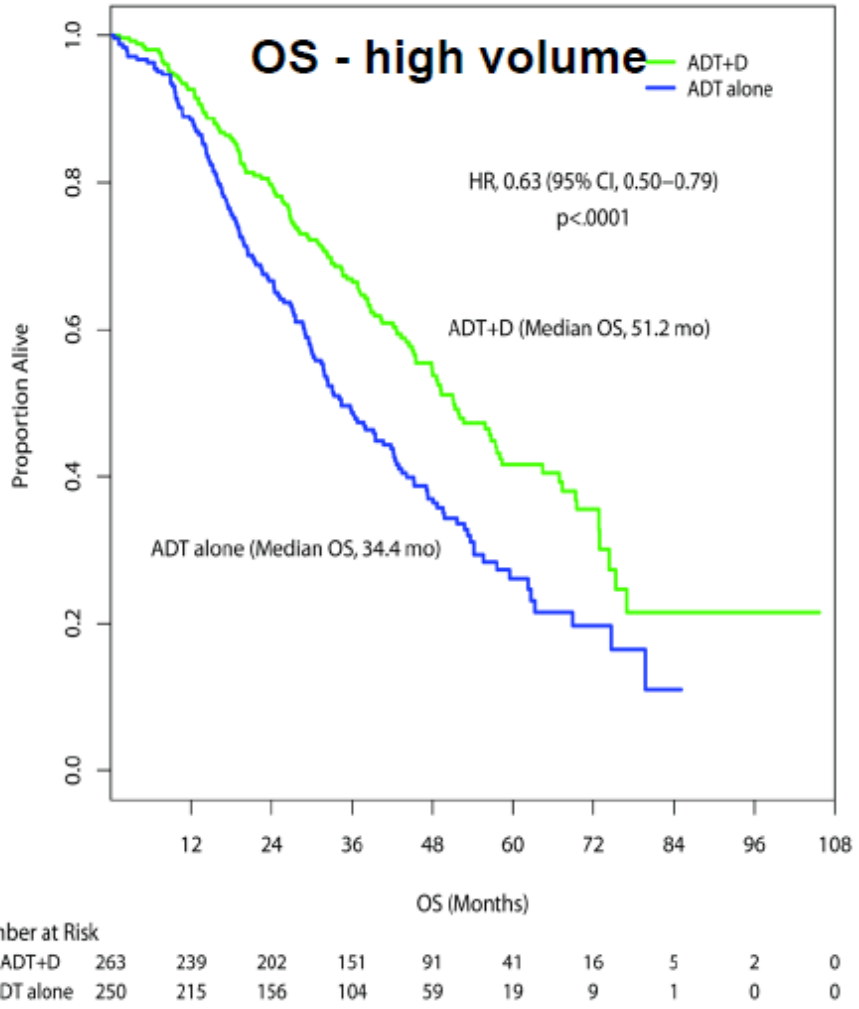
ABSTRACT 720PD: CHAARTED UPDATE

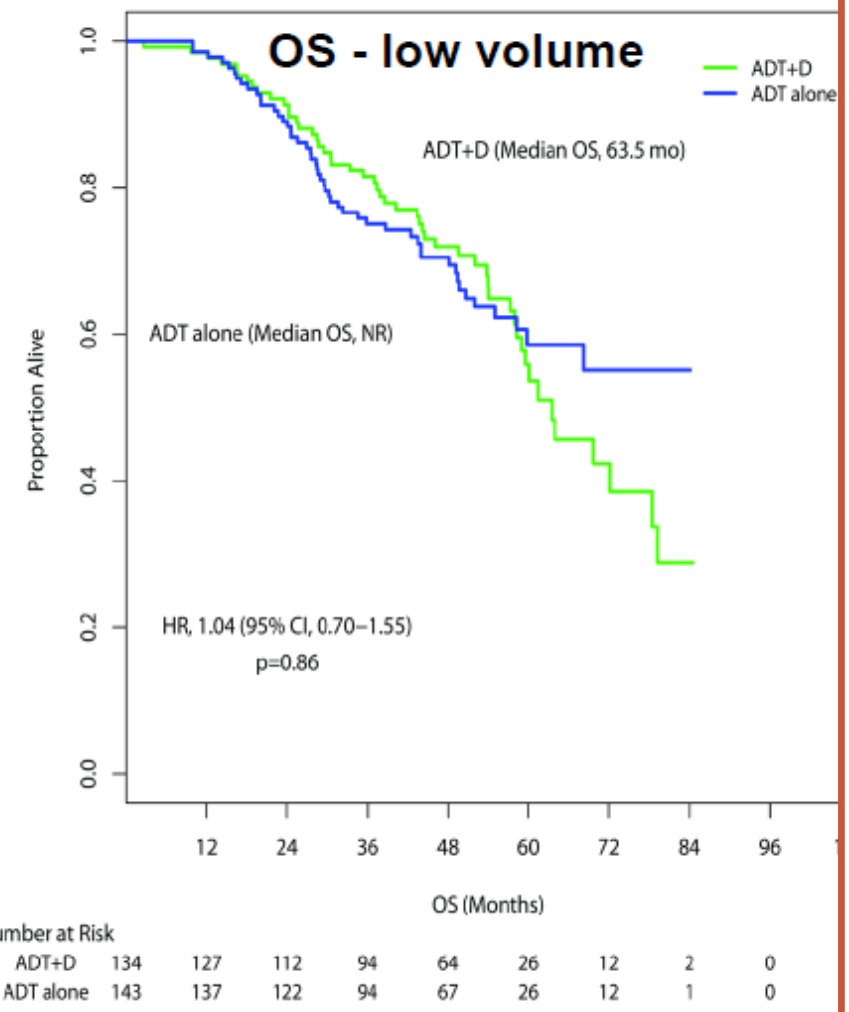
- Men with met prostate cancer treated with ADT + 6 cycles of docetaxel had median OS **57.6 months** compared to **47.2 months** for ADT alone (HR 0.73, 95% CI 0.59-0.89)

- However, men with low volume metastatic disease did not benefit with mature data (HR 1.04, 95% CI 0.79-1.55)
  - High volume disease: ≥4 bone mets with one outside axial skeleton OR visceral mets

Sweeney C et al

ABSTRACT 720PD: CHAARTED UPDATE





Sweeney C et al

IN CONTEXT: ADDITION OF DOCETAXEL IN MHSPC, RECENTLY REPORTED TRIALS

Study	Overall Survival High Vol pts ADT alone	Overall survival High Vol pts ADT + Docetaxel	Overall survival low vol pts ADT alone	Overall survival low vol pts ADT + D
GETUG-15 (n=385)	35 months (n=91)	39 months (n=92)	Not reached (n=102)	83.1 months (n=100)
CHAARTED (n=790)	32 months (n=250)	49 months (n=263)	Not reached (n=143)	63.5 months (n=134)

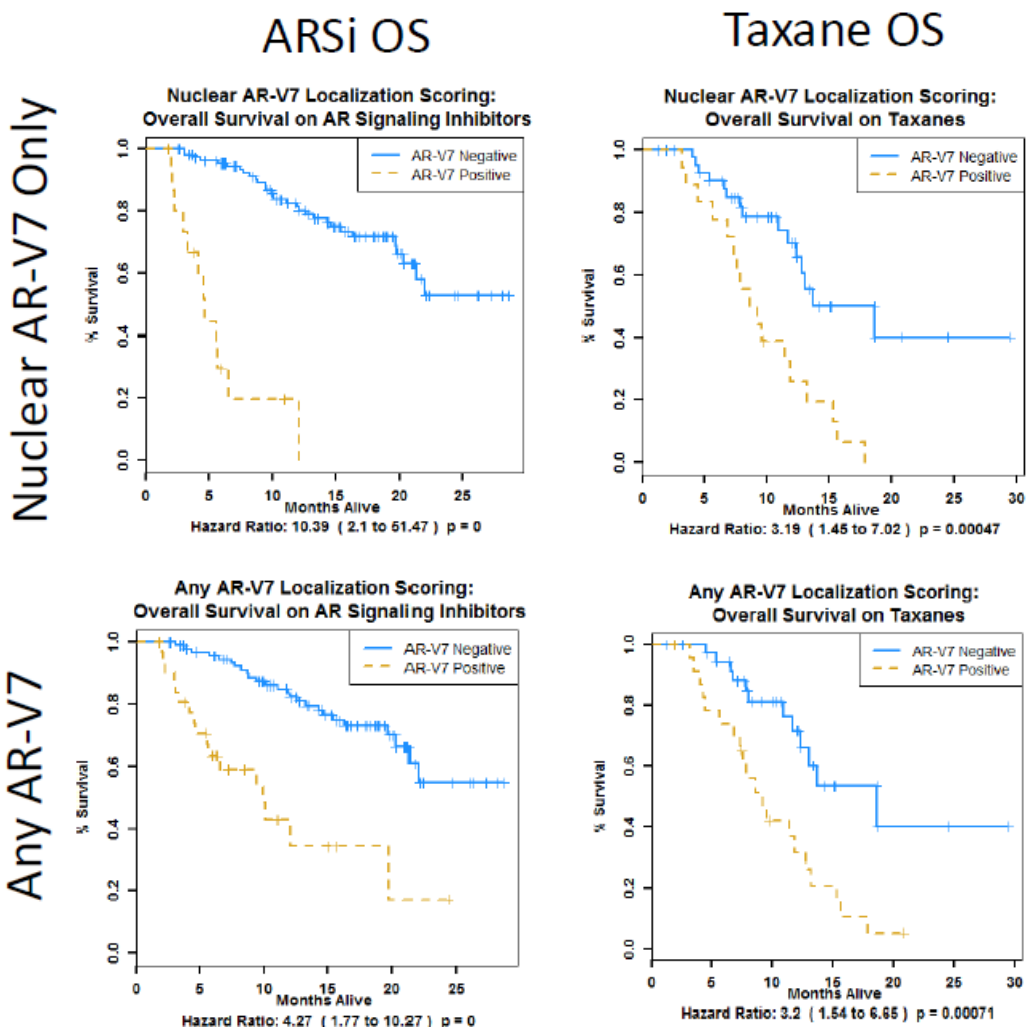
Note: STAMPEDE (James N et al Lancet Oncol 2016; 387:1163) did not report OS by volume of disease

1. Gravis G et al. 2015 ASCO GU abstract 140
2. Sweeney C et al. 2016 ESMO abstract 720PD and NEJM 2015; 373:8

ARV7 PRESENCE ALONE DOES NOT PREDICT LACK OF RESPONSE TO AR-TARGETED THERAPY

- Using EPIC platform, Scher et al. identified that ARv7 presence did not predict response/OS with AR-targeted therapy versus to taxane therapy… but nuclear localization of ARv7 did (abstract 728PD)
- SOGUG identified 8 patients with ARv7 by rtPCR and 4/8 (50%) had PSA response to enzalutamide (abstract 726PD)
- **Bottom line:** ARv7 assays require validation so we can ensure not to deny potentially effective therapy from patients with mCRPC

ABSTRACT 728PD: ARV7 ASSAY



Comparisons of OS by AR-V7 Localization by Therapy type		
AR-V7 Localization	**HR of ARSi**	**HR of Taxane**
Nuclear AR-V7 Only	**10.39** P<0.0001	**3.19** p=0.00047
ANyAR-V7	**4.27** P<0.0001	**3.2** P=0.00071

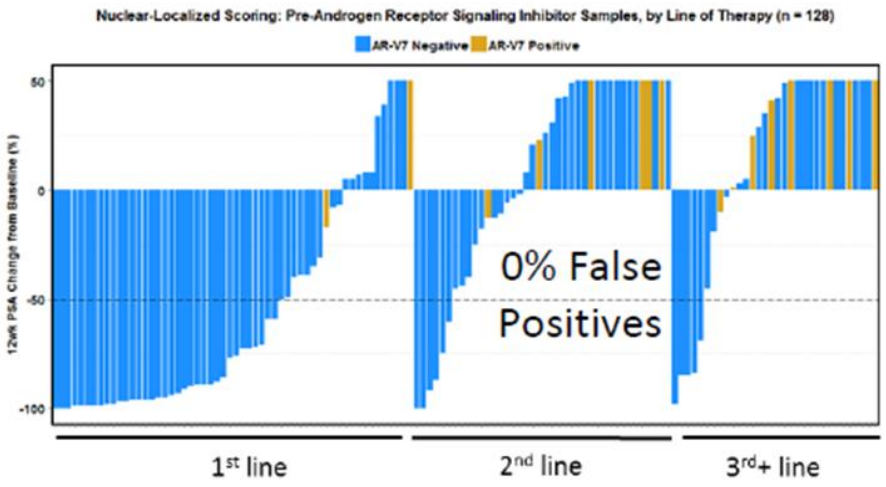
Scher et al

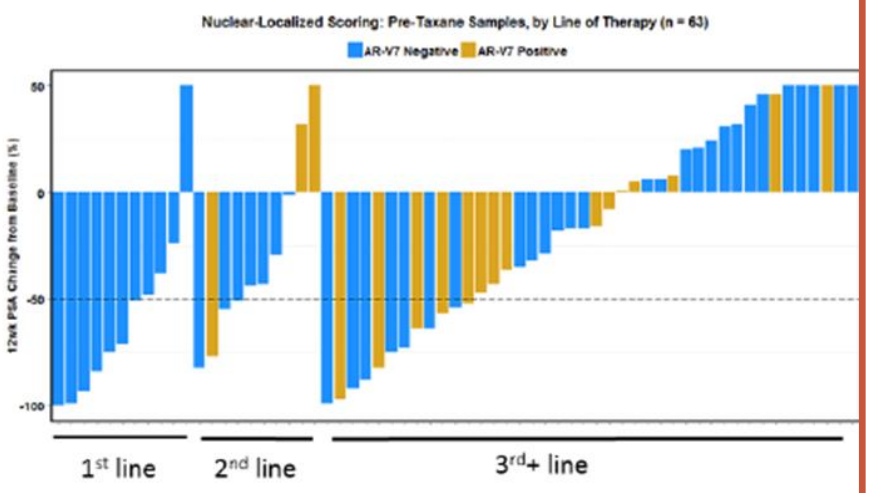
NUCLEAR ARV7 PREDICTS FOR LACK OF RESPONSE TO ABI/ENZA BUT NOT TAXANE THERAPY

ARSi PSA Responses

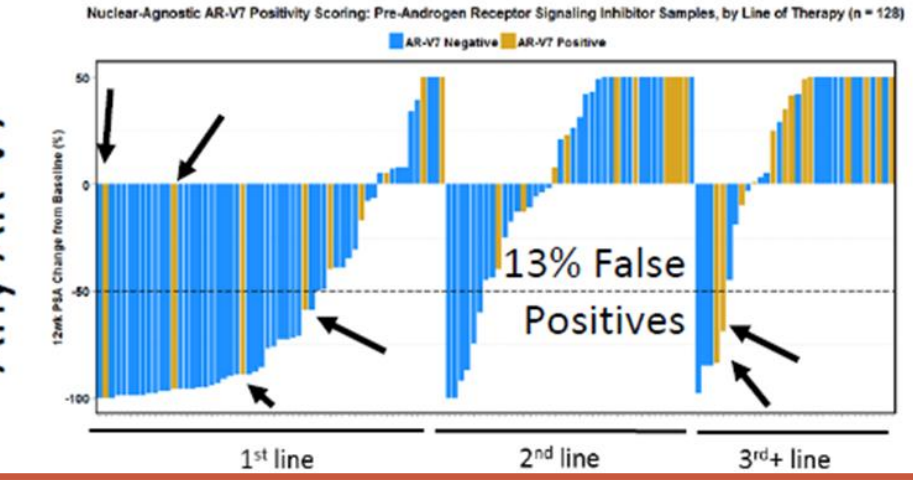
Taxane PSA Responses

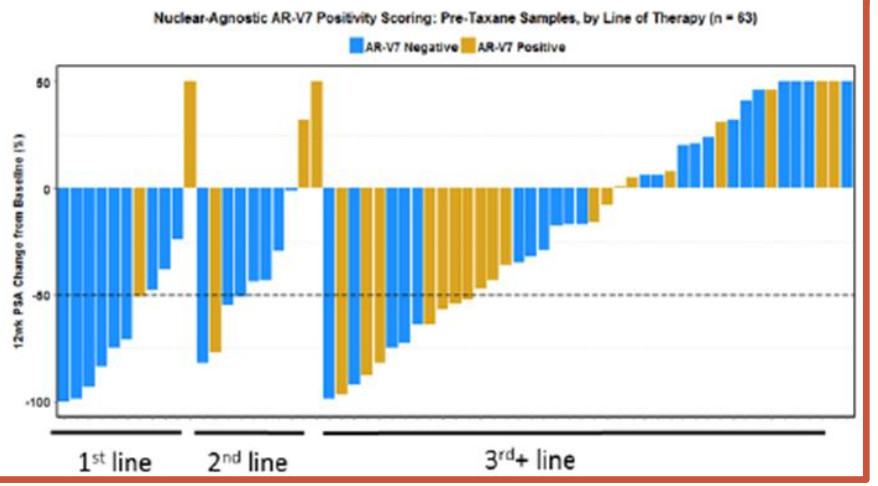
Nuclear AR-V7 Only



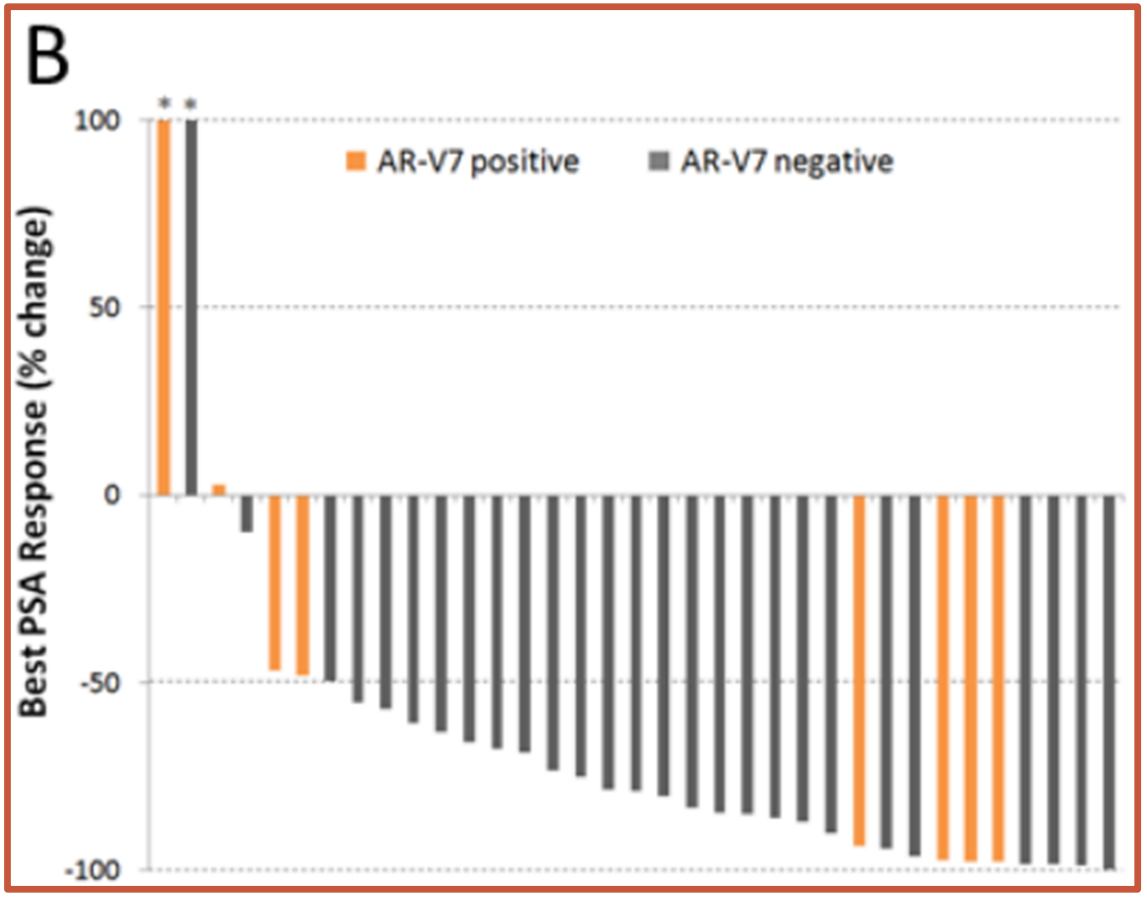


Any AR-V7





GRANDE E ET AL SOGUG 'PREMIERE' TRIAL DOCETAXEL-NAÏVE MCRPC RECEIVING ENZALUTAMIDE



Most had low ratio of ARv7 to full length AR

...need to establish a 'cutpoint' for ARv7 PCR based assay

PEMBROLIZUMAB SHOWS PROMISE IN TREATING PATIENTS WITH MCRPC

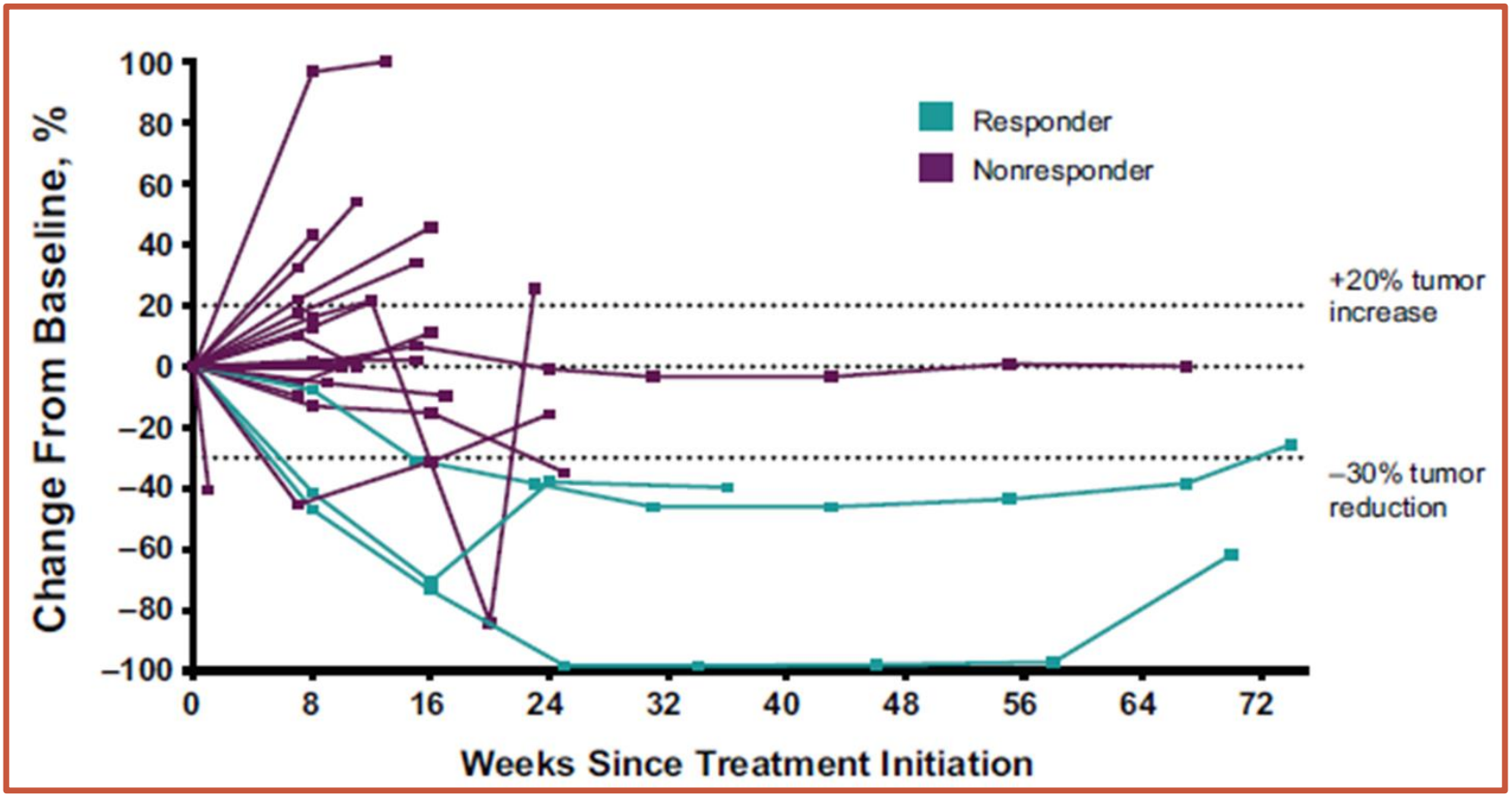
- Early findings, small sets of patients, but very encouraging
- Graff et al. (abstract 719O) found 4/20 men progressing on enzalutamide had significant responses to pembrolizumab
- Hansen et al. (abstract 725PD) found 3/23 had objective responses
- Ongoing studies: KEYNOTE-199 (single agent) and KEYNOTE-046 (with ADXS31-142)

RESPONSE AND ADVERSE EVENTS WITH PEMBROLIZUMAB FOR MCRPC

	Graff (abstract 719O)	Hansen (abstract725PD)
Taxane pretreated	No	Yes
PDL1 staining	Not required*	≥ 1%
Dosing of pembro	200 mg IV q3 wk x 4	10 mg/kg q2 wk x 24 mo
PSA response (50% reduction)	4/20 (20%)	NR
RECIST response	2/20 (10%)	3/23 (13%)
Med PFS	NR	3.6 months
TEAEs Grd 3-4 irAEs noted	3 (15%) Myositis, thyroid, colitis	4 (17%) Edema, thyroid, pneumonitis

*On study biopsy for 2 of the responders showed PDL1+
TEAE = treatment emergent adverse events

ABSTRACT 725PD: PEMBROLIZUMAB IN MCRPC – KINETICS OF RESPONSE



Plan to combine data with other KEYNOTE studies to identify predictive gene signature

Hansen A et al

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