IX Congresso Internacional de Uro-Oncologia

IV SIMPÓSIO MULTIPROFISSIONAL DE URO-ONCOLOGIA

1 a 3 de Março de 2018

SHERATON SÃO PAULO WTC HOTEL

mCRPC – quest for personalized medicine

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Centro de Oncologia e Hematologia
Família Dayan - Daycoval
Hospital Israelita Albert Einstein

MAR/2018

Potential Conflicts of Interest

- **Honoraria: sanofi, janssen, bayer, astellas**
- **Research Funding: janssen, astellas**
- **Travel, Accomodation, Expenses: bayer, sanofi, AstraZeneca, MSD, astellas, janssen**
- **Consultant or Advisory Board: sanofi, bayer, Janssen, astellas**

Treatment options in mCPRC

	Agent	Mechanism of action	Comparator	HR	Δsurvival (mos)	P
2004	Docetaxel	Taxane	Mitoxantrone	0.76	2.4	0.009
2010	Sipuleucel - T	Vaccine	Placebo	0.78	4.1	0.03
2010	Cabazi-post	Taxane	Mitoxantrone	0.72	2.4	<.0001
2011	Abi-post	CYP 17	Prednisone	0.74	4.6	<.0001
2013	Abi-pre	CYP 17	Prednisone	0.79	5.2	0.0151
2012	Enza-post	AR	placebo	0.63	4.8	<.001
2014	Enza-pre	AR	placebo	0.71	2.2	<0.001
2013	Radium-223	α-emission	placebo	0.70	3.6	<.001

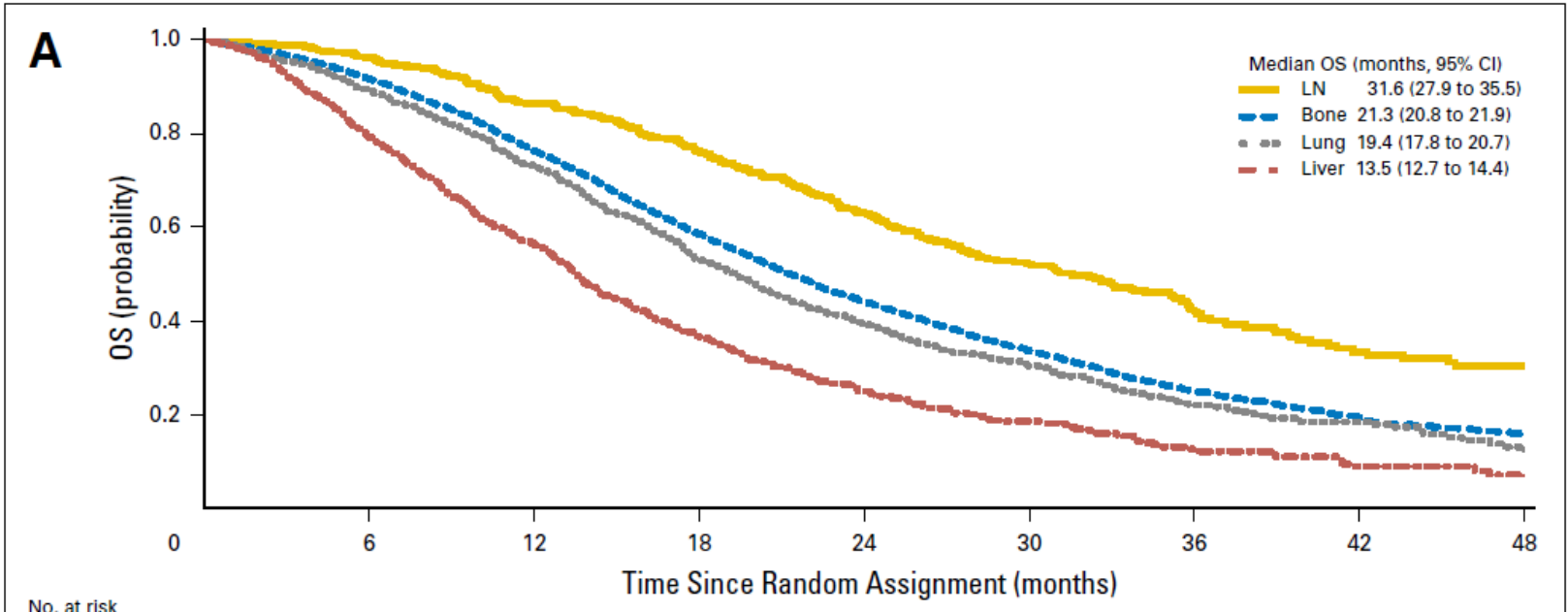
VOLUME 34 · NUMBER 14 · MAY 10, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Meta-Analysis Evaluating the Impact of Site of Metastasis on Overall Survival in Men With Castration-Resistant Prostate Cancer

Susan Halabi, William Kevin Kelly, Hua Ma, Haojin Zhou, Nicole C. Solomon, Karim Fizazi, Catherine M. Tangen, Mark Rosenthal, Daniel P. Petrylak, Maha Hussain, Nicholas J. Vogelzang, Ian M. Thompson, Kim N. Chi, Johann de Bono, Andrew J. Armstrong, Mario A. Eisenberger, Abderrahim Fandi, Shaoyi Li, John C. Araujo, Christopher J. Logothetis, David I. Quinn, Michael J. Morris, Celestia S. Higano, Ian F. Tannock, and Eric J. Small



No. at risk									
LN	565	510	424	345	250	162	91	50	37
Bone	6,356	5,602	4,406	3,079	1,932	1,083	556	278	165
Lung	791	669	508	347	225	126	65	36	16
Liver	752	551	367	219	128	66	27	13	5

PCa: Lack of a biomarker

	NON SMALL CELL LUNG CANCER	BREAST	COLON-RECTUM	STOMACH	PROSTATE
Worldwide incidence[1], 2008 (thousands)	1,600	1,400	1,200	989	903
Estabilished adjuvante chemoRx	Y	Y	Y	Y	N
Metastatic disease predictive marker	EGFR, ALK, ROS	ER/PR, Her-2-neu	RAS gene	Her-2-neu	N

1. Jemal et al. *CA Cancer J Clin* 2011

Prostate Cancer 0x4 BIG 4

	NON SMALL CELL LUNG CANCER	BREAST	COLON-RECTUM	STOMACH	PROSTATE
Worldwide incidence[1], 2008 (thousands)	1,600	1,400	1,200	989	903
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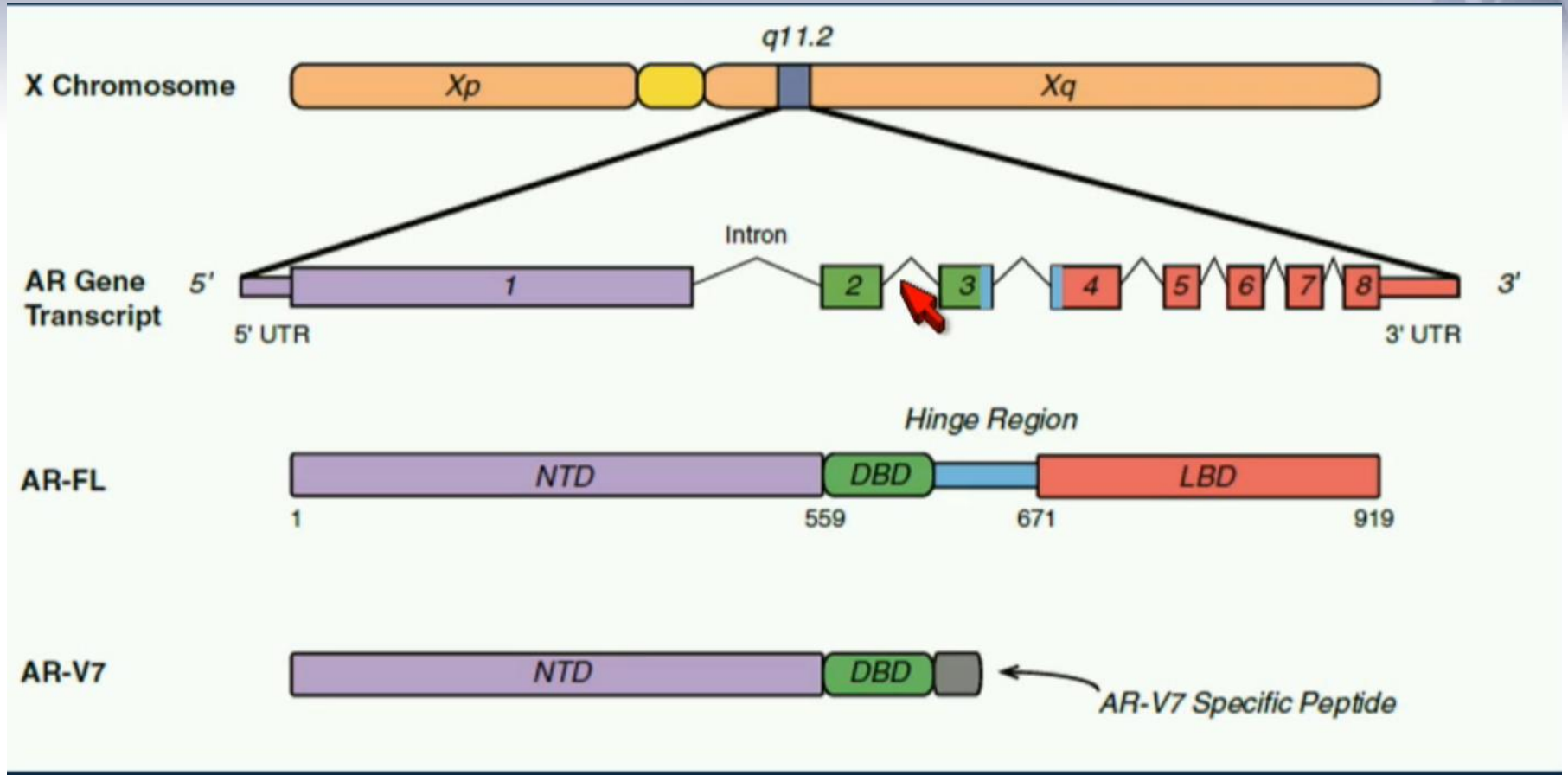
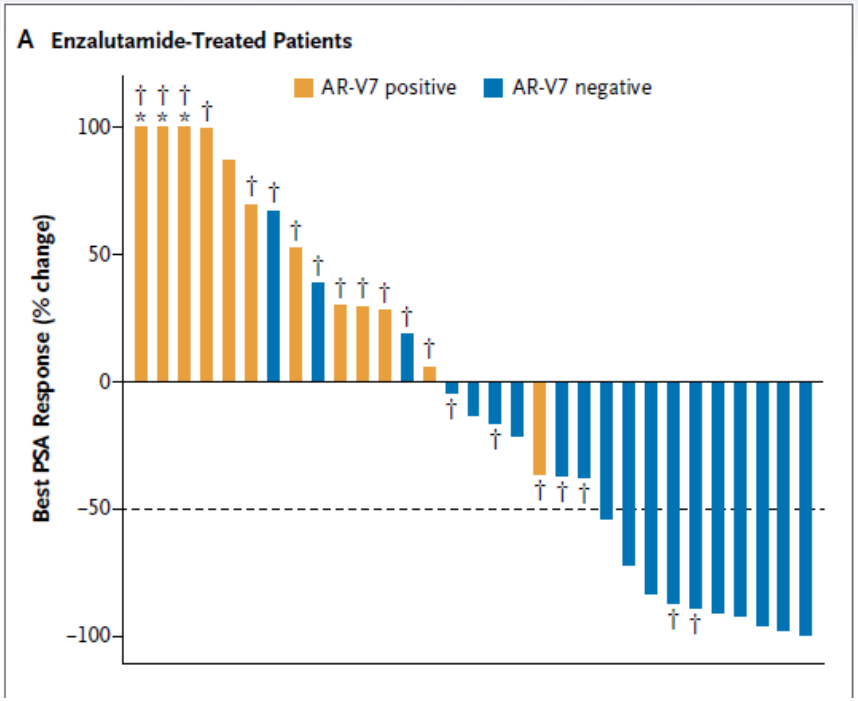
1. Jemal et al. *CA Cancer J Clin* 2011

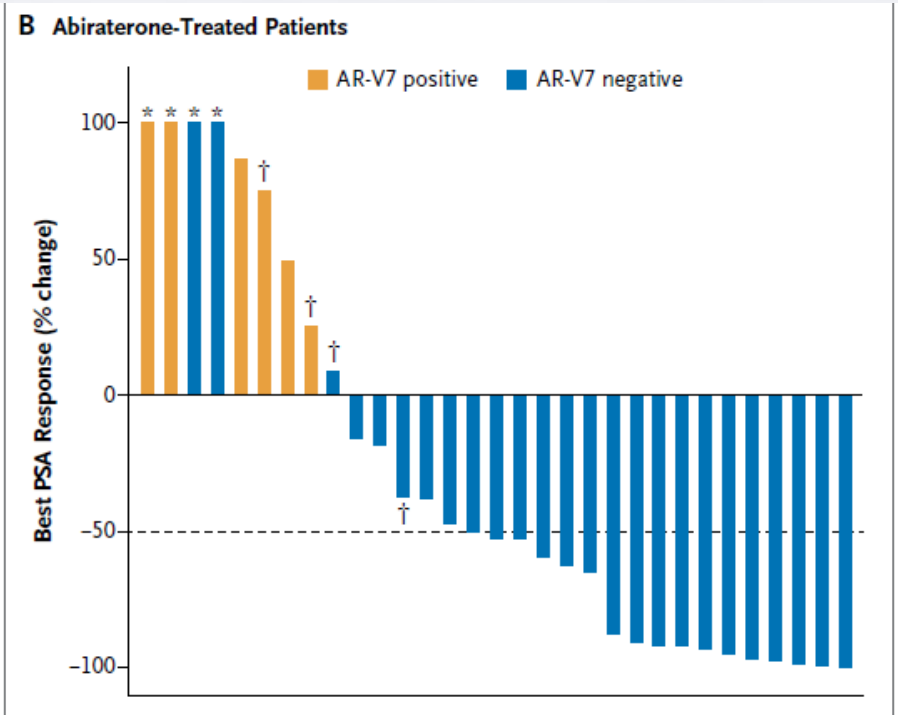
AR-V7 lacks the Ligand Binding Domain



Nakazawa M, et al. *Horm Cancer* 2014; 5: 265-273.

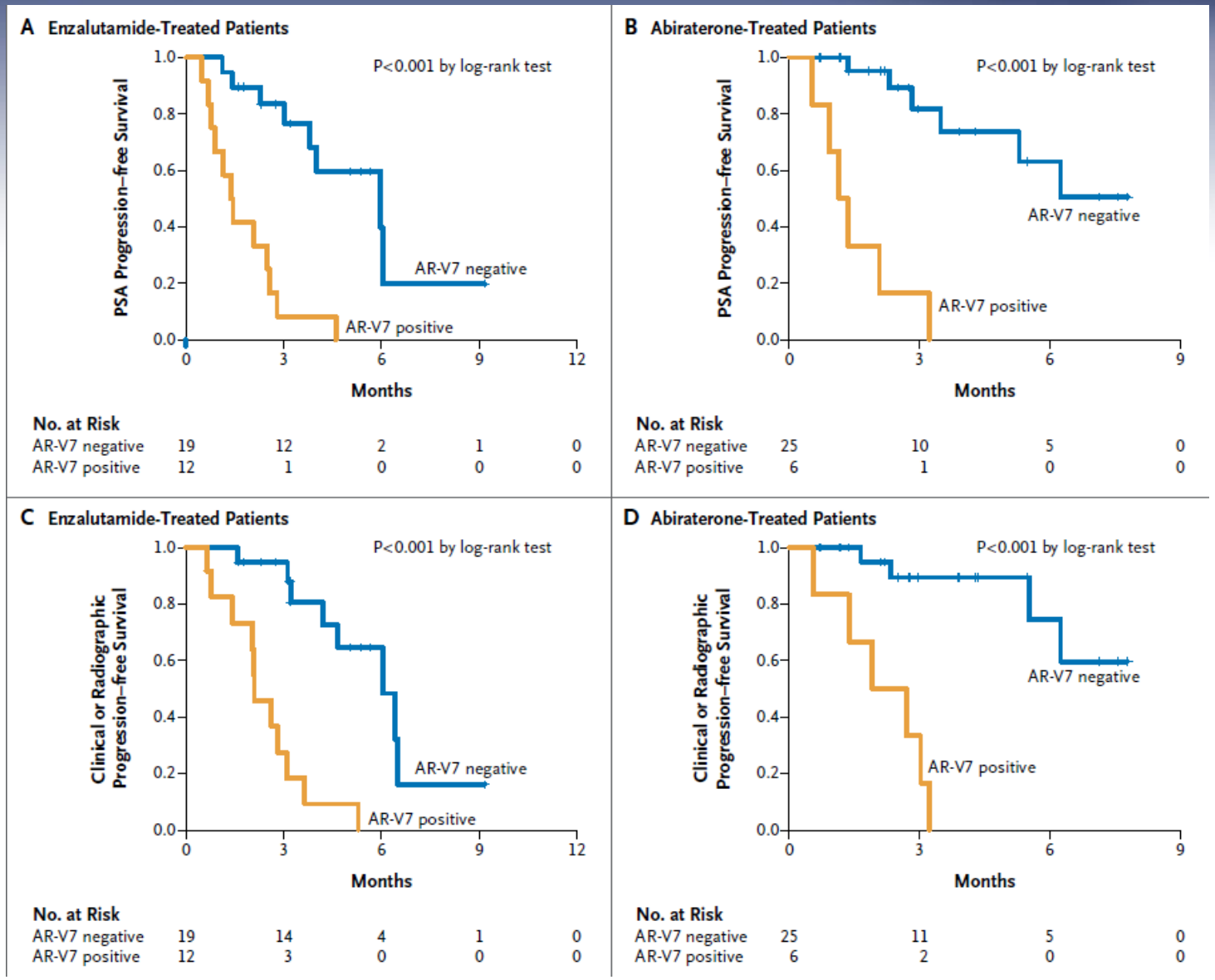
Primary Resistance to Androgen Signaling Inhbition and ARV7 status





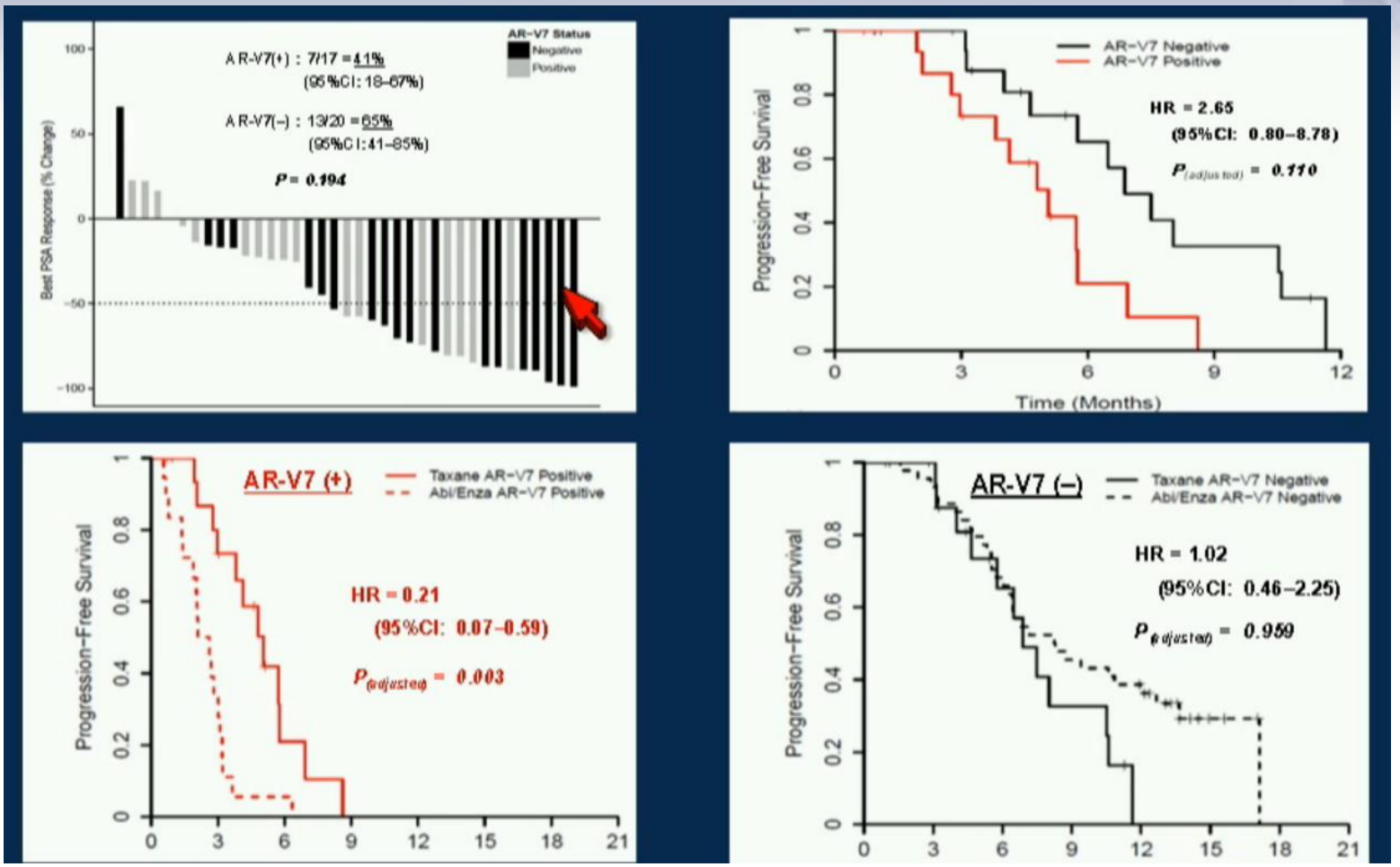
Antonarakis et al New Engl J Med 20

ARV7 presence equals to primary resistance



Antonarakis et al New Engl J Med 2014

AR-V7 and Taxanes



Antonarakis et al JAMA Oncol 2015

AR-V7 - treatment-selection marker??

- **AR-V7+: taxanes may be more efficacious than AR-directed therapies**
- **AR-V7-: taxanes may have comparable efficacy to AR-directed therapies**

Antonarakis ASCO 2016

original report

Clinical Utility of CLIA-Grade AR-V7 Testing in Patients With Metastatic Castration-Resistant Prostate Cancer

Table 2. Clinical Utility of AR-V7 Testing in Patients With mCRPC

	Did the AR-V7 Assay Result in a Change in Management for This Patient?			
	Yes		No	
Test Result	n/N	%	n/N	%
CTC–	18/40	45.0	22/40	55.0
CTC+/AR-V7–	20/42	47.62	22/42	52.38
CTC+/AR-V7+	37/60	61.67	23/60	38.33

Abbreviations: AR-V7, androgen receptor splice variant 7; CTC, circulating tumor; mCRPC, metastatic castration-resistant prostate cancer; n/N, number of patients in that category divided by total number of patients.

Table 4. PSA_{50} Response Rate to Next-Line Therapy Based on Change in Clinical Practice After AR-V7 Testing

	Did the Patient Achieve a PSA_{50} Response on Next-Line Therapy?			
	Yes		No	
Management	n/N	%	n/N	%
Changed	34/63	53.97	29/63	46.03
Did not change	16/52	30.77	36/52	69.23

NOTE. Fisher's exact test $P = .015$.
Abbreviations: AR-V7, androgen receptor splice variant 7; n/N, number of patients in that category divided by total number of patients; PSA_{50}, 50% decline in prostate-specific antigen.

Antonarakis et al JCO Precis Oncol. 2017

BRCA1/2, ATM, CHK2 as biomarkers for PARPi?

The NEW ENGLAND JOURNAL of MEDICINE

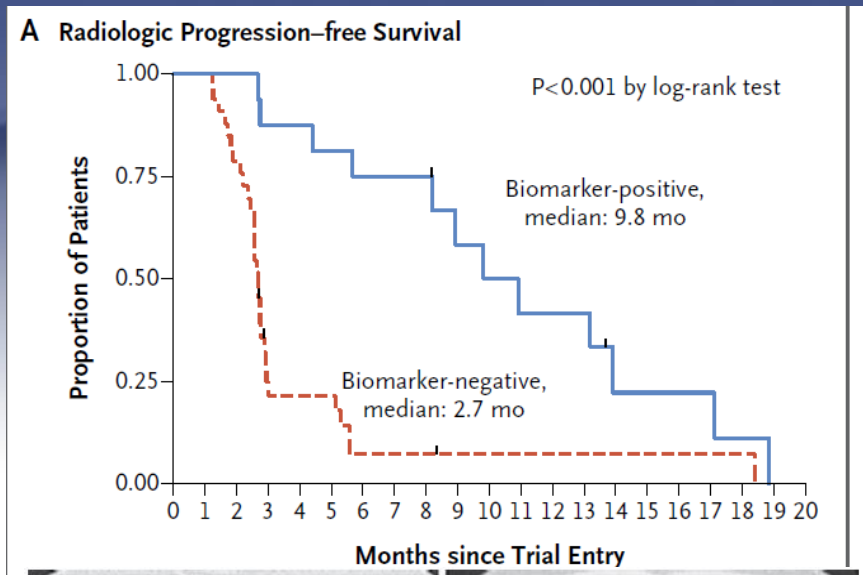
ESTABLISHED IN 1812 OCTOBER 29, 2015 VOL. 373 NO. 18

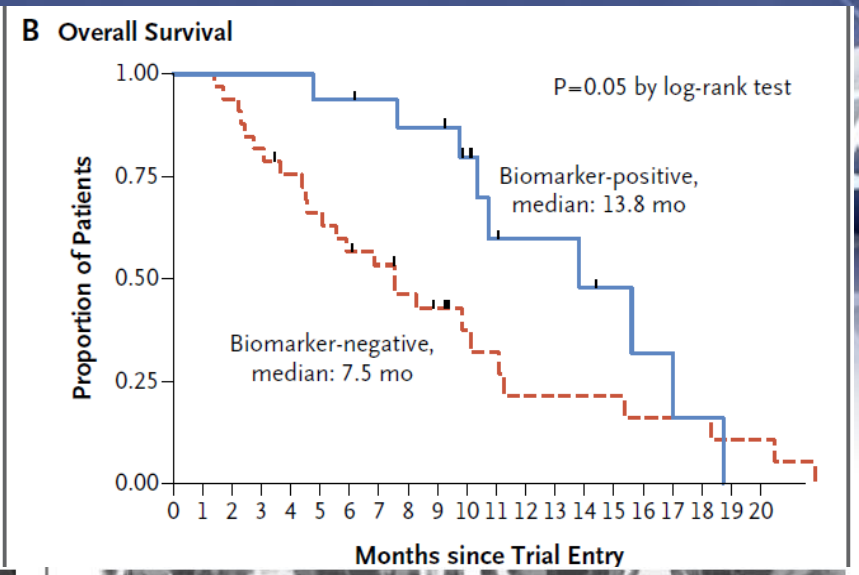
DNA-Repair Defects and Olaparib in Metastatic Prostate Cancer

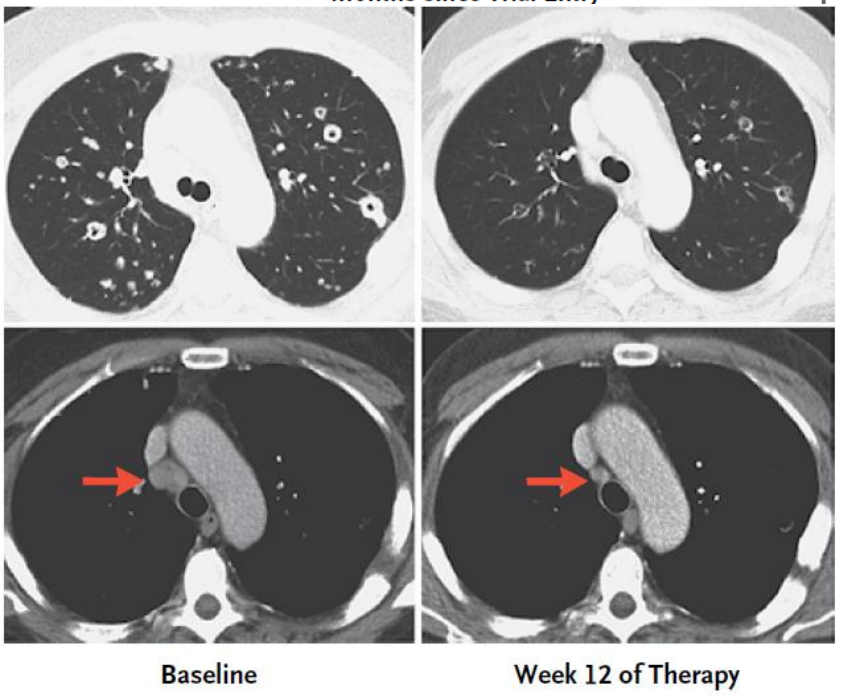
J. Mateo, S. Carreira, S. Sandhu, S. Miranda, H. Mossop, R. Perez-Lopez, D. Nava Rodrigues, D. Robinson, A. Omlin, N. Tunariu, G. Boysen, N. Porta, P. Flohr, A. Gillman, I. Figueiredo, C. Paulding, G. Seed, S. Jain, C. Ralph, A. Protheroe, S. Hussain, R. Jones, T. Elliott, U. McGovern, D. Bianchini, J. Goodall, Z. Zafeiriou, C.T. Williamson, R. Ferraldeschi, R. Riisnaes, B. Ebbs, G. Fowler, D. Roda, W. Yuan, Y.-M. Wu, X. Cao, R. Brough, H. Pemberton, R. A'Hern, A. Swain, L.P. Kunju, R. Eeles, G. Attard, C.J. Lord, A. Ashworth, M.A. Rubin, K.E. Knudsen, F.Y. Feng, A.M. Chinnaiyan, E. Hall, and J.S. de Bono

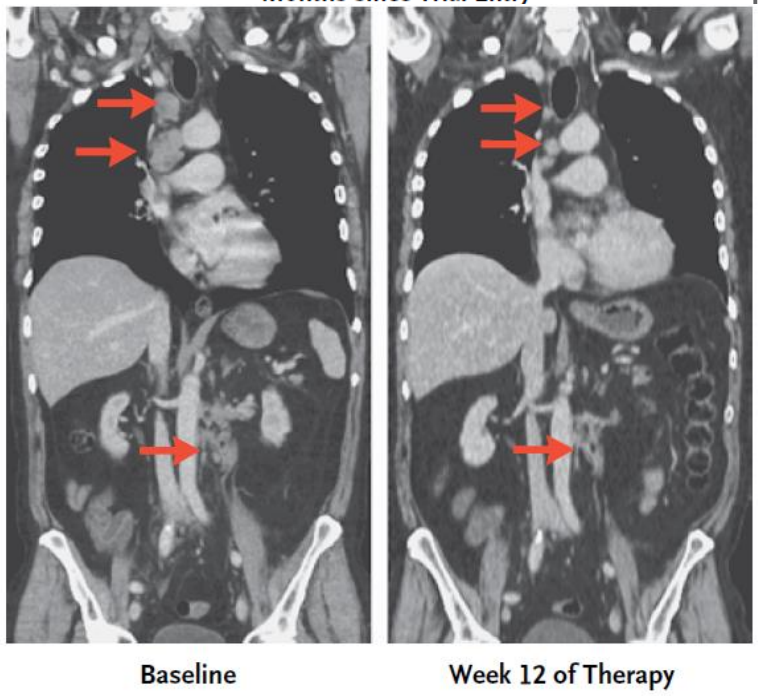
ABSTRACT

BACKGROUND









- **↓PSA: 88% (14/16)**

Mateo et al New Engl J Med 2015

PARPi current trials

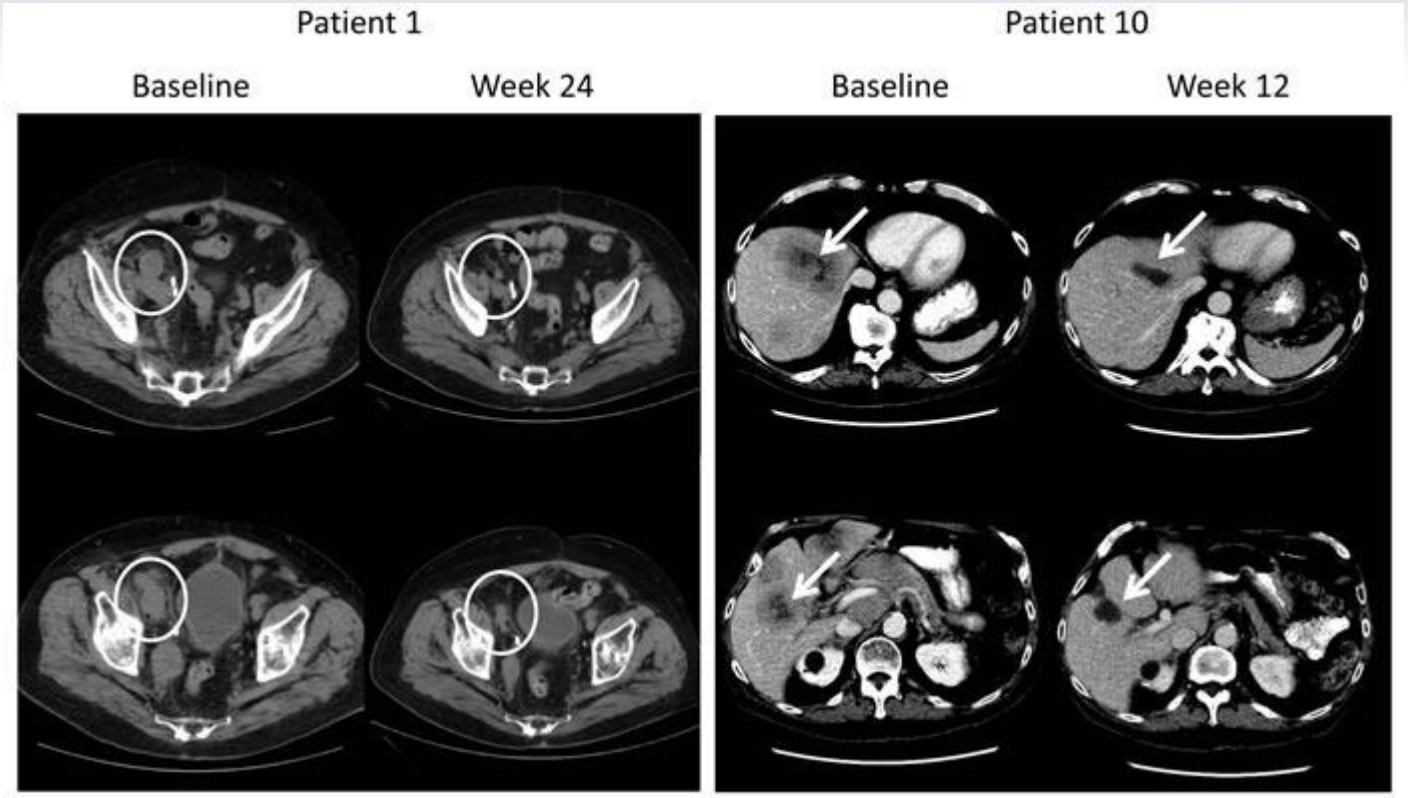
- **Rucaparib - TRITON**
- **Niraparib - Galahad**
- **Olaparib - PROfound**

Anti-PD1 – what is the right biomarker?

- **Hanssen et al. KEYNOTE-028, 2016**
  - **Pembrolizumab phase II / anti-PD-L1 +ve**
  - **23 pts: 3PR (mDOR: 59 wks); 9SD**

- **MSI-High Trials, 2017**
  - **2/59 pts non-CRC: 1PR, 1 SD (DOR 9.8+ months)**

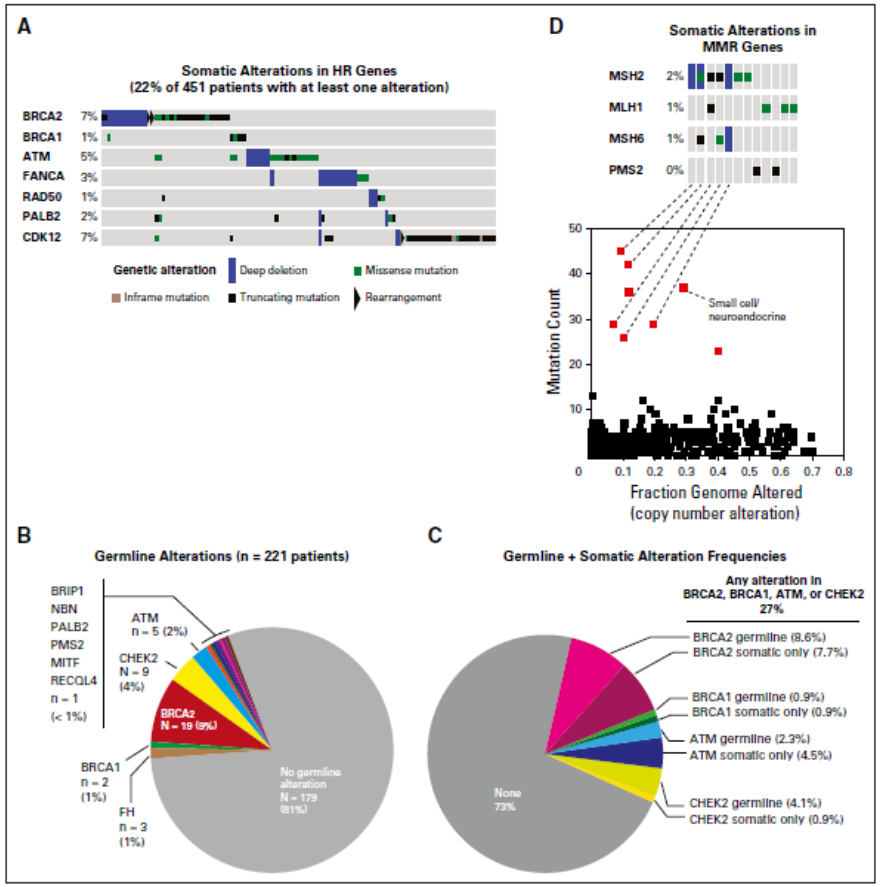
Early evidence of anti-PD-1 activity in enzalutamide-resistant prostate cancer

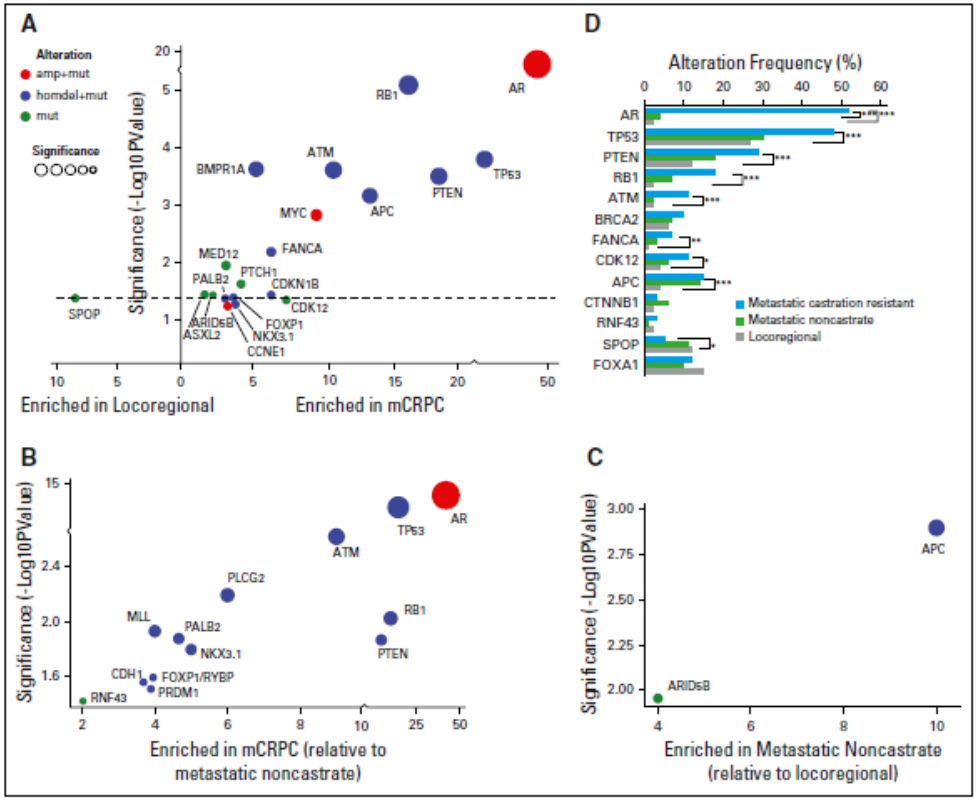


Graff et al Oncotarget 2016

original report

Prospective Genomic Profiling of Prostate Cancer Across Disease States Reveals Germline and Somatic Alterations That May Affect Clinical Decision Making





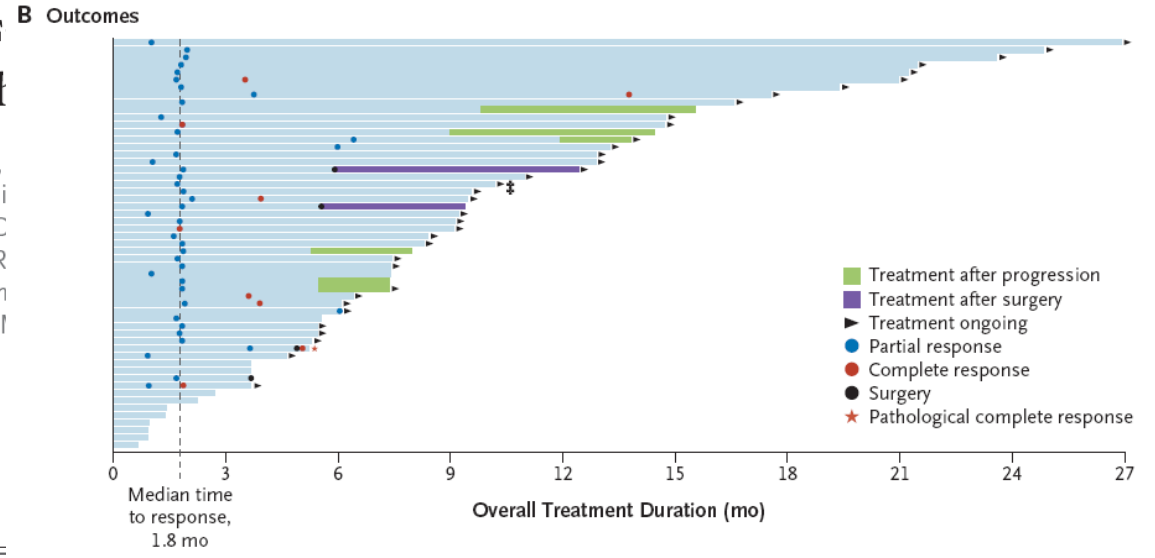
Adiba et al JCO Precis Oncol. 2017

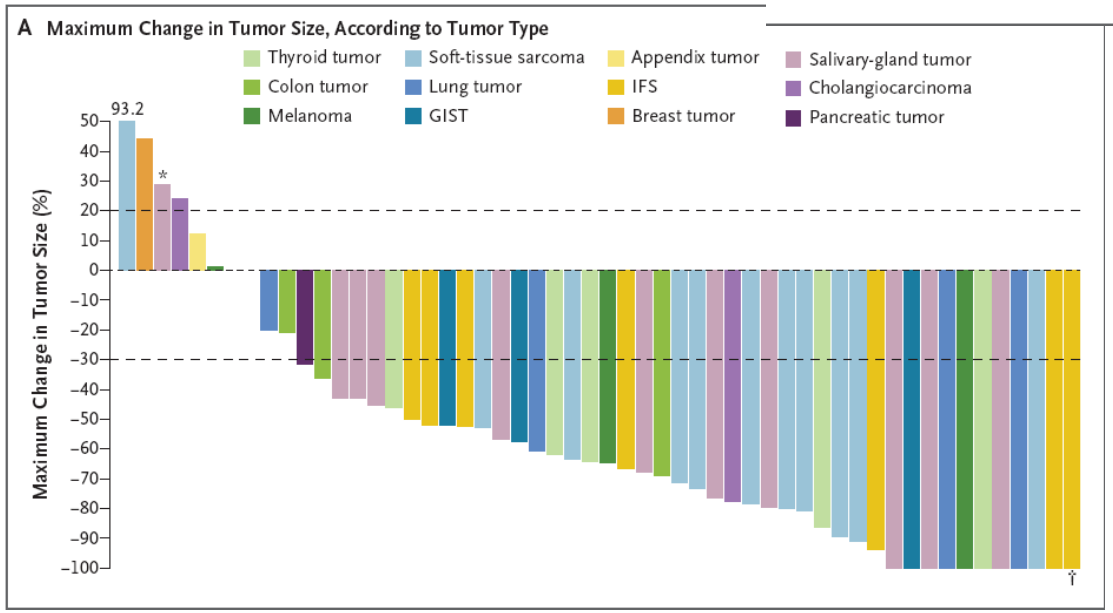
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of Larotrectinib in *TRK* F
Positive Cancers in Adults and Cl

A. Drilon, T.W. Laetsch, S. Kummar, S.G. DuBois, U.N. Lassen,
M. Nathenson, R.C. Doebele, A.F. Farago, A.S. Pappo, B. Turpi
M.S. Brose, L. Mascarenhas, N. Federman, J. Berlin, W.S. El-D
J. Deeken, V. Boni, R. Nagasubramanian, M. Taylor, E.R. R
F. Meric-Bernstam, D.P.S. Sohal, P.C. Ma, L.E. Raez, J.F. Hechtm
M. Ladanyi, B.B. Tuch, K. Ebata, S. Cruickshank, N.C. Ku, I
D.S. Hawkins, D.S. Hong, and D.M. Hyman





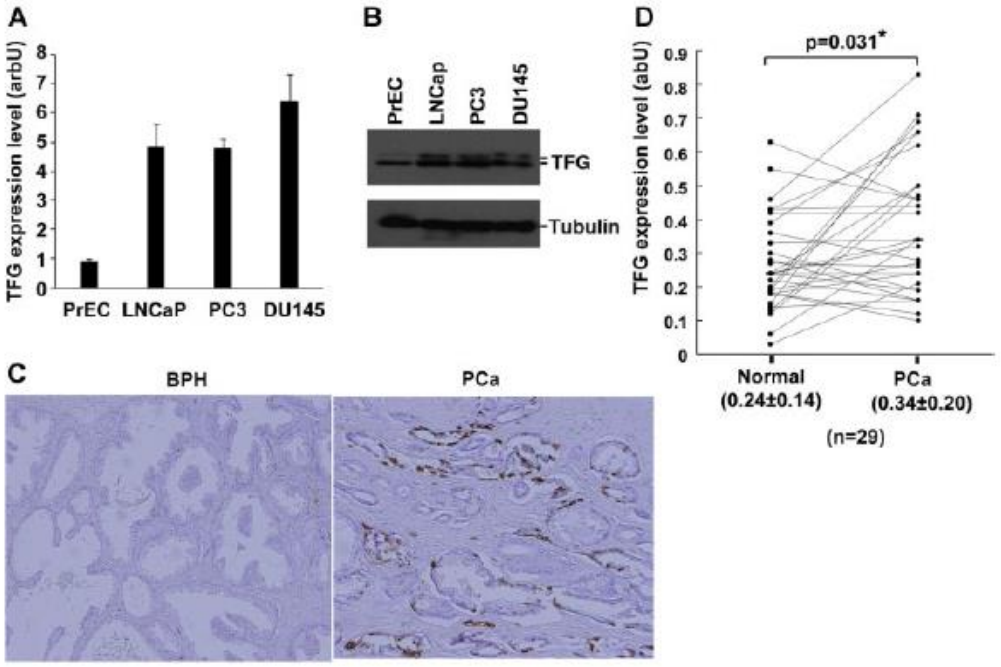
Drilon et al New Engl J Med 2018

The Prostate 72:626–637 (2012)

Identification of Phosphorylated Proteins Involved in the Oncogenesis of Prostate Cancer Via PinI-Proteomic Analysis

Kanji Endoh,[1,2] Mayuko Nishi,[2] Hitoshi Ishiguro,[3,4] Hiroji Uemura,[3] Yohei Miyagi,[5] Ichiro Aoki,[6] Hisashi Hirano,[7] Yoshinobu Kubota,[3] and Akihide Ryo[2]*

[1]Drug Discovery Research Center, Taiho Pharmaceutical Co., Ltd, Tsukuba, Japan
[2]Department of Microbiology, Yokohama City University School of Medicine, Yokohama, Japan
[3]Department of Urology, Yokohama City University School of Medicine, Yokohama, Japan
[4]Photocatalyst Group, Kanagawa Academy of Science and Technology, Takatsu-ku, Kawasaki, Kanagawa, Japan
[5]Molecular Pathology and Genetics Division, Kanagawa Cancer Center Research institute, Yokohama, Japan
[6]Department of Molecular Pathology, Yokohama City University School of Medicine, Yokohama, Japan
[7]Department of Nanobioscience, Yokohama City University, Yokohama, Japan



. 2. TFG is overexpressed in prostate cancer cells and tissues. **A**, **B**: TFG mRNA expression levels were monitored by quantitative RT-

Endoch et al The Prostate 2012

Klinikum rechts der Isar
Technical University Munich

2018 Genitourinary Cancers Symposium

Abstr. 206

Clinical experience with 100 consecutive patients treated with Lu-177-labeled PSMA-I&T radioligand therapy for metastatic castration-resistant prostate cancer

Matthias M. Heck[1], Sebastian Schwaiger[1,2], Karina Knorr[2], Margitta Retz[1], Tobias Maurer[1], Friederike Janssen[1,2], Calogero D´Alessandria[2], Hans-Jürgen Wester[3], Jürgen E. Gschwend[1], Markus Schwaiger[2], Robert Tauber[1], Matthias Eiber[2]
[1] Department of Urology and [2] Department of Nuclear Medicine, Rechts der Isar University Hospital, Technical University of Munich, Germany
[3] Pharmaceutical Radiochemistry, Technical University of Munich, Germany
Contact: matthias.heck@tum.de

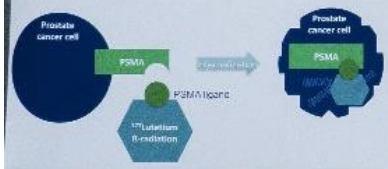
Objective

To report our clinical experience with a ^{177}Lutetium-labeled prostate-specific membrane antigen ligand (^{177}Lu-PSMA-I&T) for systemic radioligand therapy in 100 consecutive patients with metastatic castration-resistant prostate cancer (mCRPC).

Methods

All patients were treated under a review board-approved compassionate use protocol. Eligibility criteria for ^{177}Lu-PSMA-I&T therapy included previous treatment with abiraterone or enzalutamide, previous taxane-based chemotherapy or unsuitability for taxanes as well as positive ^{68}Ga-PSMA tracer uptake of metastases in a baseline PET-scan. Intravenous treatment with ^{177}Lu-PSMA-I&T was given 6- to 8-weekly with an activity of 7.4GBq up to 6 cycles in patients without clinical or radiographic progression. We report prostate-specific antigen (PSA) decline, PSA progression-free survival (PSA-PFS), clinical progression-free survival (cPFS) and overall survival (OS) as well as toxicity.

Mode of action of radioligand therapy with ^{177}Lu-PSMA-I&T



A ^{177}Lu labeled PSMA ligand binds to the extracellular part of PSMA expressed on prostate cancer cells. It is subsequently internalized and beta-radiation emitted from ^{177}Lu decay leads to cell damage.

Baseline patient characteristics

Median age was 72 years (range 46-85) and median PSA level was 164 ng/ml (range 0-6178). Bone, lymph node and visceral metastases were present in 94%, 85% and 33% of patients, respectively. The median number of previous treatment regimens for mCRPC was 3 (range 1-6) and 84% of patients were pretreated with chemotherapy.

No. patients	100
Age, years, median (range)	72 (46-85)
PSA, ng/ml, median (range)	164 (0-6178)
ECOG, No. (%), median (range)	1 (0-2)
Prior systemic treatments, No. (%)	
Docetaxel	83 (83)
Cabazitaxel	20 (20)
Abiraterone	89 (89)
Enzalutamide	61 (61)
Radium 223	19 (19)
Prior lines of systemic treatment, No. (%)	
1	7 (7)
2	38 (38)
3	34 (34)
4	15 (15)
5	7 (7)
6	1 (1)
Site of metastasis, No. (%)	
lymph nodes	85 (85)
bone	94 (94)
visceral	33 (33)

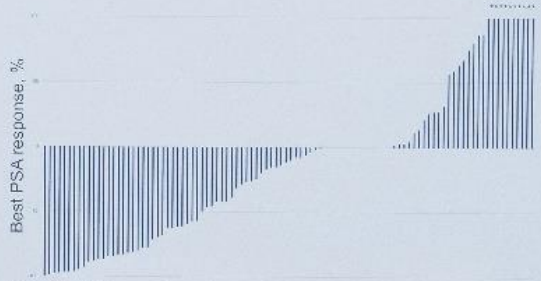
Adverse events

Treatment-emergent hematologic grade 3/4 toxicities were anemia in 7%, thrombocytopenia in 5% and neutropenia in 4% of patients. Grade 3/4-non-hematologic toxicities were not observed. The main non-hematologic grade 1/2 toxicities were dry mouth in 18%, fatigue in 16% and loss of appetite in 16% of patients.

Adverse events	Grade 1-2 No. (%)	Grade 3-4 No. (%)
Hematologic toxicities		
Anemia	36 (36)	7 (7)
Neutropenia	18 (18)	4 (4)
Thrombopenia	20 (20)	5 (5)
Non-hematologic toxicities		
Dry mouth	18 (18)	-
Fatigue	16 (16)	-
Loss of appetite	16 (16)	-

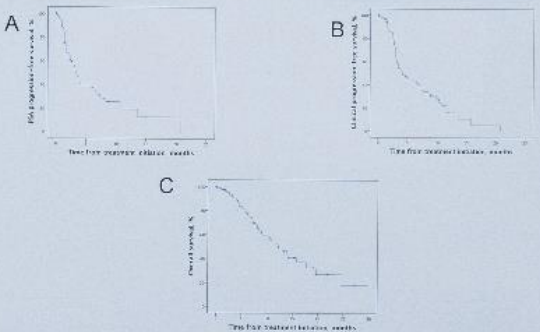
PSA response

At the time of evaluation, 286 cycles with ^{177}Lu-PSMA-I&T were applied (median 2 cycles per patient, range 1-6), while treatment was still ongoing in 27% of patients. Overall, 4 and 6 cycles were applied in 33 and 15 patients, respectively. PSA decline ≥30%, ≥50% and ≥90% was achieved in 40%, 32% and 9% of patients, respectively.



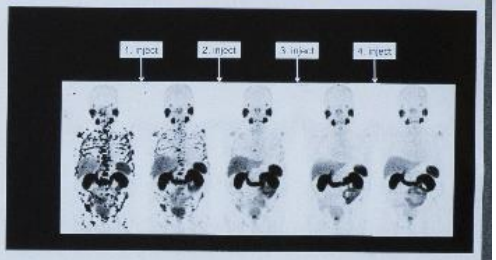
Waterfall plot for maximum change of prostate-specific antigen (PSA) levels under 7.4 GBq ^{177}Lu-PSMA-I&T radioligand therapy. Asterisks indicate an increase of >100%.

Survival analysis



Median PSA-PFS was 3.4 months (95%CI 2.7-4.0) (A), median cPFS was 4.1 months (95%CI 2.5-5.7) (B) and median OS was 12.2 months (95%CI 8.8-15.7) (C).

Patient example



^{68}Ga-PSMA PET/CT-scans of a 72 y/o patient who nearly achieved complete remission under 7.4GBq ^{177}Lu-PSMA-I&T radioligand therapy as fifth line therapy. He was pretreated with abiraterone, docetaxel, radium-223 and enzalutamide. His PSA level decreased from 1200 ng/ml to 10 ng/ml at the end of the fourth cycle. He had multiple bone metastases at baseline which became nearly undetectable after the fourth cycle.

Conclusion

Radioligand therapy with ^{177}Lu-PSMA I&T appears to be safe and active in late-stage mCRPC.

Literature on ^{177}Lu-PSMA-I&T:

•Weineisen M, Simecek J, Schottelius M, Schwaiger M, Wester H-J. Synthesis and preclinical evaluation of DOTAGA-conjugated PSMA ligands for functional imaging and endoradiotherapy of prostate cancer. EJNMMI Res 2014;4:63.

•Weineisen M, Schottelius M, Simecek J, et al. 68Ga- and 177Lu-labeled PSMA I&T: Optimization of a PSMA targeted theranostic concept and first proof of concept human studies. J Nucl Med J Nucl Med 56, 8 (2015), 1169-1176 2015.

•Heck MM, Retz M, D'Alessandria C, Rauscher I, Scheidhauer K, Maurer T, et al. Systemic radioligand therapy with (177)Lu-PSMA-I&T in patients with metastatic castration-resistant prostate cancer. J Urol. 2016 Mar 8.

German Multicenter Study Investigating ^{177}Lu-PSMA-617 Radioligand Therapy in Advanced Prostate Cancer Patients

Kambiz Rahbar*[1], Hojjat Ahmadzadehfar*[2], Clemens Kratochwil[3], Uwe Haberkorn[3], Michael Schäfers[1], Markus Essler[2], Richard P. Baum[4], Harshad R. Kulkarni[4], Matthias Schmidt[5], Alexander Drzezga[5], Peter Bartenstein[6], Andreas Pfestroff[7], Markus Luster[7], Ulf Lützen[8], Marlies Marx[8], Vikas Prasad[9], Winfried Brenner[9], Alexander Heinzel[10], Felix M. Mottaghy[10], Juri Ruf[11], Philipp Tobias Meyer[11], Martin Heuschkel[12], Maria Eveslage[13], Martin Bögemann[14], Wolfgang Peter Fendler†[6], and Bernd Joachim Krause†[12,15]

TABLE 1
Patient Characteristics at Baseline (n = 145)

Characteristic	Data
Age (y)	73 (43–88)
PSA (ng/mL)	214 (0.35–5,436)
Alkaline phosphatase (U/L)	120 (38–1,607)
Hemoglobin (g/dL)	11.3 (6–16)
White blood cells (10^3/μL)	6.2 (2.4–14.3)
Platelets (10^3/μL)	235 (55–557)
Creatinine (mg/dL)	0.9 (0.3–3.1)
Site of metastases (n)	
Bone	126 (87%)
Lymph node	112 (77%)
Liver	30 (20%)
Lung	20 (14%)
Other	3 (2%)
Previous therapy of mCRPC (n)	
Androgen-deprivation therapy	145 (100%)
Chemotherapy	79 (54%)
Abiraterone	93 (64%)
Ezalutamide	76 (52%)
^{223}Ra	24 (17%)
External-beam radiation therapy to bone	51 (35%)

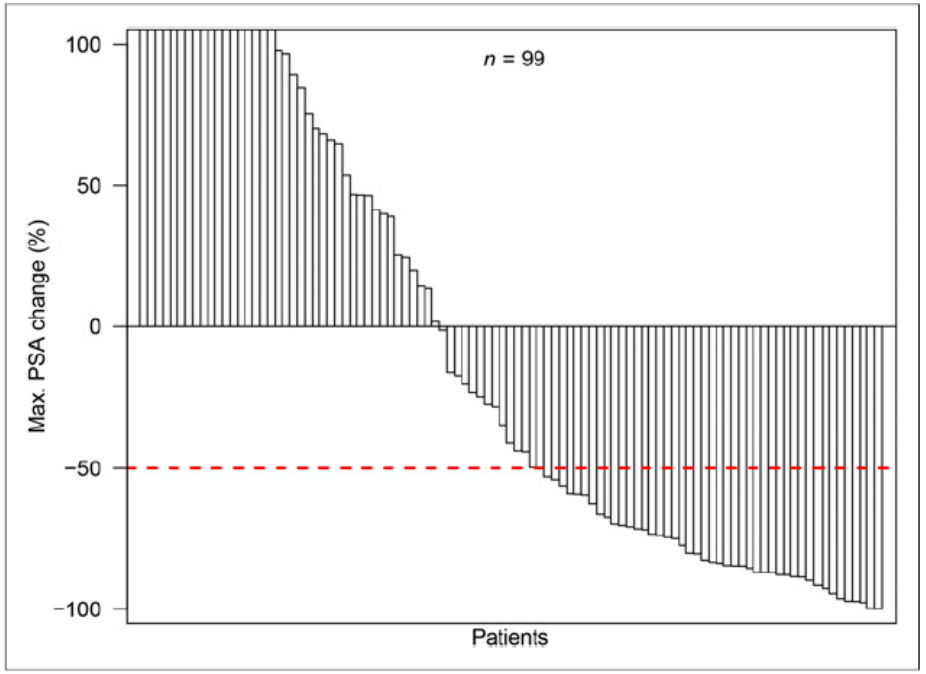


FIGURE 2. Waterfall plot of maximum PSA change (%) from baseline over total follow-up period. PSA increase > 100% was cropped due to simplification.

Clinical experience with PSMA-Actinium-225 radioligand therapy in end-stage metastatic castration-resistant prostate cancer patients

abstract 344

Maarten J. van der Doelen[1,2], Niven Mehra[2], Minke Smits[2], Inge M. van Oort[1], Linda Heijmen[3], Marcel J.R. Janssen[3], Uwe Haberkorn[4], Clemens Kratochwil[4], Winald R. Gerritsen[2]

Departments of Urology[1], Medical Oncology[2], and Nuclear Medicine[3], Radboud University Medical Center, Nijmegen, The Netherlands. [4]Department of Nuclear Medicine, University Hospital Heidelberg, Germany

BACKGROUND

- Prostate-specific membrane antigen (PSMA) is an ideal target for imaging and radioligand therapy (RLT) in metastatic castration resistant prostate cancer (mCRPC) patients[1]
- Alpha-emitting radioisotope Actinium-225 (^{225}Ac) may be more efficacious than beta-emitting Lutetium-177 (^{177}Lu)[2,3]:
  - Higher rates of double-strand DNA breaks in cancer cells
  - Less tissue penetration
  - Minimal bystander effects in PSMA-negative cells
- **Limited data is available on the clinical efficacy and side effects of ^{225}Ac-PSMA RLT and mechanisms of resistance to therapy**

OBJECTIVES

- To describe our initial clinical experience of mCRPC patients referred and treated with ^{225}Ac-PSMA RLT
- **Primary endpoint:** overall survival (OS): months from start of therapy to death or censoring
- **Secondary endpoints:**
  - Changes in alkaline phosphatase (ALP), prostate specific antigen (PSA), and lactate dehydrogenase (LD) levels
  - Hematological toxicity
  - Radiological response: RECIST 1.1 and PSMA-PET response
  - Xerostomia evaluation by the Xerostomia Inventory[4]
  - Molecular signature by next generation DNA sequencing (NGS)

PATIENTS AND METHODS

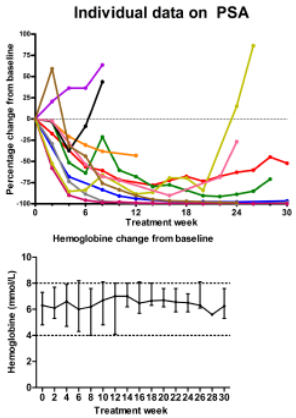
- **Design** observational cohort study
- **Therapy** PSMA-617 was labeled with Actinium-225 (^{225}Ac)
- **Treatment schedule** 100 kBq/kg bodyweight, every two months, up to four cycles, February 2016 to November 2017
- **Laboratory evaluation** approximately every two weeks
- **Metastatic biopsies** were taken per institution protocol for:
  - Neuroendocrine tissue markers: chromogranin, CD56 antigen and synaptophysin
  - Next-generation sequencing by Hartwig Medical Foundation (whole genome sequencing) or by Foundation Medicine (Foundation One)
- **Xerostomia evaluation** by Xerostomia Inventory, every 4 weeks
- **Statistics** Kaplan-Meier analysis to calculate OS and the Wilcoxon signed-rank test for paired data in the Xerostomia Inventory

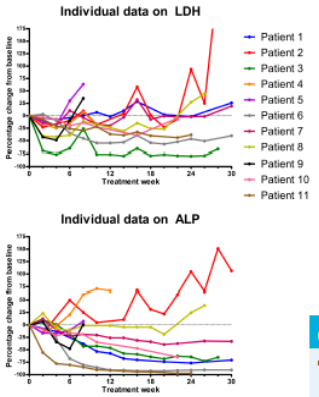
RESULTS

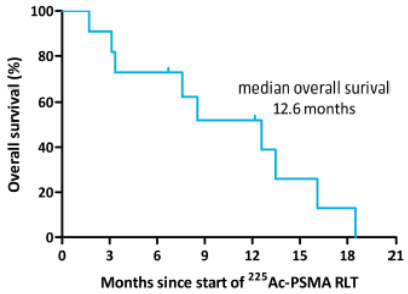
- 11 mCRPC patients were referred for ^{225}Ac-PSMA RLT
- No grade 3-4 hematologic toxicity occurred
- Xerostomia score deteriorated significantly (P 0.027)

PATIENT CHARACTERISTICS	median [range], n [%]
Age (years)	71 [56-81]
Gleason score 8-10	5 (45.5)
Number of prior therapies for mCRPC	4 [2-5]
Opioid use	7 (63.6)
ECOG performance score 1-2	8 (72.7)
Baseline PSA	878 [6-2249]
Baseline ALP	356 [90-2148]
Baseline LDH	294 [189-1346]

OUTCOMES	median [range], median (95% confidence interval)
Number of ^{225}Ac-PSMA RLT cycles	3 [1-4]
Injected activity (MBq)	8 [6-10]
Overall survival (months)	12.6 (5.7-19.4)







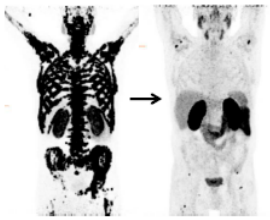
Patient	Prior therapies	Disease sites	NE markers	NGS results	Max PSA decline	RECIST 1.1 response	PSMA PET response
1	A – D – R – E	B, L, V	-	BRCA1	-97,8 %	PR	PR
2	D – A – E – C	B, L, V	++	PTEN	-78,1 %	PR	PR
3	D – C	B, L	-	- **	-91,3 %	no target lesions	PR
4	A – E – D	B, L, V	*	*	-43,0 %	SD	n/a
5	A – E – D – C – Cp	B, L, V	*	*	no decline	n/a	n/a
6	D – C – A	B, L	+	RB1	-99,9 %	no target lesions	PR
7	D – A – E – C – R	B, L, V	-	RAD51C	-99,8 %	PR	PR
8	D	B, L	++	- **	-84,1 %	PD	PD
9	D – A – C – E - Cp	B, L, V	?	FANCM, PTEN	-37,2 %	n/a	n/a
10	D – R – E – A	B	+	TP53	-90,1 %	n/a	n/a
11	D – R – E – A – C	B	-	BRCA1, PTEN	-98,5 %	no target lesions	PR

Abbreviations: A, Abiraterone; C, Cabazitaxel; Cp, Carboplatin; D, Docetaxel ; E, Enzalutamide; R, Radium-223; B, bone metastases; L, lymph node metastases; V, Visceral metastases; NE, neuroendocrine; NGS, Next Generation Sequencing; PR, Partial Response; SD, Stable Disease; PD, Progressive Disease; n/a, not assessed (no scan)

** results pending or ongoing*

*** no aberrations in oncogenes, tumour suppressor and DNA damage response genes*

PATIENT 6



Prior to ^{225}Ac-PSMA radioligand therapy PSA 946 µg/L (September 2016)

After 3 injections ^{225}Ac-PSMA RLT PSA 0.29 µg/L (May 2017)

CONCLUSIONS

- ^{225}Ac-PSMA RLT resulted in remarkable clinical, biochemical and radiological responses in end-stage mCRPC patients
- Therefore, ^{225}Ac-PSMA RLT may be considered a promising therapy for mCRPC patients
- These findings warrant further investigation, especially in to optimal patient selection, protection against xerostomia, mechanisms of resistance to radioligand therapy, and next generation sequencing in patients with an ongoing response

REFERENCES

1. Benešová M, et al. J Nucl Med 2015; 56: 914–920
2. Kratochwil C, et al. J Nucl Med 2016; 57: 1941-1944
3. Kratochwil C, et al. J Nucl Med 2018; Epub ahead of print
4. Thomson WR, et al. Community Dental Health 1999; 16: 12-17

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Clinical experience with PSMA-Actinium-225 radioligand therapy in end-stage metastatic castration-resistant prostate cancer patients

abstract 344

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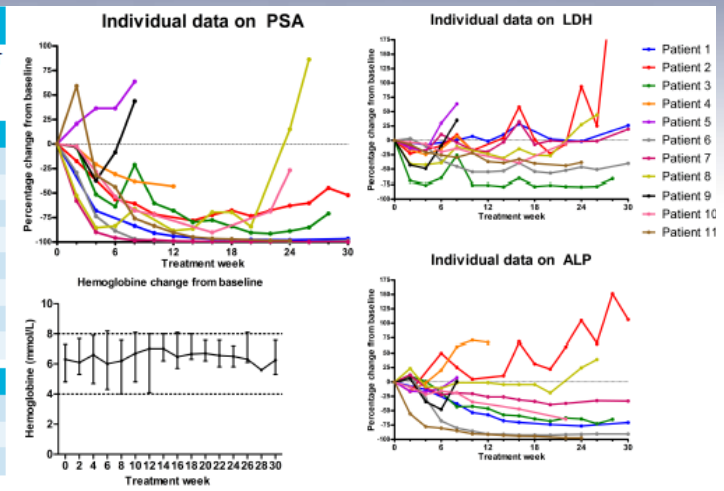
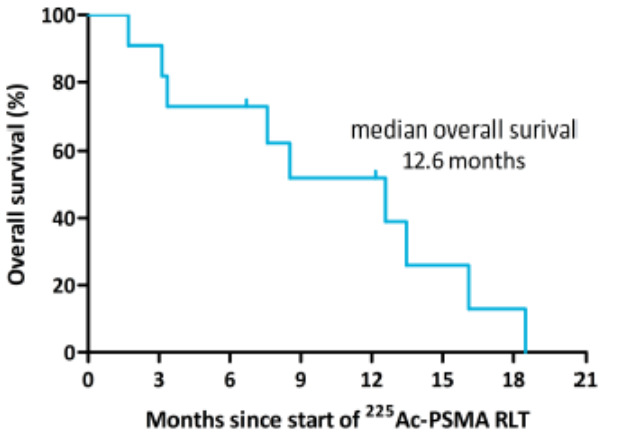
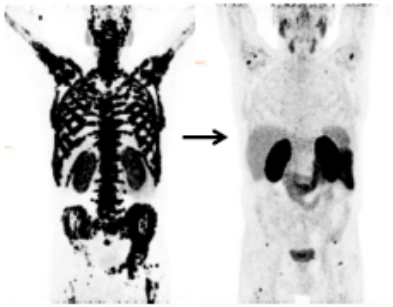




PATIENT 6



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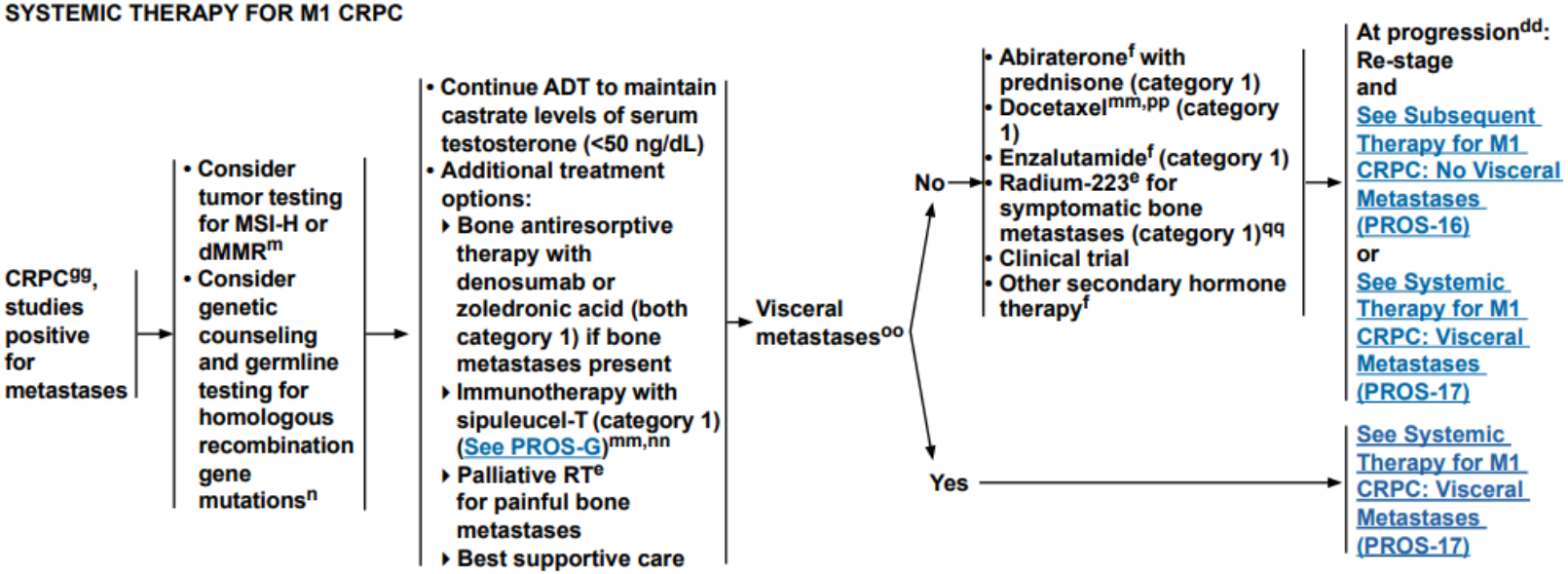
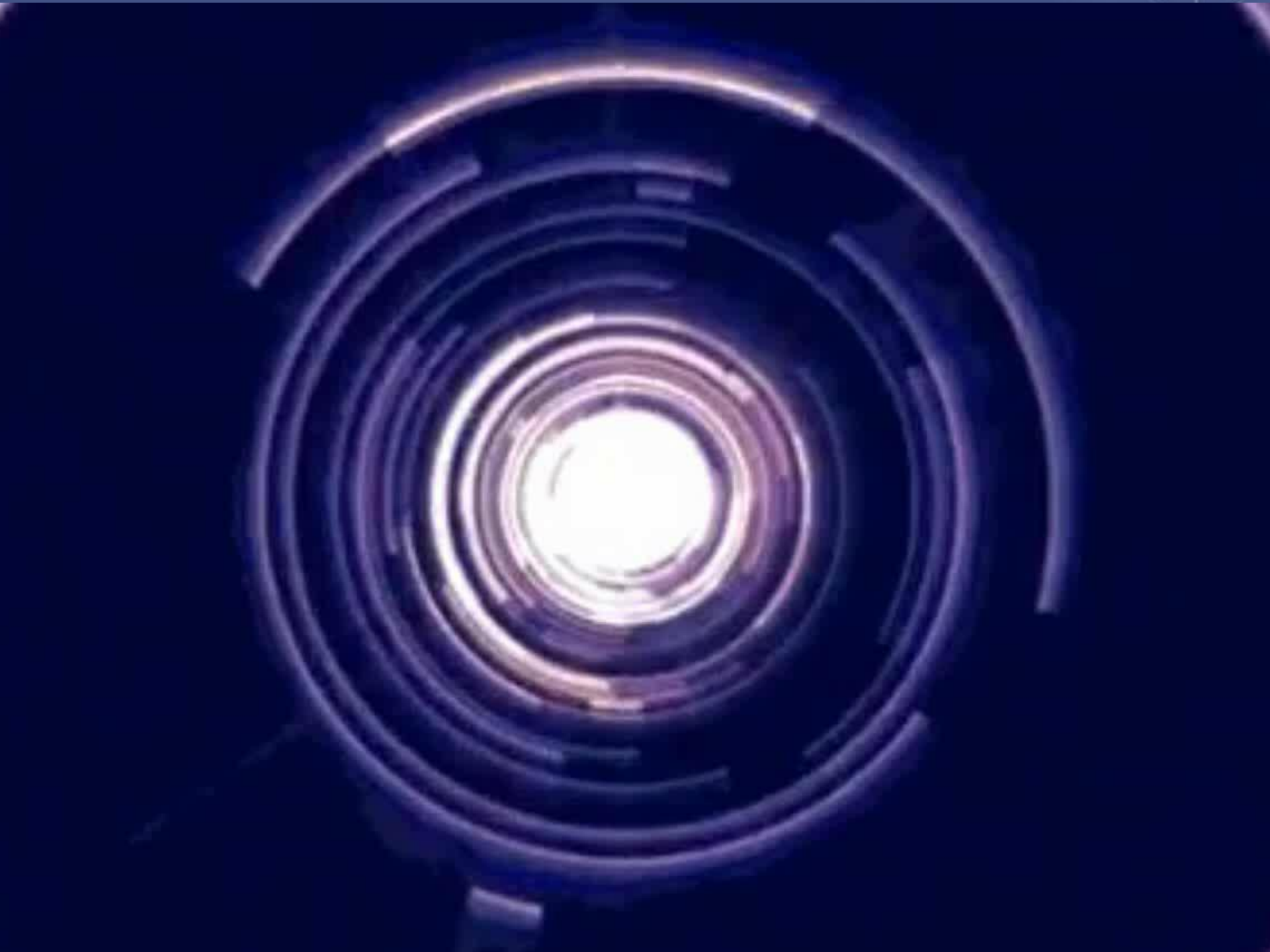
SYSTEMIC THERAPY FOR M1 CRPC



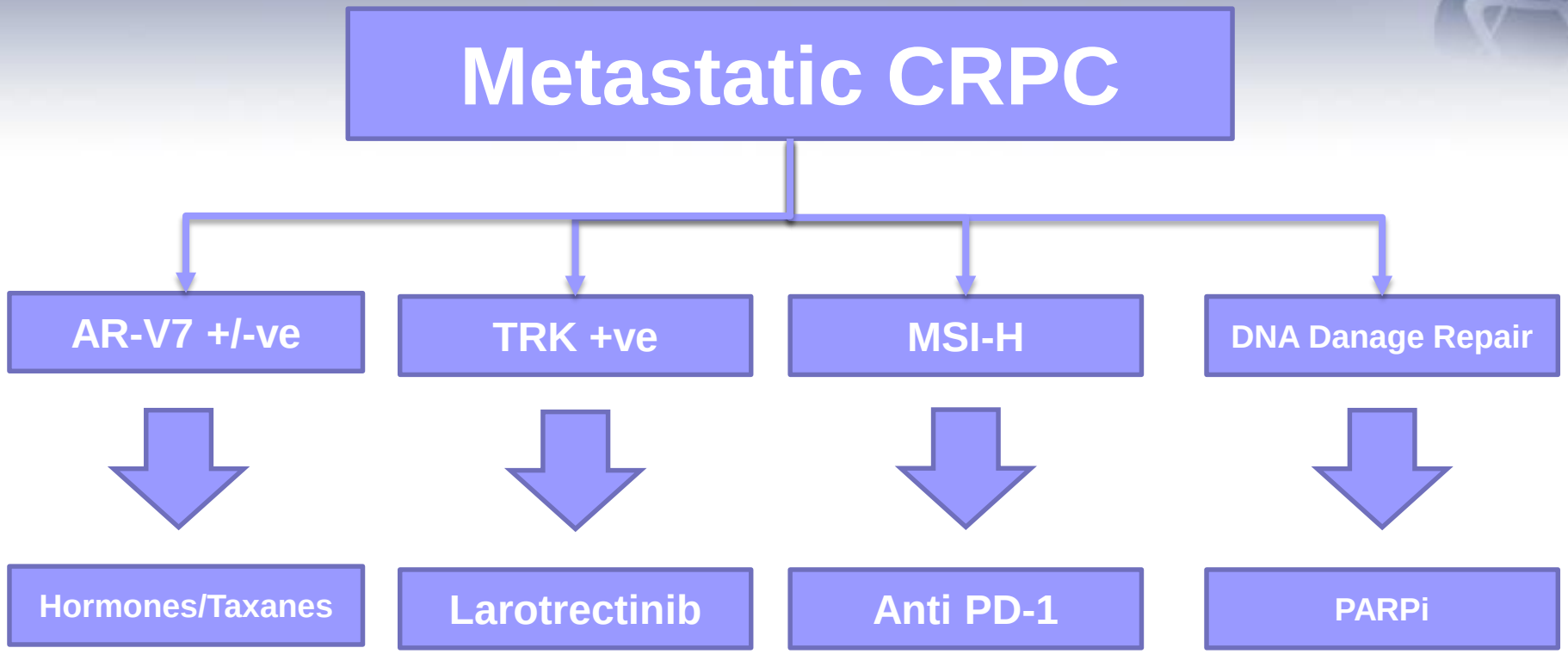
[e] See Principles of Radiation Therapy (PROS-D).
[f] See Principles of Androgen Deprivation Therapy (PROS-F).
[m] DNA analysis for MSI and IHC for MMR are different assays measuring the same biological effect. If MSI-H or dMMR is found, refer to genetic counseling to assess for the possibility of Lynch syndrome. MSI-H or dMMR indicate eligibility for pembrolizumab in later lines of treatment for CRPC (see PROS-16 and PROS-17).
[n] Consider testing for mutation in these genes (germline and somatic): *BRCA1, BRCA2, ATM, PALB2, FANCA;* refer to genetic counseling if positive. At present, this information may be used for genetic counseling, early use of platinum chemotherapy, or eligibility for clinical trials (e.g., PARP inhibitors) [dd] Workup for progression should include chest x-ray or chest CT, bone imaging, and abdominal/pelvic CT or MRI with and without contrast. Consider C-11 choline PET/CT or PET/MRI or F-18 fluciclovine PET/CT or PET/MRI for further soft tissue evaluation or F-18 sodium fluoride PET/CT for further bone evaluation. See Principles of Imaging (PROS-B) and Discussion.

[gg] Castration-resistant prostate cancer (CRPC) is prostate cancer that progresses clinically, radiographically, or biochemically despite castrate levels of serum testosterone (<50 ng/dL). Scher HI, Halabi S, Tannock I, et al. Design and end points of clinical trials for patients with progressive prostate cancer and castrate levels of testosterone: recommendations of the Prostate Cancer Clinical Trials Working Group. J Clin Oncol 2008;26:1148-1159.
[mm] See Principles of Immunotherapy and Chemotherapy (PROS-G).
[nn] Sipuleucel-T has not been studied in patients with visceral metastases.
[oo] Visceral metastases refers to liver, lung, adrenal, peritoneal, and brain metastases. Soft tissue/lymph node sites are not considered visceral metastases.
[pp] Although most patients without symptoms are not treated with chemotherapy, the survival benefit reported for docetaxel applies to those with or without symptoms. Docetaxel may be considered for patients with signs of rapid progression or visceral metastases despite lack of symptoms.
[qq] Radium-223 is not approved for use in combination with docetaxel or any other chemotherapy. See Principles of Radiation Therapy (PROS-D, page 2 of 3).

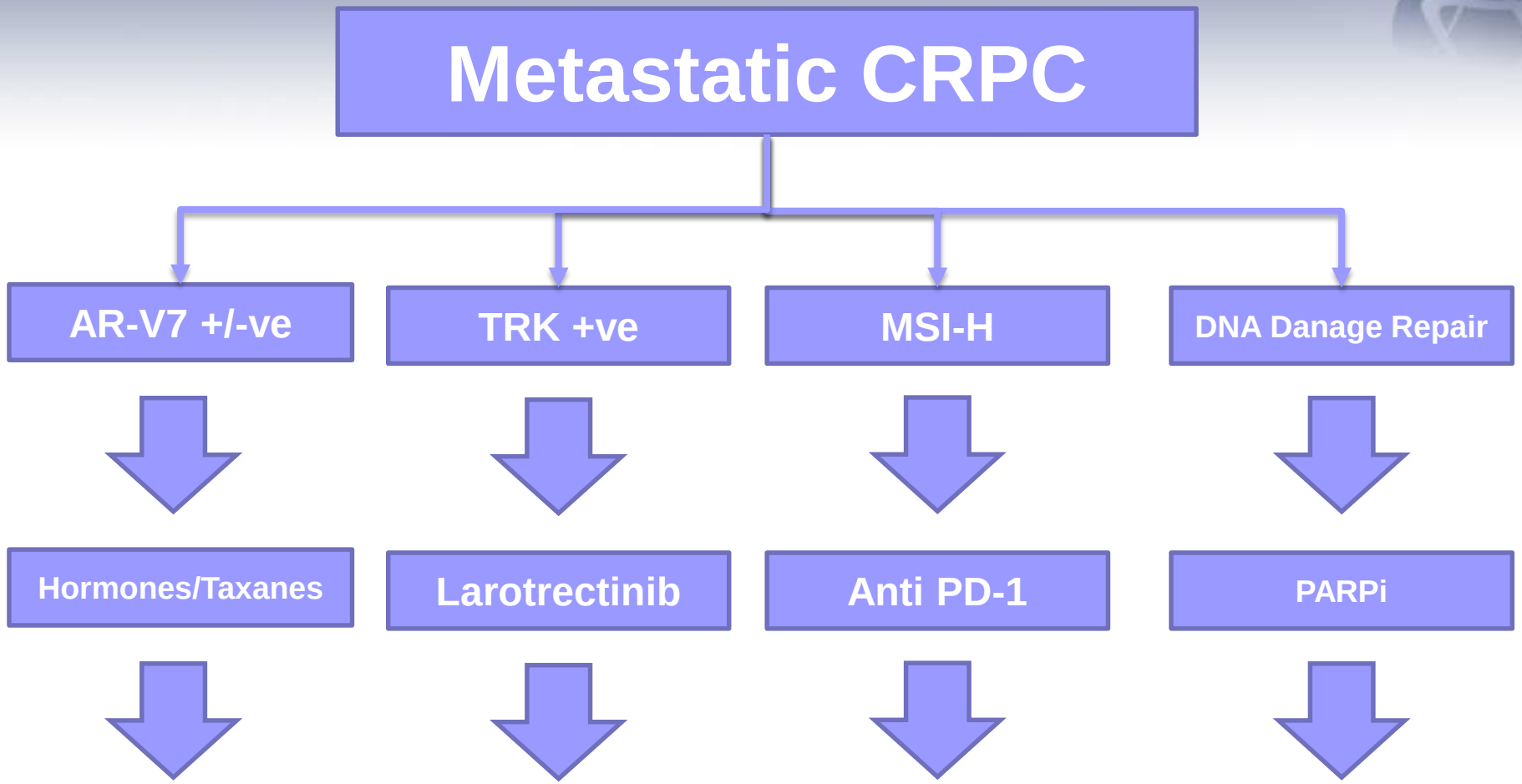
Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.



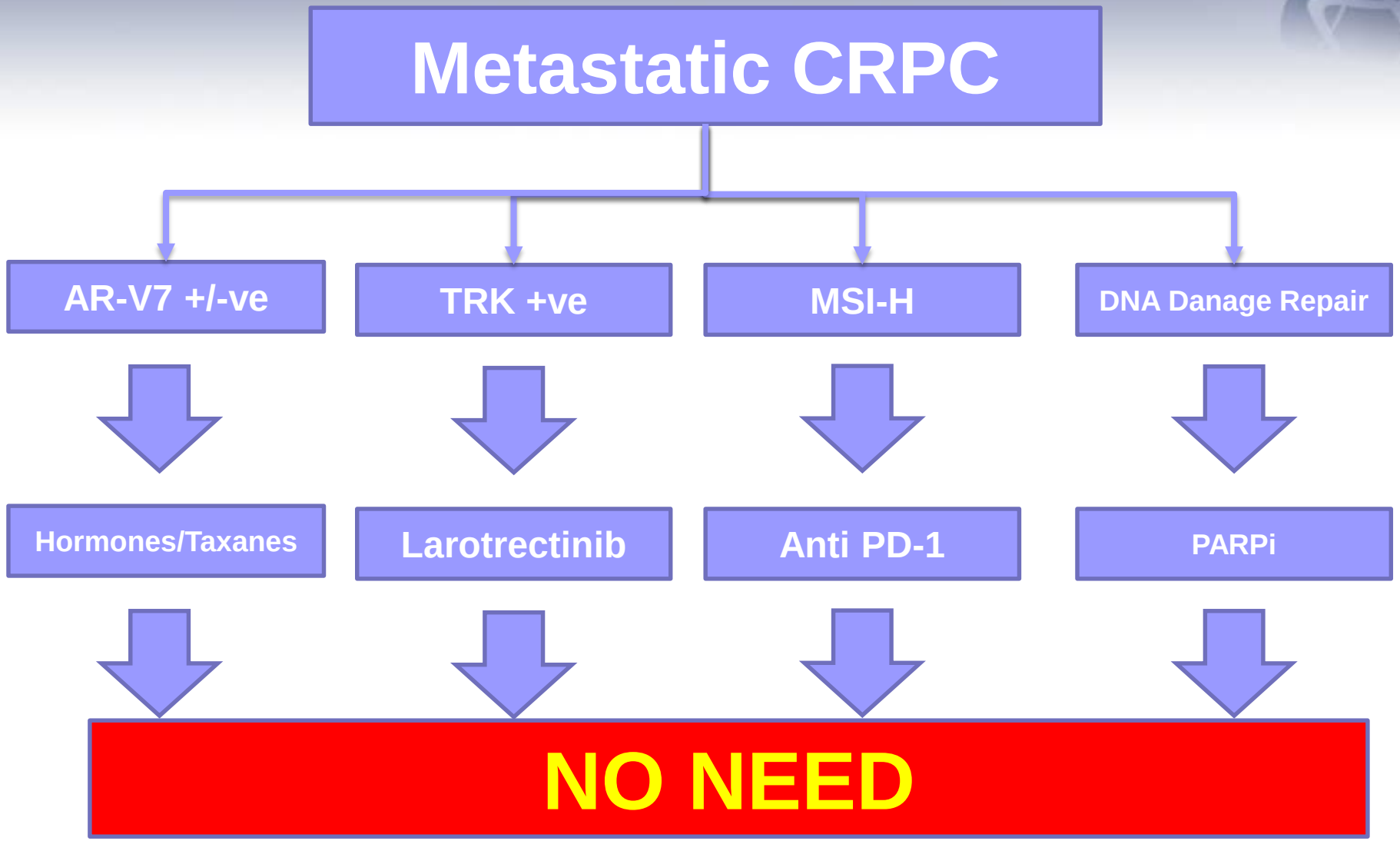
Are we ready – 1st line Rx?



Are we ready – 2nd line Rx?



Are we ready – 2nd line Rx?



Obrigado

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