Metastatic Prostate Cancer

February 1, 2020

Alex Niu

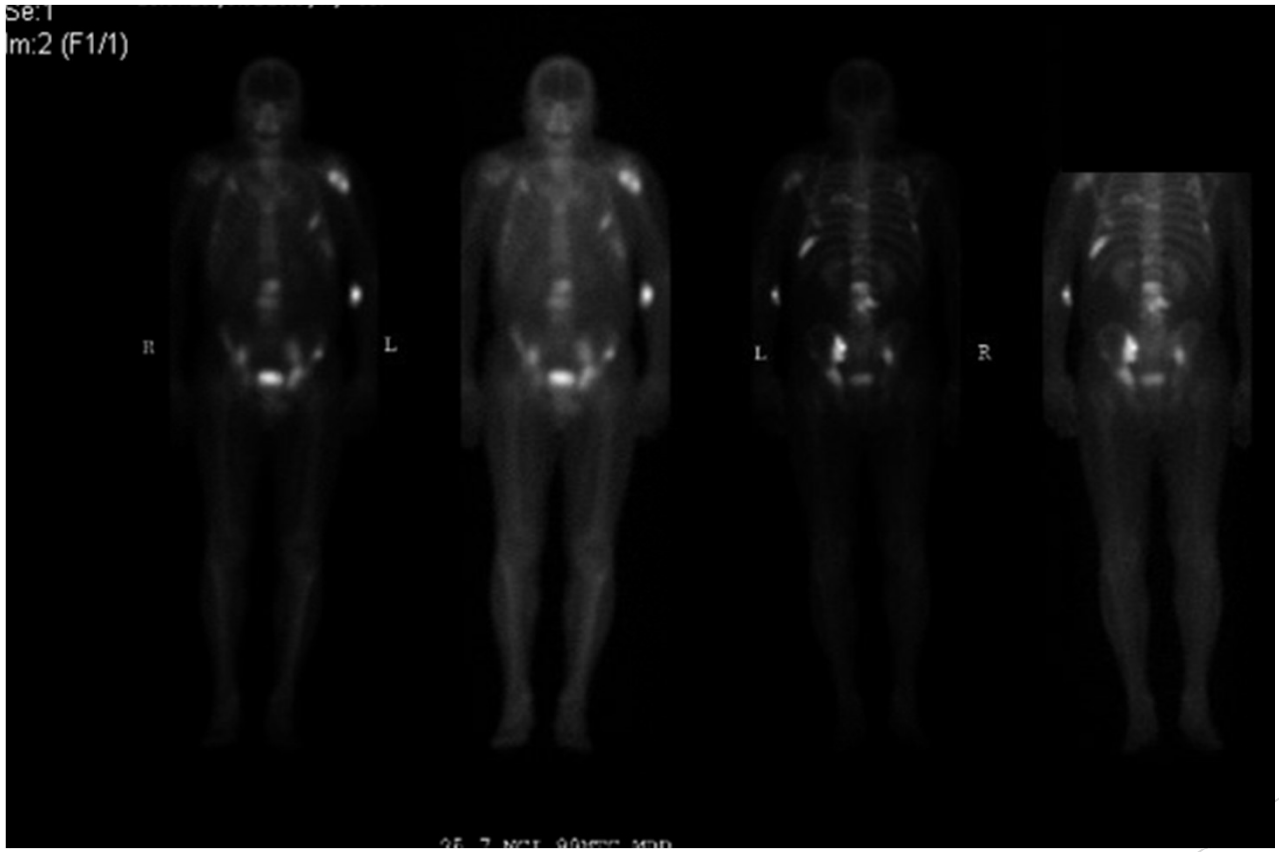
Tulane Hem-Onc Fellow IV

Case: Mr. RB

- 59 yr old male
- No significant PMH
- Truck-driver
- July 2017: Lower back pain
- Bone scan: diagnosed with metastatic prostate cancer to bones.
- Initial PSA 371; Gl 5+4

Tulane University

Initial Bone Scan (Jul 2017)



Reproduced with pt permission

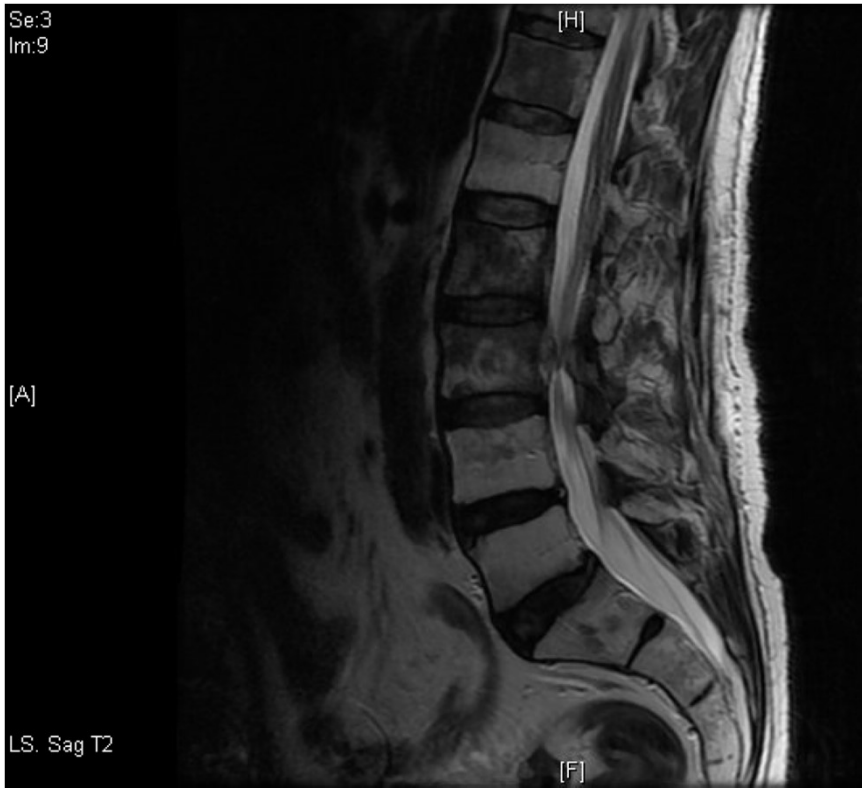
Tulane University

Treatment Timeline

- Aug 2017: Orchiectomy and Bicalutamide. Initial response but PSA progression few weeks later. Started XRT to T5 and T8.
- Nov 2017: Antiandrogen withdrawal. PSA response. Minimal symptoms.
- May 2018: Palliative XRT to left shoulder and started enzalutamide. Bone pain severe.
- July 2018: No PSA response. Docetaxel started. 6 total cycles given. XRT to ilium.
- Nov 2018: Palliative XRT to L3. Pain better controlled.
- Dec 2018: rising PSA. 283. VISION trial at Tulane – Lu177 + Abiraterone/dexamethasone

Tulane University

- May 2019 – PSA 260. Hospital admission with cord compression (L2-L3)



Reproduced with pt permission

Tulane University

Treatment Timeline

- July 2019: Surgical decompression.
- Ordered genetic germline and somatic NGS testing

Tulane University

PATIENT	SPECIMEN INFORMATION	ORDERED BY
[redacted]		
Case Number: TN18-129442 **Diagnosis:** Adenocarcinoma, NOS	[redacted]	New Orleans, LA 70112 USA (504) 988-7869

BIOMARKER HIGHLIGHTS (SEE PAGE 2 AND APPENDIX FOR MORE DETAILS)

Biomarker	Method	Result
MSI	NGS	High
Tumor Mutational Burden		High | 25 Mutations/Mb
ATM	NGS	Mutation Not Detected
BRCA1	NGS	Mutation Not Detected
BRCA2	NGS	Mutation Not Detected
FANCA	NGS	Mutation Not Detected
PALB2	NGS	Mutation Not Detected
PTEN	NGS	Mutated, Variant of Unknown Significance Exon 6 | p.P190L
AR	IHC	Positive | 2+, 95%
	NGS	Mutation Not Detected

Biomarker	Method	Result
Mismatch Repair Status*		Deficient
MLH1	IHC	Positive | 2+, 65%
MSH2	IHC	Negative | 0, 100%
MSH6	IHC	Negative | 0, 100%
PMS2	IHC	Positive | 1+, 85%
PD-L1	IHC	Negative | 0, 100%
ASXL1	NGS	Mutated, Pathogenic Exon 12 | p.G646fs
BMPR1A	NGS	Mutated, Pathogenic Exon 4 | p.L59fs
PIK3R1	NGS	Mutated, Pathogenic Exon 9 | p.R348*
SETD2	NGS	Mutated, Pathogenic Exon 14 | p.R2040*
TP53	NGS	Mutated, Pathogenic Exon 5 | p.R175H

* Mismatch repair status is determined by the presence or absence of the repair proteins MLH1, MSH2, MSH6 and PMS2 by IHC. If any of these IHC's are negative, mismatch repair status is considered deficient.

THERAPIES WITH POTENTIAL BENEFIT

pembrolizumab*	**Mismatch Repair Deficient, MSI**

* Drug/biomarker association(s) supported by the highest level of clinical evidence.

THERAPIES WITH UNCERTAIN BENEFIT

carboplatin, cisplatin	ATM, BRCA1, BRCA2

Drugs are placed in the Uncertain benefit category when a result suggests only a decreased likelihood of response (vs. little to no likelihood of response) or if there is insufficient evidence to associate the drug with either benefit or lack of benefit.

Tulane University

PATIENT	SPECIMEN INFORMATION	ORDERED BY
[redacted]		
Case Number: TN18-129442 **Diagnosis:** Adenocarcinoma, NOS	[redacted]	New Orleans, LA 70112 USA (504) 988-7869

BIOMARKER HIGHLIGHTS (SEE PAGE 2 AND APPENDIX FOR MORE DETAILS)

Biomarker	Method	Result
MSI	NGS	High
Tumor Mutational Burden		High | 25 Mutations/Mb
ATM	NGS	Mutation Not Detected
BRCA1	NGS	Mutation Not Detected
BRCA2	NGS	Mutation Not Detected
FANCA	NGS	Mutation Not Detected
PALB2	NGS	Mutation Not Detected
PTEN	NGS	Mutated, Variant of Unknown Significance Exon 6 | p.P190L
AR	IHC	Positive | 2+, 95%
	NGS	Mutation Not Detected

Biomarker	Method	Result
Mismatch Repair Status*		Deficient
MLH1	IHC	Positive | 2+, 65%
MSH2	IHC	Negative | 0, 100%
MSH6	IHC	Negative | 0, 100%
PMS2	IHC	Positive | 1+, 85%
PD-L1	IHC	Negative | 0, 100%
ASXL1	NGS	Mutated, Pathogenic Exon 12 | p.G646fs
BMPR1A	NGS	Mutated, Pathogenic Exon 4 | p.L59fs
PIK3R1	NGS	Mutated, Pathogenic Exon 9 | p.R348*
SETD2	NGS	Mutated, Pathogenic Exon 14 | p.R2040*
TP53	NGS	Mutated, Pathogenic Exon 5 | p.R175H

* Mismatch repair status is determined by the presence or absence of the repair proteins MLH1, MSH2, MSH6 and PMS2 by IHC. If any of these IHC's are negative, mismatch repair status is considered deficient.

THERAPIES WITH POTENTIAL BENEFIT

pembrolizumab*	**Mismatch Repair Deficient, MSI**

* Drug/biomarker association(s) supported by the highest level of clinical evidence.

THERAPIES WITH UNCERTAIN BENEFIT

carboplatin, cisplatin	ATM, BRCA1, BRCA2

Drugs are placed in the Uncertain benefit category when a result suggests only a decreased likelihood of response (vs. little to no likelihood of response) or if there is insufficient evidence to associate the drug with either benefit or lack of benefit.

Tulane University

Treatment continues

- June 2019: Pembrolizumab started.
- PSA in September 2019 undetectable
- Still on Pembro today. Minimal side effects.

Tulane University

PSA

07/26/19: < 0.1
07/01/19: 1.1
06/10/19: 82.4
05/23/19: 266, T<8 ← Cord compression. Pembro started
05/15/19: 220
04/04/19: 164
03/21/19: 127
02/21/19: 146 – T <8
01/10/19: 138
12/13/18: 150.7
11/29/18: 283 ← Lu177 + zytiga/dex
10/31/18: 262
10/08/18: 232
09/04/18: 147 ← Completed Docetaxel

Tulane University

Pembrolizumab for MSI-H Tumors

ORIGINAL ARTICLE

PD-1 Blockade in Tumors with Mismatch-Repair Deficiency

FDA Approves (pembrolizumab) for Adult and Pediatric Patients with Unresectable or Metastatic, Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient Cancer

May 23, 2017

- **Pembrolizumab for Microsatellite Instability-High (MSI-H) Cancer**

- "Treatment of adult and pediatric patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair (MMR)-deficient:
  - Solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or
  - Colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan"

D le et al, NEJM 2015

MSI-H in Prostate Cancer

“Analysis of the Prevalence of Microsatellite Instability in Prostate Cancer and Response to Immune Checkpoint Blockade.” **Abida W et al.**

December 27, 2018

Tulane University

Summary

- Worth ordering genetic germline and somatic NGS testing on patients with prostate cancer
- MSI-H/dMMR is uncommon in prostate cancer.
- However, MSI-H can be meaningful target in prostate cancer.
- Need more evaluation into utilization of MSI-H/dMMR and PD1/PDL1 in prostate cancer

Tulane University

Thanks!!

Special thanks to Dr. Barata!