Updates in the Management of Prostate Cancer with a Focus on Radiopharmaceuticals

Grant Wintheiser, M.D.
Allina Health Cancer Institute

AHCI Oncology Symposium
9/26/2025

Allina Health

1

DISCLOSURES

I have no relevant financial disclosures.

Allina Health

2

OBJECTIVES

Metastatic castration resistant prostate cancer (mCRPC)

- Background on Pluvicto
- Pluvicto before chemotherapy - **PSMAfore**

Metastatic hormone sensitive prostate cancer (mHSPC)

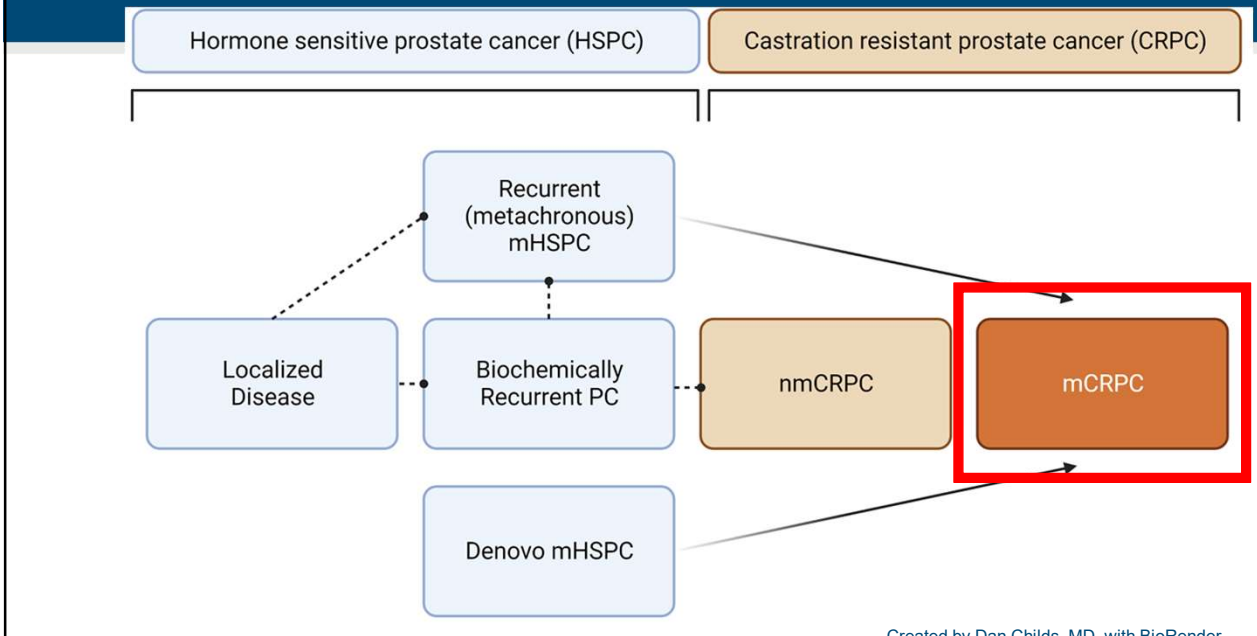
- Darolutamide doublet - **ARANOTE**
- ARPI selection practices - **STOPCAP**
- PARPi for mHSPC - **AMPLITUDE**

Looking ahead

- Pluvicto in mHSPC
- Doublet vs triplet therapy in high volume mHSPC
- Using PSA response to tailor therapy in mHSPC

Allina Health

3

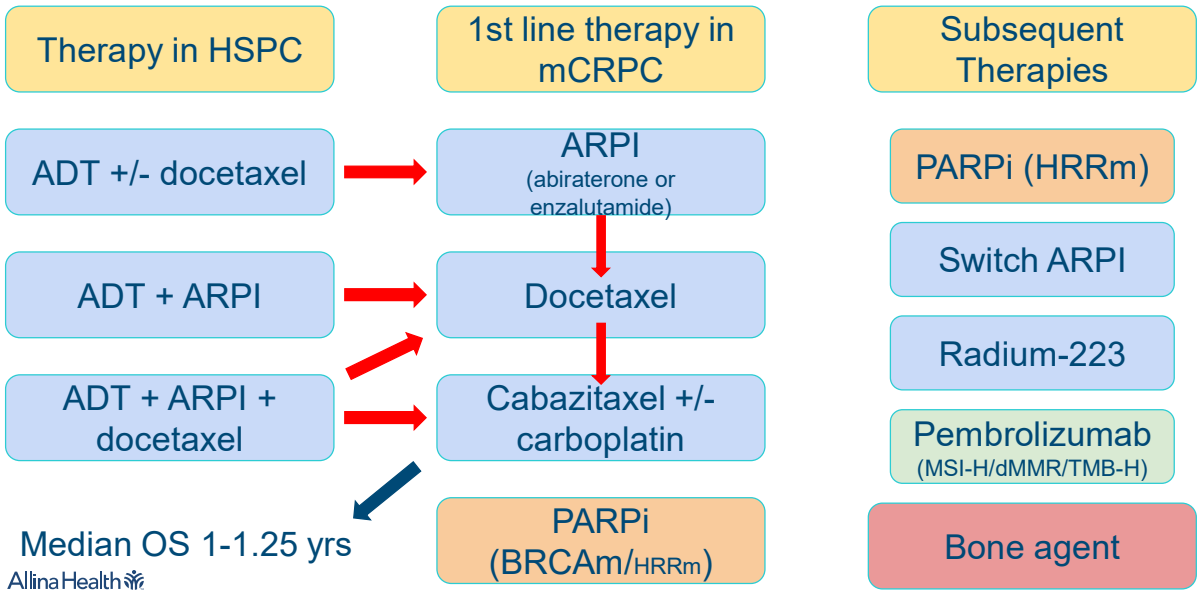


Created by Dan Childs, MD, with BioRender

Allina Health

4

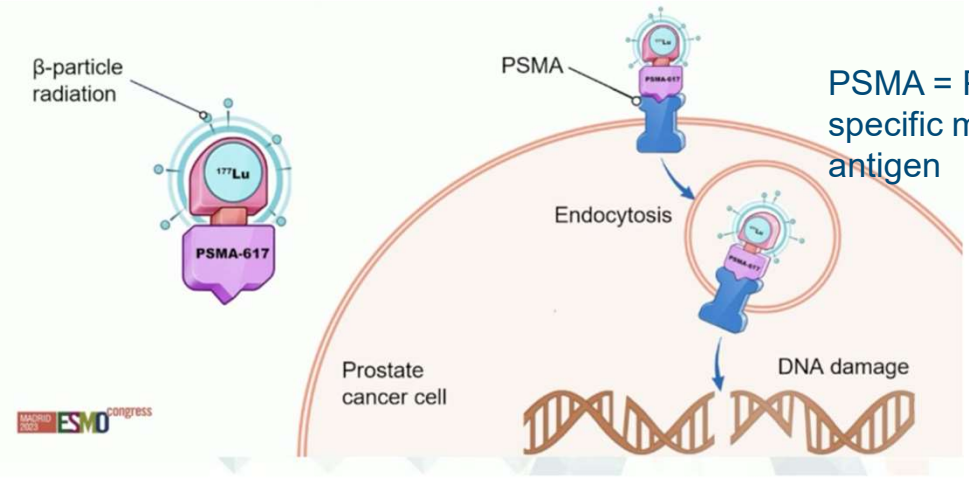
Summary of mCRPC management prior to Pluvicto



AllinaHealth

5

What is Pluvicto (Lutetium Lu 177 vipivotide tetraxetan)?



PSMA = Prostate specific membrane antigen

Recommended dose is 200 mCi intravenously every 6 weeks for up to 6 doses, or until disease progression or unacceptable toxicity

AllinaHealth

6

Toxicity profile of Pluvicto

Toxicities (>20%)

- Fatigue
- Dry mouth/dry eyes
- Nausea
- Decreased appetite
- Anemia

Grade 3 and 4 toxicities largely limited to cytopenias

- Anemia and thrombocytopenia (~10-15%) > leukopenia (~5%)
- Risk of inducing tCCUS and tMN is small, but present (1-5%)[1]
  - Short latency time

* Closely monitor kidney function, high grade kidney toxicity has been reported

Allina Health

7

Initial FDA approval after chemotherapy[2]

FDA approves Pluvicto for metastatic castration-resistant prostate cancer

On March 23, 2022, the Food and Drug Administration approved Pluvicto (lutetium Lu 177 vipivotide tetraxetan, Advanced Accelerator Applications USA, Inc., a Novartis company) for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy.

Allina Health

8

VISION[3]

Key Eligibility
- mCRPC
- Prior treatment:
  - 1+ ARPI
  - 1 or 2 taxane regimens
- ECOG 0-2
- Not a candidate for second taxane regimen
- PSMA-PET+*

SOC**

SOC + 177Lu-PSMA617

7.4 GBq (200miC) Q6wks x4-6 cycles

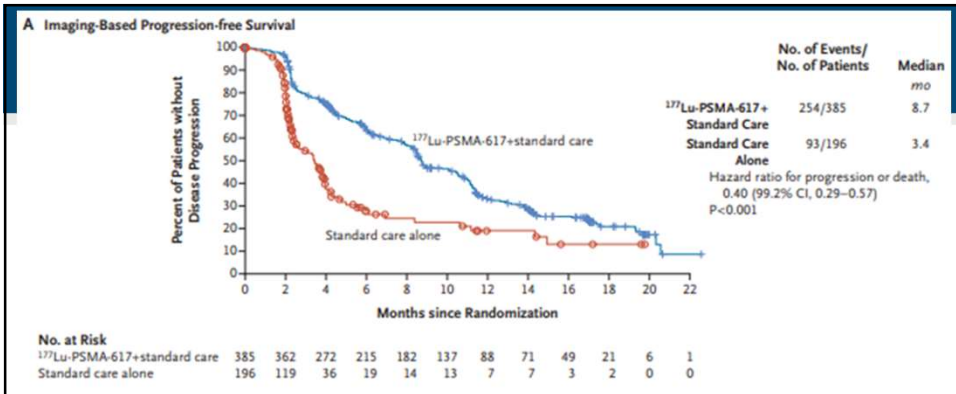
iPFS and OS

*1+ PSMA+ lesion (68Ga uptake>liver)
No PSMA- lesions (LN.2cm, solid organ>1cm)

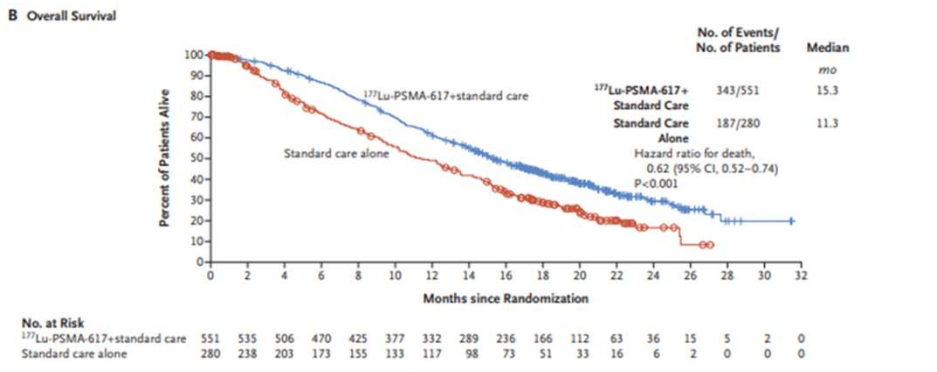
**Not permitted: chemotherapy, immunotherapy, radium-223
Permitted: ARPI (68 vs 53%), steroid, bone agent, radiation therapy

AllinaHealth

9

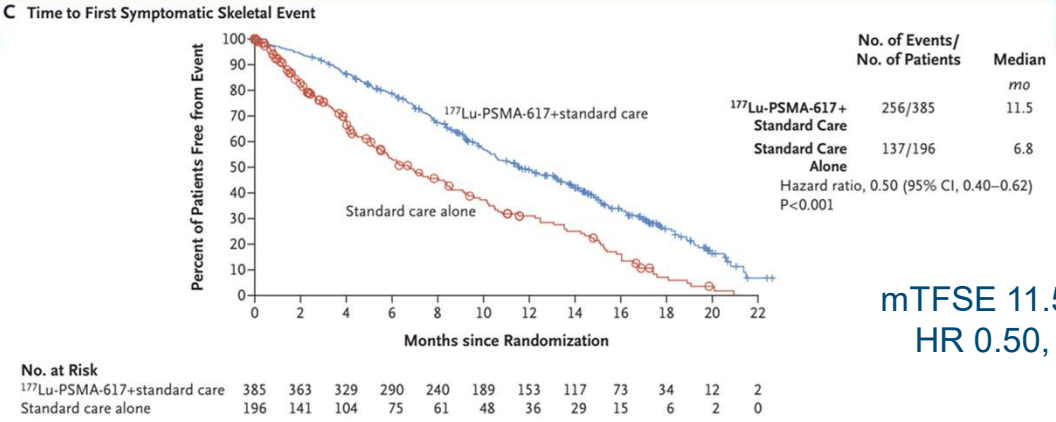


mIPFS 8.7 vs 3.4 mo.
HR 0.40, p<0.001



mOS 15.3 vs 11.3 mo.
HR 0.62, p<0.001

10



mTFSE 11.5 vs 6.8mo
HR 0.50, p<0.001

PSA response (50+% decrease) - 46% vs 7.1%

RECIST 1.1 ORR - 51% vs 3%

AllinaHealth

11

TheraP[4]

Key Eligibility
- mCRPC
- Prior treatment:
  - Docetaxel
- Eligible for cabazitaxel
- Rising PSA (PSA >20ng/dL)
- ECOG 0-2
- Adequate organ function
- PSMA-PET+*

Cabazitaxel

20mg/m2 IV q3wks, up to 10 cycles

177Lu-PSMA617

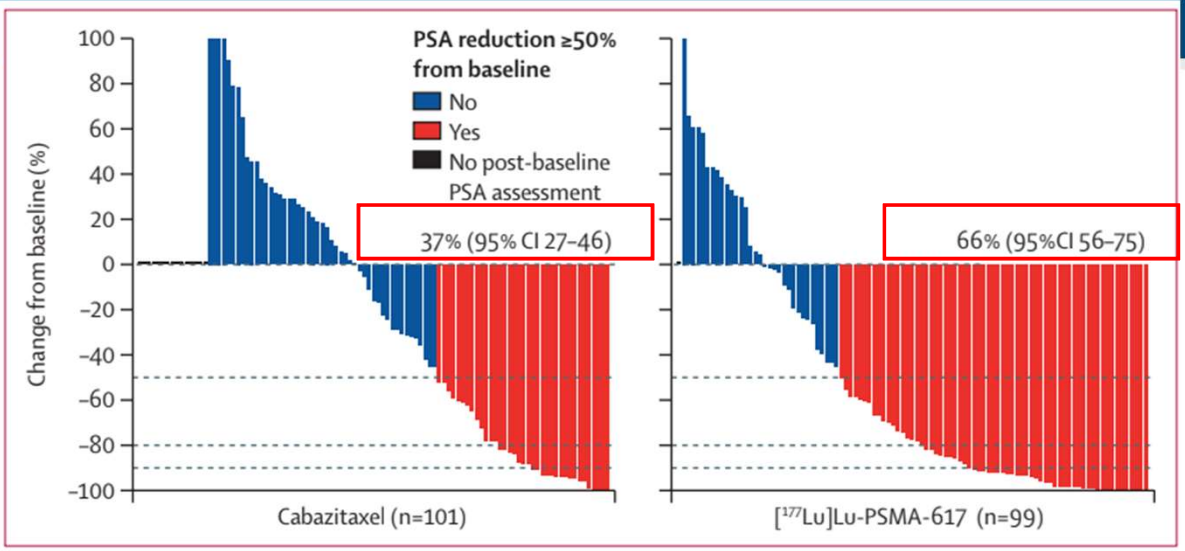
Q6wks x 6 cycles, starting at 8.5 GBq and decreasing 0.5GBq each cycle

PSA response rate

*PSMA SUV max >20
All measurable sites SUV max >10
No FDG+/PSMA- sites

AllinaHealth

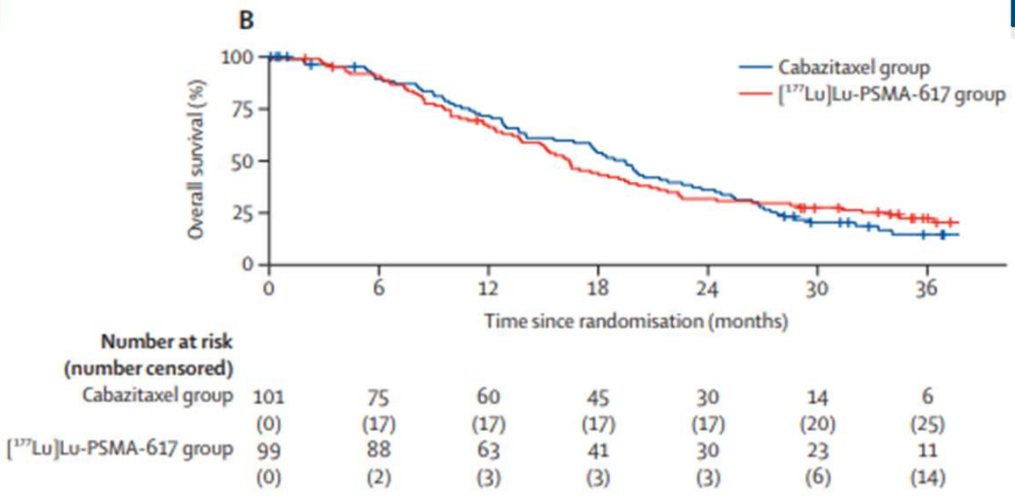
12



RECIST v1.1 ORR 49% vs 24%

AllinaHealth

13



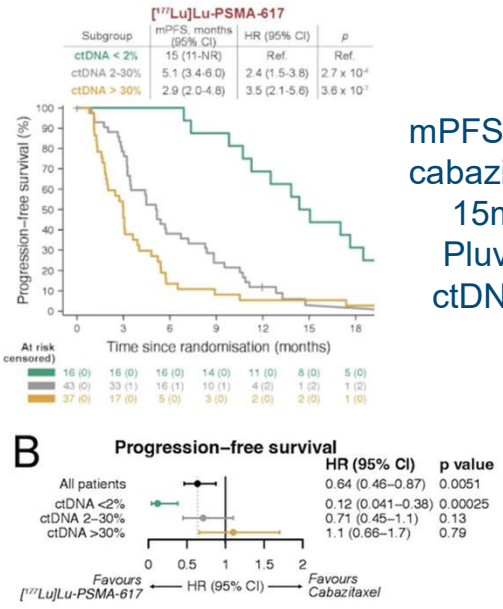
Number at risk (number censored)							
Cabazitaxel group	101	75	60	45	30	14	6
	(0)	(17)	(17)	(17)	(17)	(20)	(25)
[177Lu]Lu-PSMA-617 group	99	88	63	41	30	23	11
	(0)	(2)	(3)	(3)	(3)	(6)	(14)

mOS 19.1 vs 19.6 mo.
p=0.77

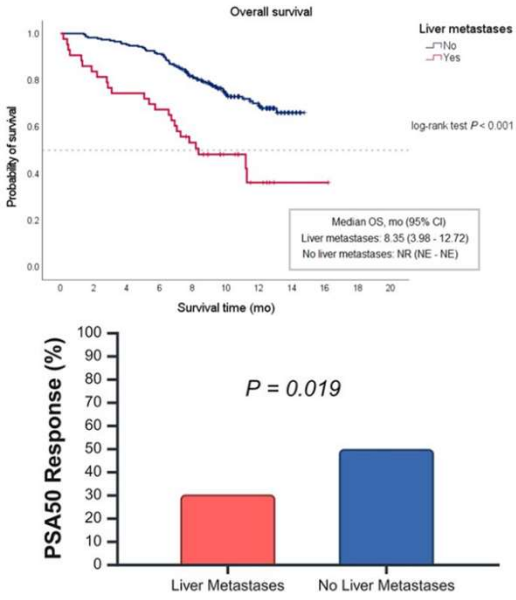
AllinaHealth

14

Predictors of Pluvicto response - ctDNA[5] and liver mets[6]



mPFS 6mo w/ cabazitaxel vs 15mo w/ Pluvicto if ctDNA<2%



15

Pluvicto now FDA approved before chemotherapy[7]

FDA expands Pluvicto's metastatic castration-resistant prostate cancer indication

On March 28, 2025, the Food and Drug Administration expanded the indication for lutetium Lu 177 vipivotide tetraxetan (Pluvicto, Novartis Pharmaceuticals Corporation) to include adults with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor pathway inhibitor (ARPI) therapy and are considered appropriate to delay taxane-based chemotherapy.

Allina

16

UPDATE #1 - PSMAfore[8] (Pluvicto before chemo in mHSPC)

Key Eligibility
- Progressive mCRPC
- Prior treatment:
  - Progressed once on prior ARPI
  - Taxane naive ([neo]adjuvant >12mo prior permitted)
- ECOG 0-1
- Not a candidate for PARPi
- PSMA-PET+

Switch ARPI

Abiraterone or enzalutamide

177Lu-PSMA617

Q6wks x 6 cycles, 7.4 GBq +/-10% each cycle

rPFS

Crossover was allowed upon progression

17

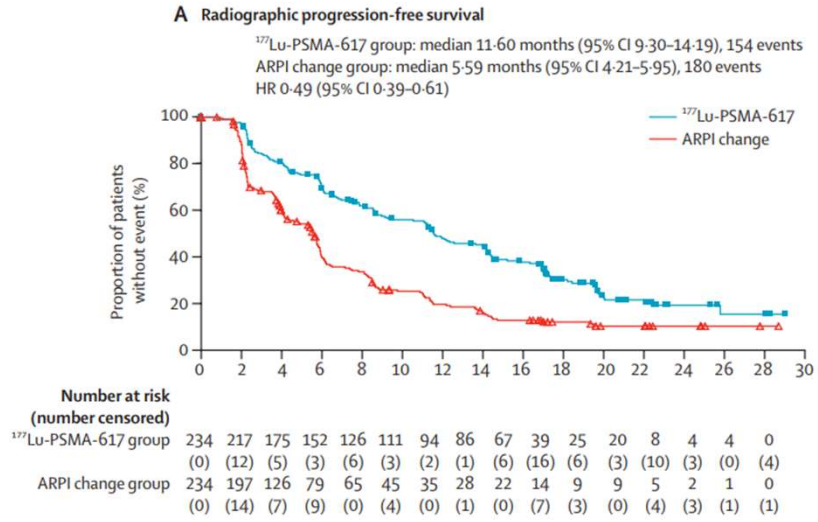
Patient characteristics

	^{177}Lu-PSMA-617 (n = 234)	ARPI change (n = 234)
Age, median (range), years	71 (43–94)	72 (53–91)
White, n (%)	211 (90.2)	214 (91.5)
ECOG performance status, n (%)		
0	146 (62.4)	115 (49.1)
1	86 (36.8)	114 (48.7)
Gleason score 8–10, n (%)	136 (58.1)	107 (45.7)
PSA, median (range), µg/L	18.4 (0–1197)	14.9 (0–4224)
Haemoglobin, median (range), g/L	128.0 (88–155)	129.0 (88–156)
Alkaline phosphatase, median (range), IU/L	100.0 (36–1727)	103.5 (28–1319)
Site of disease, n (%)		
Liver	13 (5.6)	7 (3.0)
Lymph node	76 (32.5)	74 (31.6)
Bone	205 (87.6)	203 (86.8)
Prior ARPI, n (%)		
Abiraterone	119 (50.9)	130 (55.6)
Enzalutamide	94 (40.2)	84 (35.9)
Other	21 (9.0)	20 (8.5)

AllinaHealth

18

Primary endpoint - rPFS

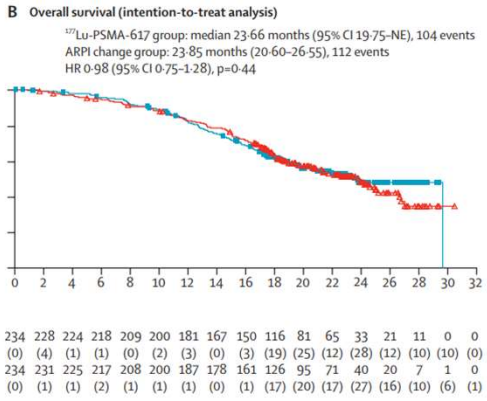


mrPFS 11.6 vs 5.6mo
HR 0.49

AllinaHealth

19

Secondary endpoints



mOS ~24mo in both groups
HR 0.98, p=0.44
*57% of patients in ARPI group crossed over

- PSA response rate (50%+ decrease)
  - Pluvicto/Switch ARPI **51%/17%**
- Recist v1.1 ORR
  - Pluvicto/Switch ARPI **50%/15%**
- Time to first skeletal related event
  - Pluvicto/Switch ARPI **NR/18mo - small # of events**
- Time to second PFS
  - Pluvicto/Switch ARPI **18mo/15.3mo - not significant**

AllinaHealth

20

Quality of life and safety

- Time to worsening of FACT-P score
  - Pluvicto/switch ARPI
    7.5/4.3mo
- Time to worsening of BPI-SF pain intensity score
  - Pluvicto/switch ARPI
    5.0/3.7mo

	^{177}Lu-PSMA-617 group (n=227)		ARPI change group (n=232)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any	224 (99%)	81 (36%)*	226 (97%)	112 (48%)*
Occurring in >10% of patients				
Dry mouth	131 (58%)†	2 (1%)	6 (3%)†	0
Asthenia	74 (33%)	2 (1%)	67 (29%)	8 (3%)
Nausea	72 (32%)	0	27 (12%)	1 (<1%)
Anaemia	61 (27%)	14 (6%)	44 (19%)	16 (7%)
Fatigue	53 (23%)	1 (<1%)	59 (25%)	4 (2%)
Constipation	50 (22%)	1 (<1%)	33 (14%)	0
Decreased appetite	49 (22%)	0	43 (19%)	1 (<1%)
Arthralgia	45 (20%)	0	54 (23%)	1 (<1%)

AE's leading to Pluvicto interruption and discontinuation 12% and 6% respectively

FACT = Functional Assessment of Cancer Therapy - Prostate
BPI-SF = Brief Pain Inventory - Short Form

Allina Health

21

Patient case #1

A 72 year old man was diagnosed with 3 years ago with low volume, de novo metastatic prostate cancer. Imaging at that time showed 5 osseous lesions confined to the spine and ribs. He was treated with ADT + abiraterone, which he continues. Recently, his PSA started to rise. Testosterone is adequately suppressed. Repeat imaging shows new enlarged lymph nodes, new osseous disease, and a solitary lung met. He has a history of seizure disorder on anti-epileptics and DM type 2 with peripheral neuropathy on duloxetine. Germline and somatic testing are negative. In addition to continuation of ADT, what treatment would you recommend next?

1) Enzalutamide
2) Docetaxel
3) Lutetium Lu 177 vipivotide tetraxetan (Pluvicto)
4) Olaparib
5) Radium 223

Allina Health

22

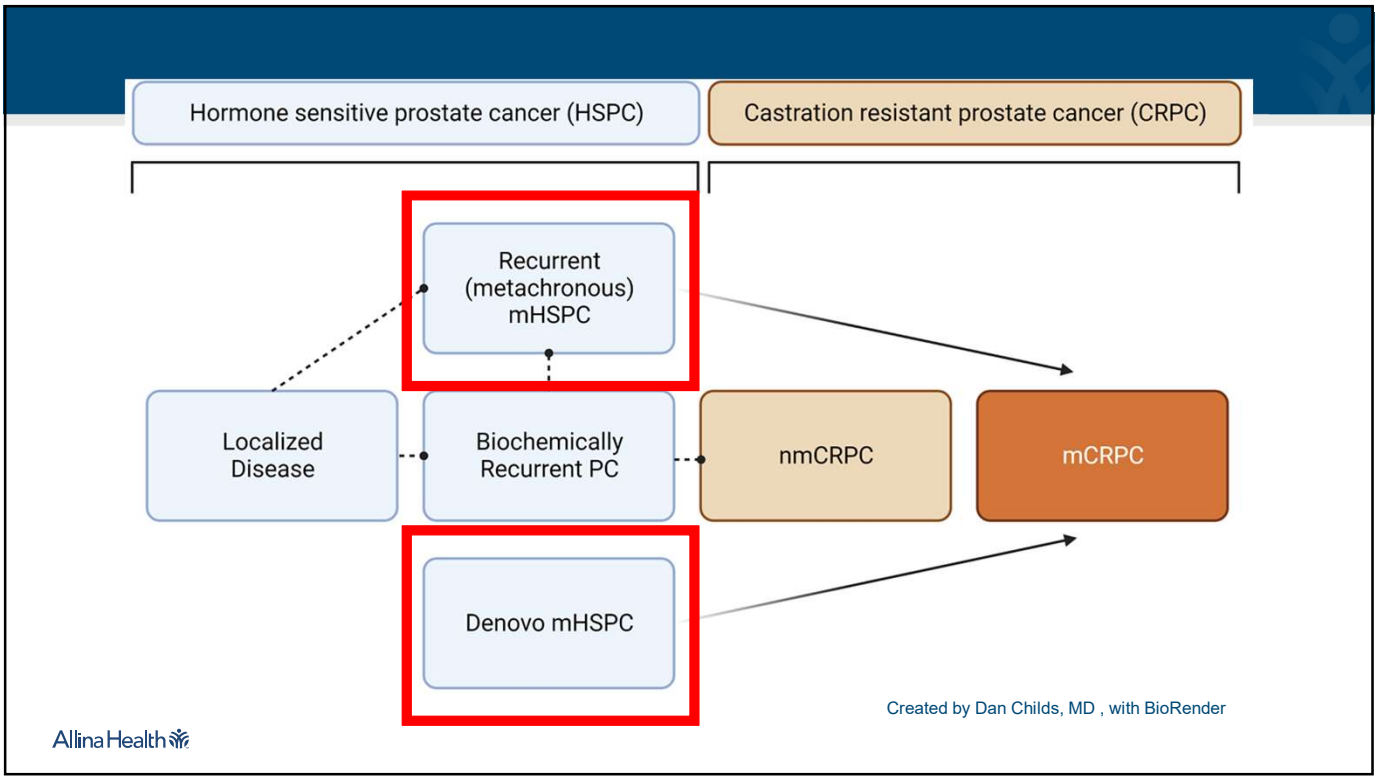
UPDATE #1 SUMMARY

Pluvicto is FDA approved in metastatic castrate resistant prostate cancer for patients who have received an ARPI, before or after chemotherapy.

Pluvicto is well tolerated and improves PSA response rates, imaging response rates, and radiographic PFS vs switch ARPI and chemotherapy, although an overall survival benefit over chemotherapy has not been demonstrated.

Allina Health

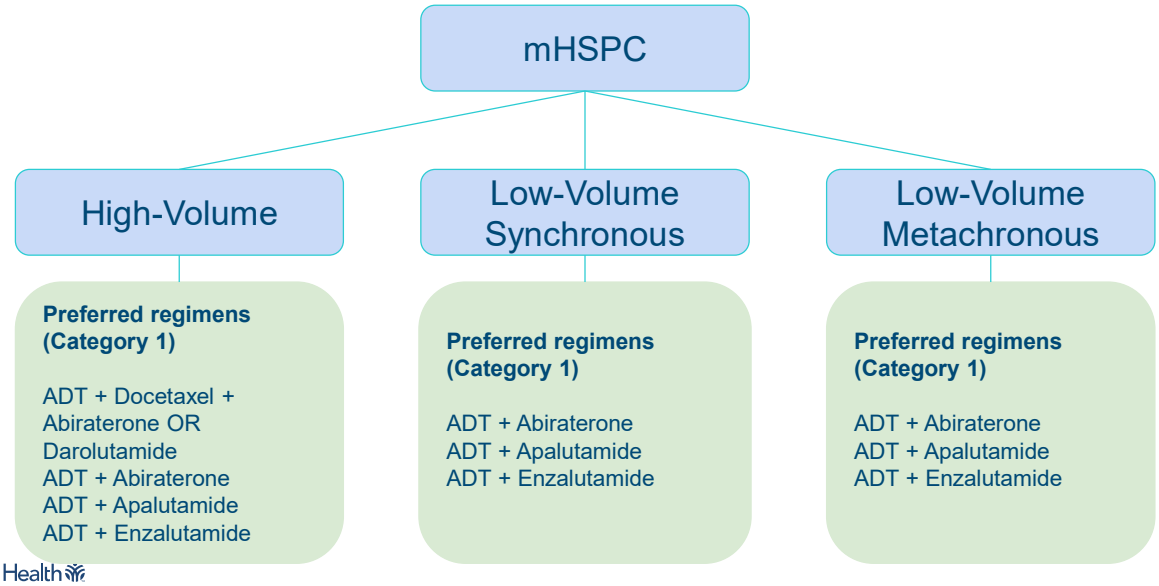
23



Allina Health

24

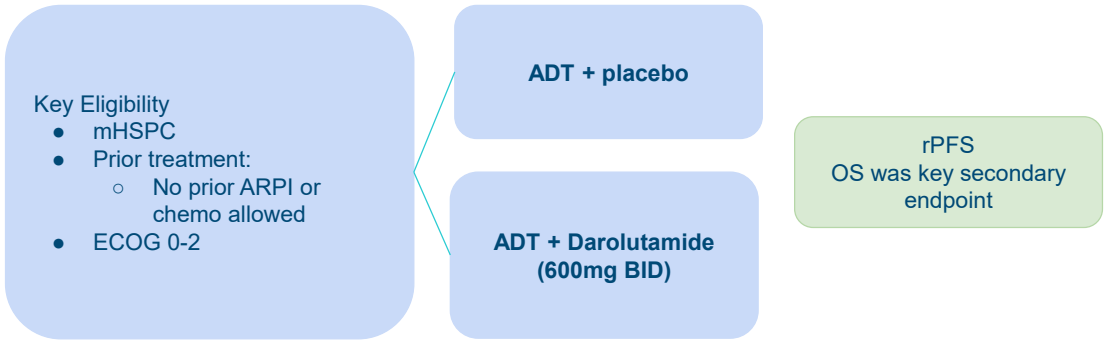
Summary of mHSPC management



AllinaHealth

25

UPDATE #2 - ARANOTE[9] (NEW ARPI DOUBLET FOR mHSPC)



* ADT without ARPI is not a standard of care in the US

AllinaHealth

26