

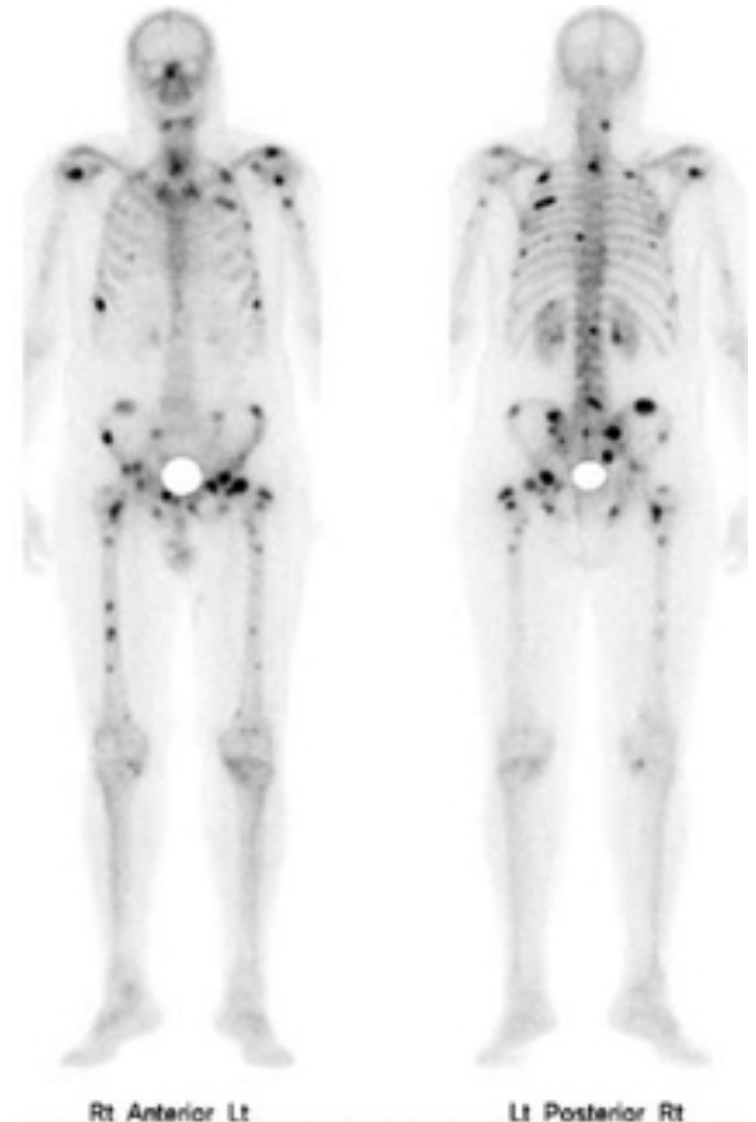
The management of advanced prostate cancer

Andre Westenberg
Swamp Urology
Tauranga



Advanced prostate cancer

- Cancer has metastasized
- Diagnosis made on PSA/scans
- ?oligometastatic disease worth treating with curative intent



Advanced prostate cancer

- Some doesn't need to be treated
- ADT works well
 - options



When to start ADT

- Symptomatic metastatic disease
- PSA DT
- Early vs delayed
- Intermittant
- ?Asymptomatic metastatic disease
- Median survival 8 years

PSA rise after 1st line AAs

- Adrenal testosterone production
- Add 2nd line agents
- Withdraw 2nd line agents
- PSA continues to rise

Standard ADT will eventually fail

- CaP heterogenous
- Population of cells
 - Make own T
 - Overexpress AR
 - Wild type AR stimulated by nonandrogens

HRCaP

- 2-3 consecutive rises in PSA
- Or clinical progression (some HG Ca does not make PSA)
- Median survival historically 18/12 (now 30/12)
- Time to symptoms once $\text{PSA} > 4$ - 8/12
- Survival once symptomatic - $< 12/12$

Management of Advanced CaP

- 1. Cancer management
- 2. Symptom management
- 3. ADT SE management
- 4. End of life care



Symptom control

- Pain - opiates, RTX
- Bleeding - surgery, tranexamic acid, ?RTX
- Fractures - stabilise
- Retention - surgery, SPC
- Ureteric obstruction - stents vs PCN
- Spinal cord compression - steroids, RTX

ADT SE

- Hot flushes
- Type 2 DM
- CVD
- Osteoporosis
 - ? Vit D + Ca supplements - probably not (no effect on bone mineralisation, ?incr more risky Ca)
 - Exercise - yes.
 - Zometa - debatable(? Denosumab better), NB dental health

EXERCISE IS IMPORTANT

End of Life Care

- Hospice - early referral
- Pain
- Edema - massage, stockings, ?RTX
- Bowels - regular laxatives
- Appetite - steroids
- Psychological

Cancer control

- Taxane chemotherapy
 - Toxic, 2/12 incr OS
 - (CHAARTED)
- Others
 - mitoxanthrone
 - Ketoconazole
 - Stuff not readily available in NZ
(enzalutamide, sipuluecel T, suramin, TKIs)

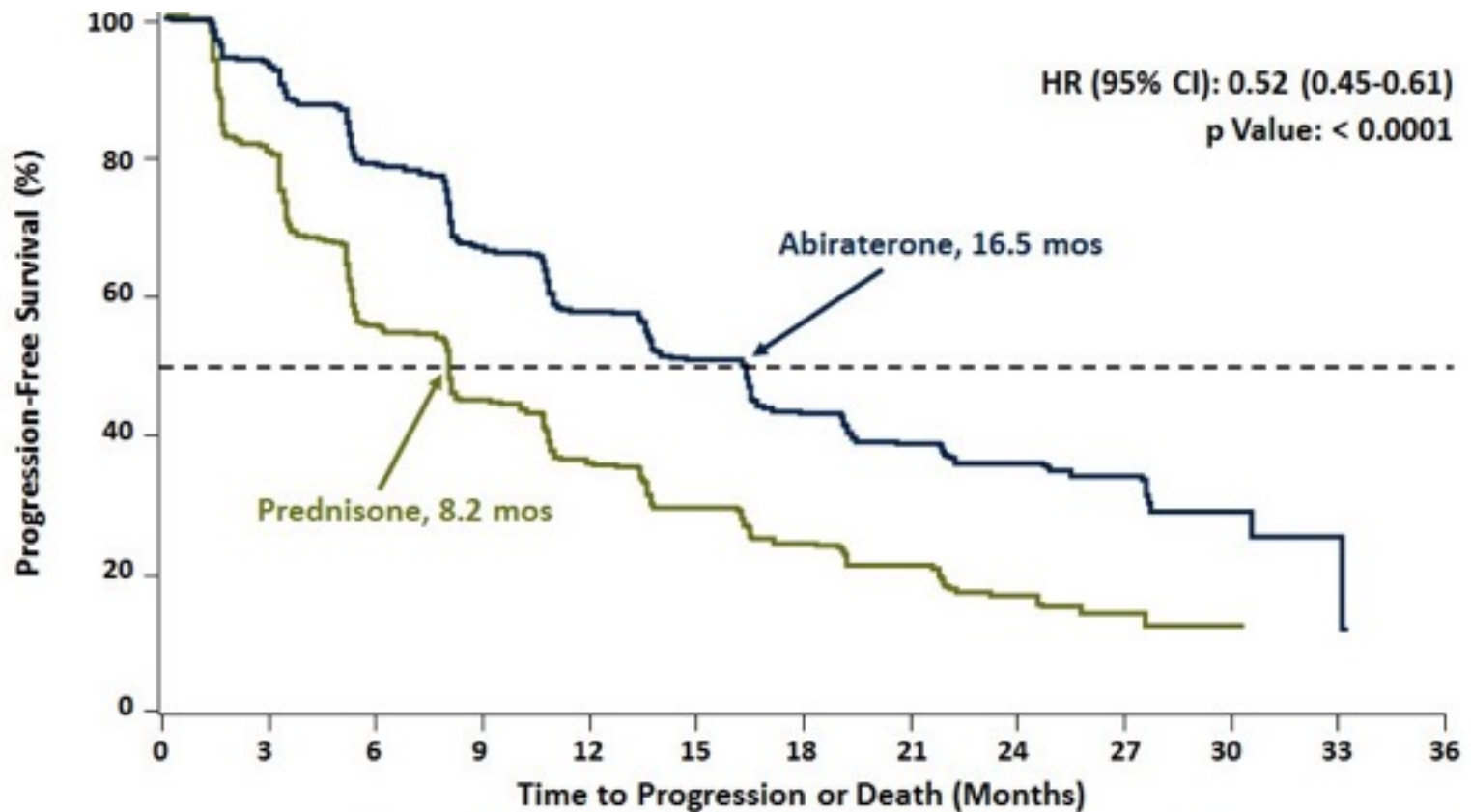
COU-AA-301 RCT Lancet 2012



Abiraterone - Zytiga

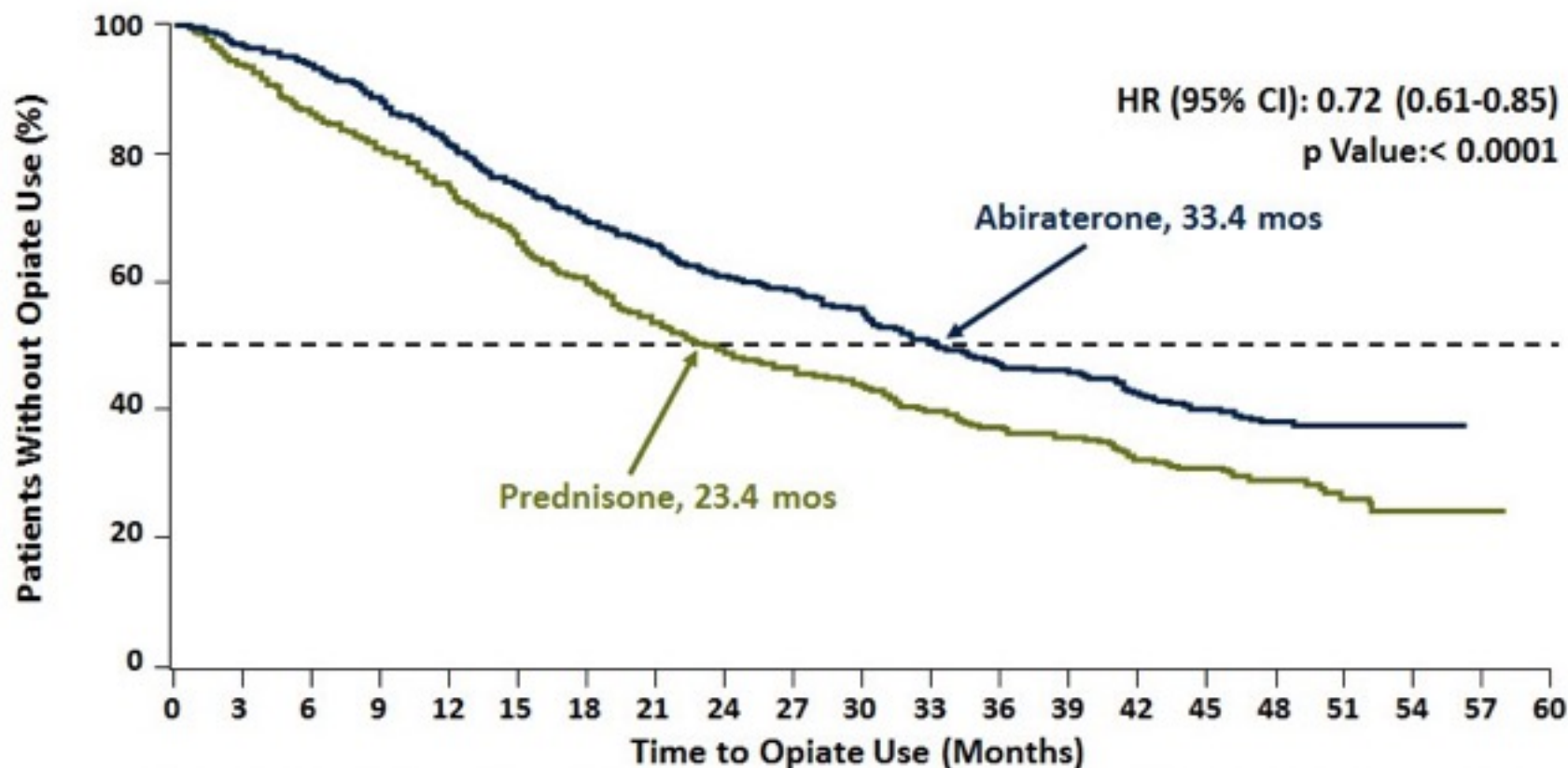
- Blocks CYP 17 in androgen synthesis pathway
 - Targets all testosterone production, including in the tumour cell itself
- Build up of precursor mineralocorticoids
- Corticosteroid insufficiency
 - take prednisone (which also decr ACTH)

Time to radiographic progression



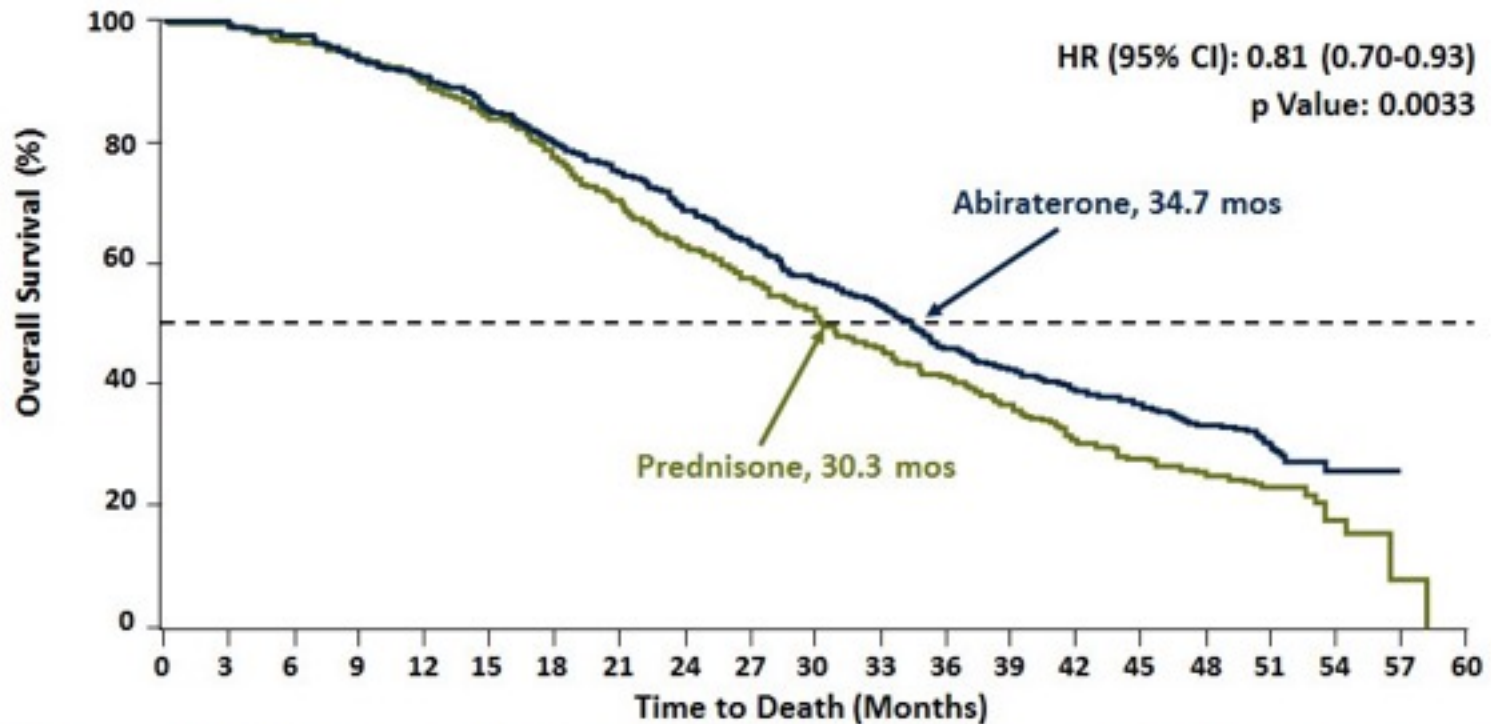
Abiraterone	546	485	389	311	240	195	157	131	117	66	20	4	0
Prednisone	542	406	244	176	133	99	78	62	45	20	7	0	0

Time to opiate use



Abiraterone	546	519	495	454	407	364	328	297	263	244	219	192	169	162	143	128	74	35	9	0	0
Prednisone	542	500	442	406	365	317	273	237	208	186	168	141	121	108	97	85	56	25	6	1	0

Overall survival



Abiraterone	546	538	525	504	483	453	422	394	359	330	296	273	235	218	202	189	118	59	15	0	0
Prednisone	542	534	509	493	466	438	401	363	322	292	261	227	201	176	148	132	84	42	10	1	0

Probably better - 44% of prednisone group had abiraterone

Monitoring required

- Mineralocorticoid excess
 - Incr BP
 - Decr K⁺
 - Fluid retention
- Hepatotoxicity

Bay U monitoring program

- Specialist nurse led
 - Check eligibility
 - Medical history
 - Physical assessment
 - Ongoing monitoring and patient point of contact
- Liaison with GP, hospice, medical and radiation oncologists

Initiation

- Make sure patient is eligible:
 - HRCaP after 2nd line AA
 - have mets
 - Performance score 0-2
 - Before or after taxanes (not at same time)

Subsequent monitoring

week	2	4	6	8	10	12
bloods	LFT,K	LFT,K	LFT,K,PSA	LFT,K	LFT,K	LFT,K,PSA
nurse	BP		BP		BP	
urologist			see			

Management of side effects

- If BP incr mildly - GP alerted to manage, continue zytiga
- If BP incr++ - stop zytiga till BP stable
- If ALT/AST inc 5x ULN, (BR 3x ULN) - stop, wait, reintroduce
- If LFTs 20x ULN -stop permanently

Failure

- Urologist and nurse discuss and liaise with colleagues
 - Taxane chemotherapy
 - Radiotherapy
 - Clinical trials
 - hospice

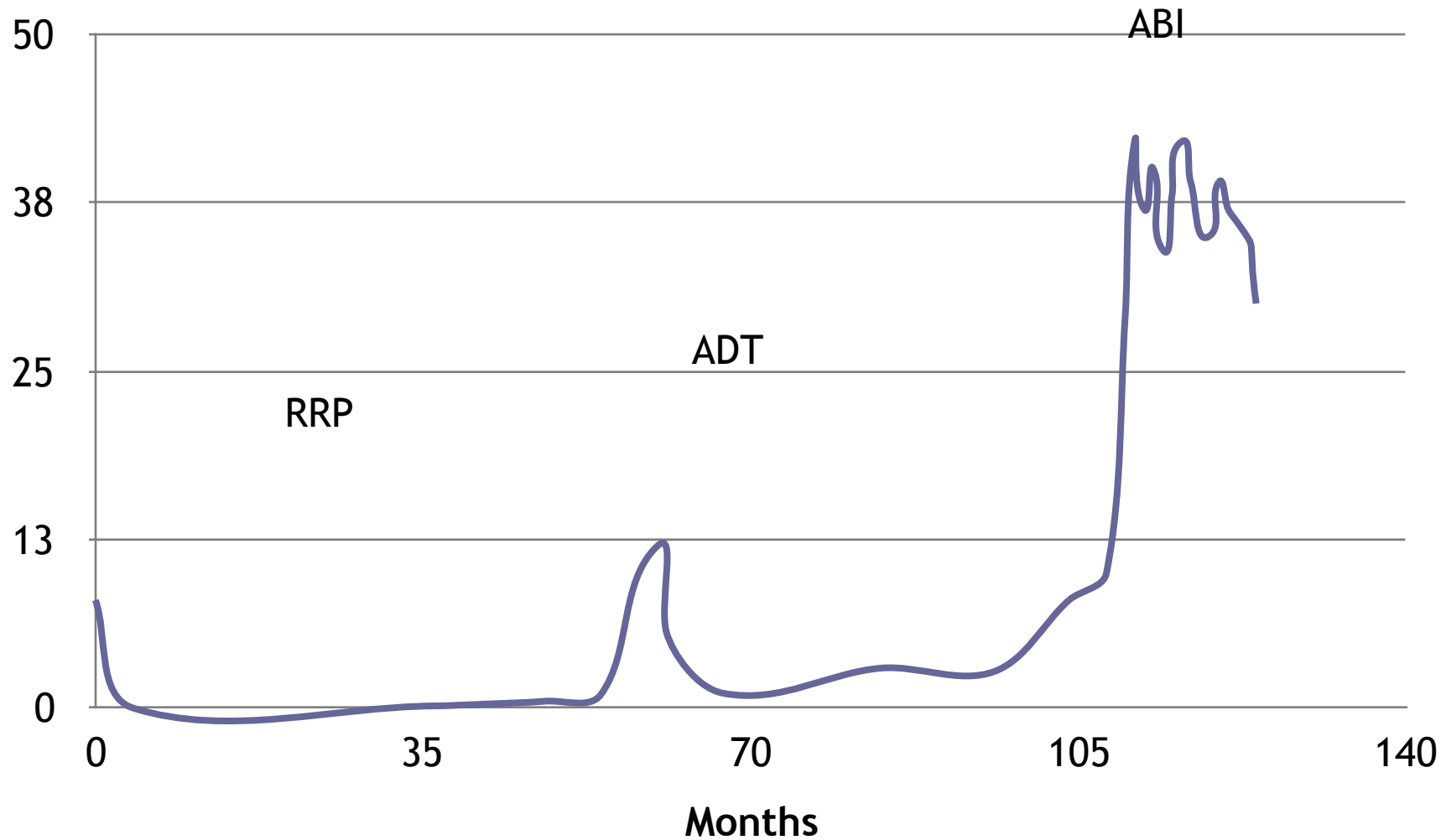
All patients to date

- 18 in total since October 2013
- 5 deceased
- All have responded to some degree
- One patient stopped due to “feeling of unwellness” (had good response, PSA stable 5 months after stopping), one stopped due to CHF
- No significant other toxicity

Case study

- BR 56y. 3+3, PSA 8, cT2
- RRP 2005 - 50% 3+4, T3b (bilat SV), nsm, Nx
- Adjuvant RTx discussed and declined
- Good functional result, spont erections at 9 mo
- Unwilling to attend followup

BR 56 at Dx



Summary - Abiraterone

- Zytiga is a valuable addition to the HRCaP armamentarium
- Close monitoring required
- Nurse led MDT approach
- Our experience to date - good PSA response, well tolerated



Take home messages

- Advanced CaP best managed in multidisciplinary setting (GP, urologist, medical and radiation oncologists, palliative care)
- Care best coordinated by GP
- Cancer control only one aspect of care
 - Symptom palliation, psychological support, ADT SE
- Early referral to hospice

When to refer (CaP px)

- Any incr in PSA after definitive therapy (surgery or radiotherapy)
- PSA DT < 3 mo
- PSA increase after withdrawal of 2nd line ADT
 - ?candidate for zytiga
- Locally invasive disease
 - Retention, bleeding, renal compromise
- Symptomatic metastatic disease
 - Bone pain, neurology



CHAARTED

- 2014
- Hormone sensitive metastatic disease
- ADT vs ADT +TAX
- OS 44 vs 57.6mo
- Better in high volume metastatic disease