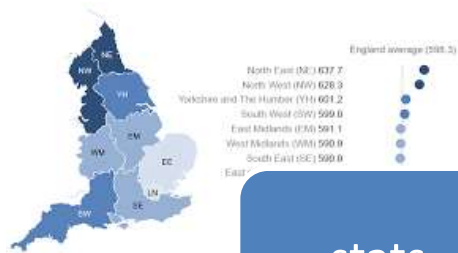


# Management of Metastatic Prostate Cancer

Dr Joe Davies

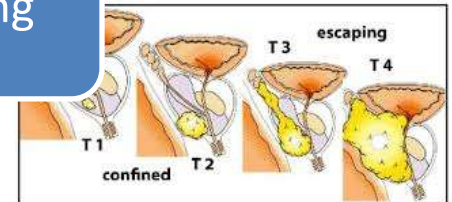
Consultant Clinical Oncologist



stats

Future

staging



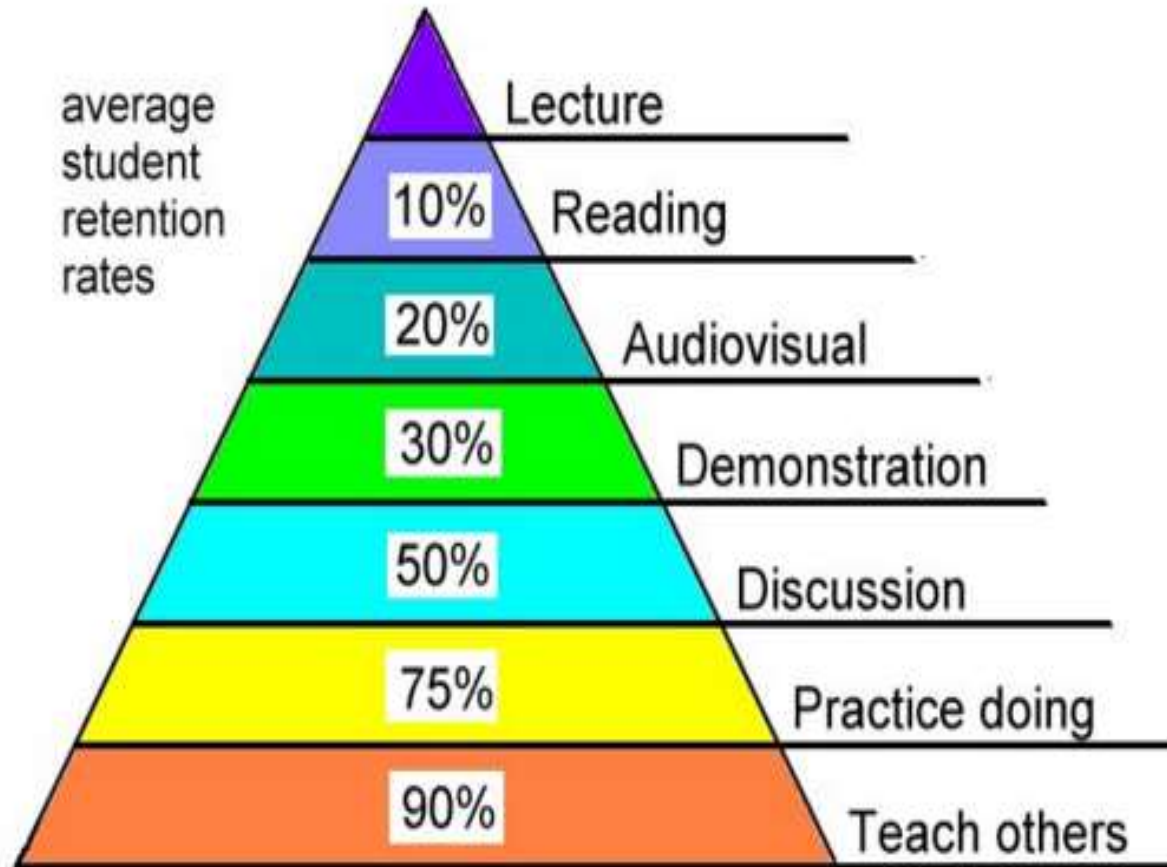
Case studies

treatments



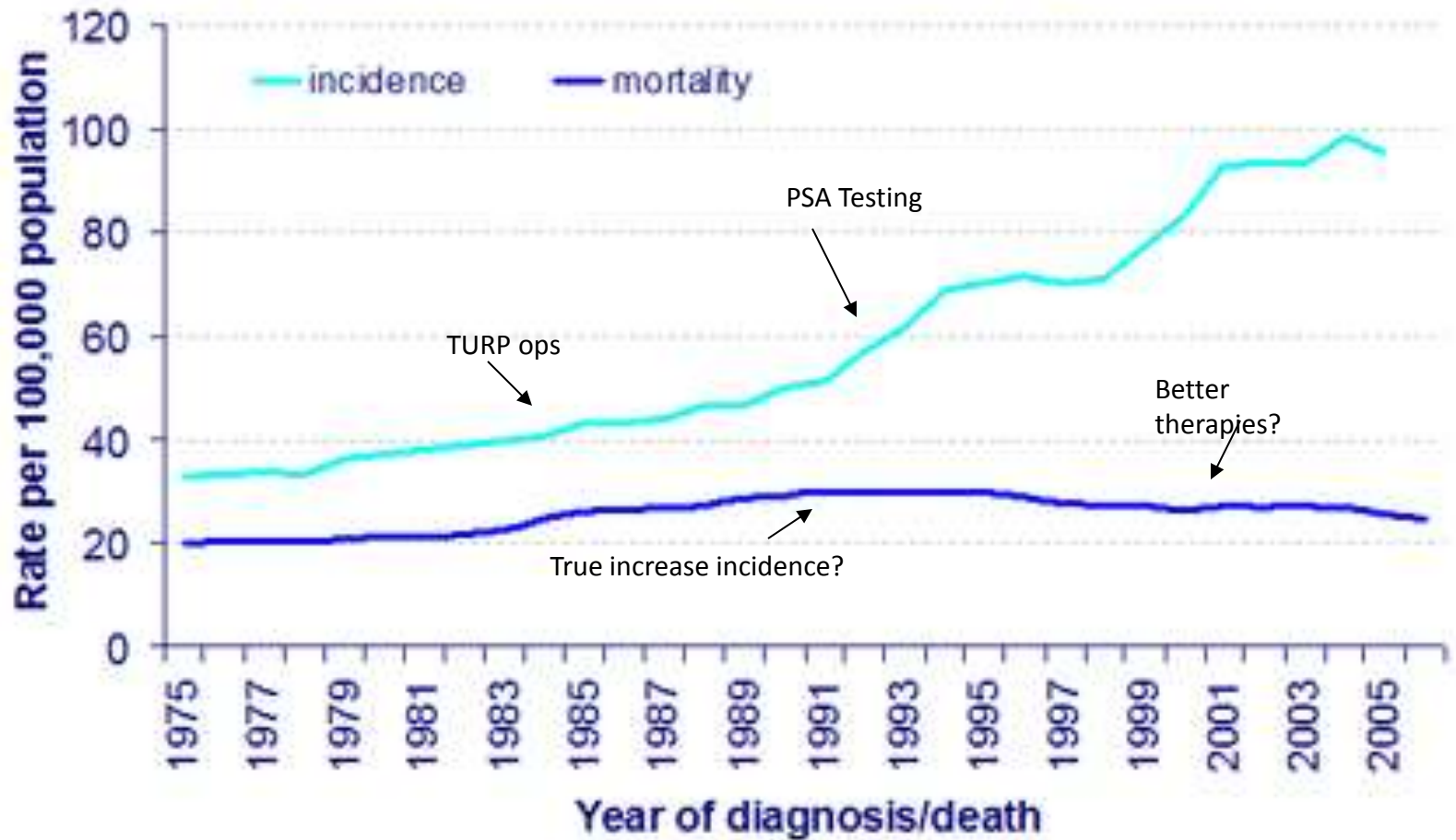
---

## Learning Pyramid



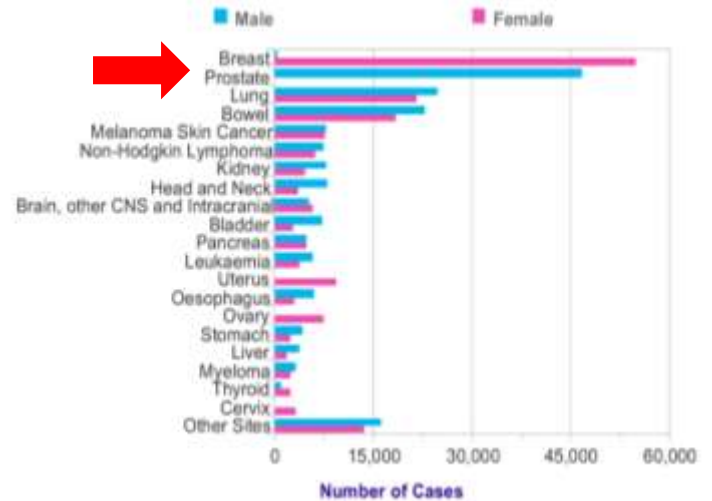
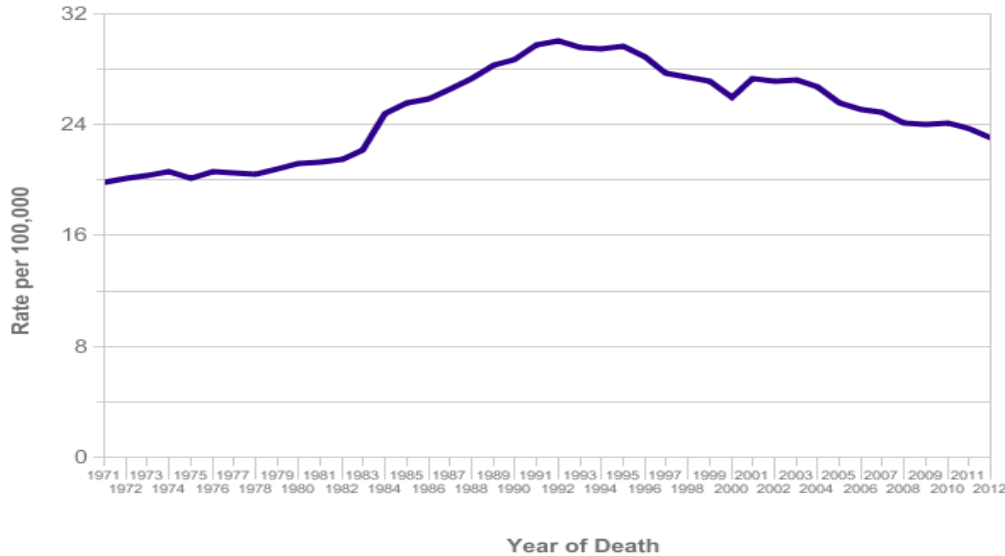
Source: National Training Laboratories, Bethel, Maine

**Figure 1.4: Age standardised (European) incidence and mortality rates, prostate cancer, males, GB, 1975-2006**

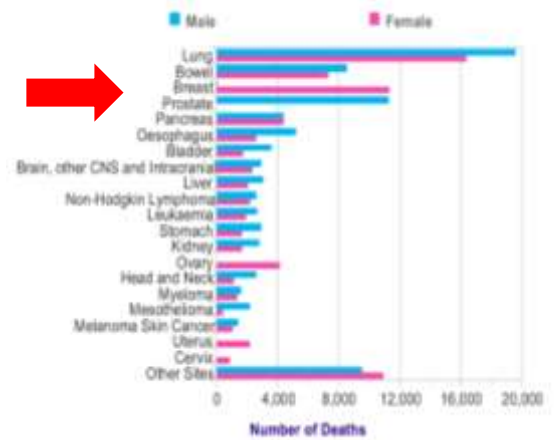


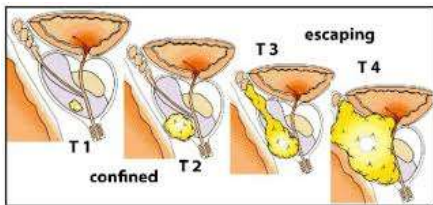
# Prostate Cancer (C61): 1971-2012

## European Age-Standardised Mortality Rates per 100,000 Population, Males, UK



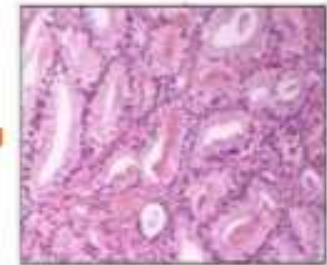
## Prostate cancer incidence statistics





# Prostate Ca : Gleason Grading:

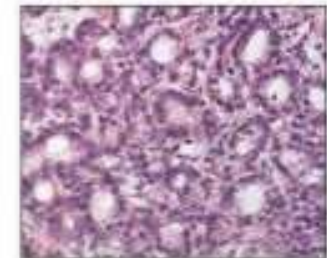
GRADE	DESCRIPTION
1	Small, uniform cells, tightly packed
2	Varied cell sizes and shapes, loosely packed
3	Increased cell size and shape irregularity, less distinction between cells
4	Large, irregular, fused cells
5	Irregular, fused cells that have invaded surrounding connective tissue cells



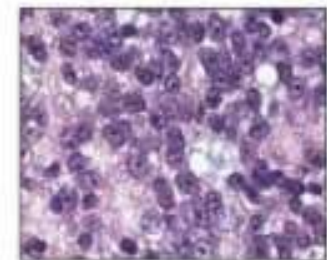
Grade 2



Grade 3



Grade 4



Grade 5



# Prostate ca staging (MRI prostate + pelvis and bone scan)

Localised prostate ca

Metastatic prostate ca

Low  
<10  
G6  
T1-2a

Inter.  
10-20  
G7  
T2b-c

High  
>20  
G8+  
T3a/b-T4

PSA>80  
Bone  
Nodal  
Visceral

Radical Rx

Hormone Rx

# Prostate ca staging (MRI prostate + pelvis and bone scan)

Localised prostate ca

Metastatic prostate ca

Low

<10

G6

T1-2a

Inter.

10-20

G7

T2b-c

High

>20

G8+

T3/4

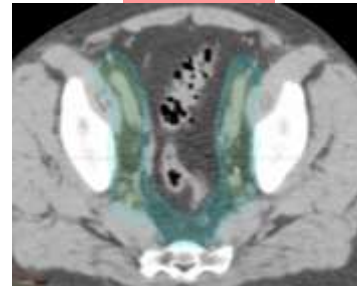
V High

2/3 High

+

PSA>40

N1



Metastatic

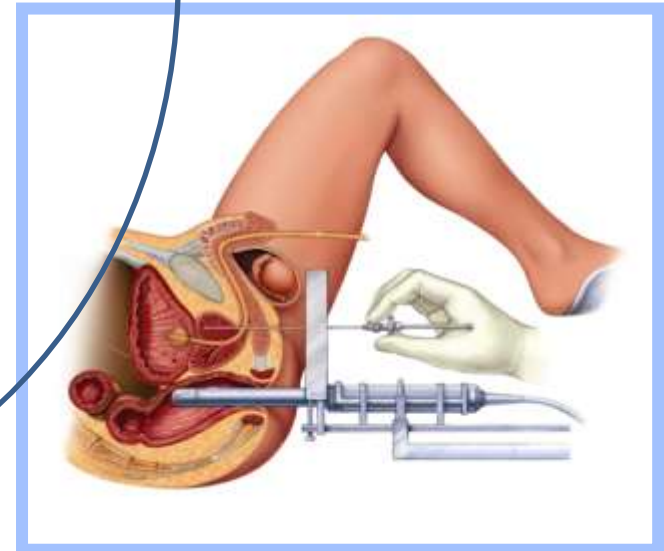
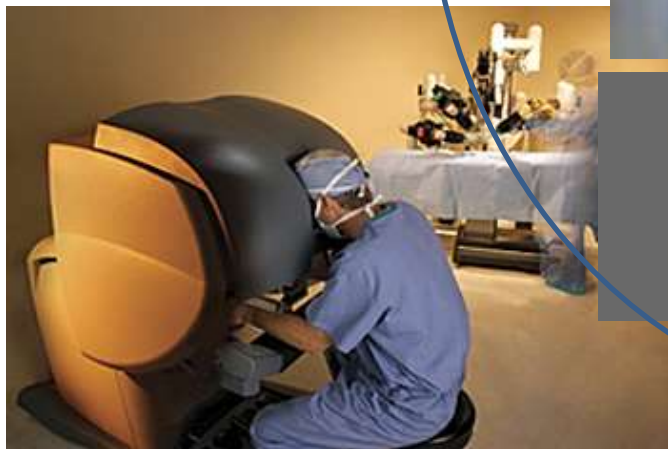
Bone

N abdo/chest

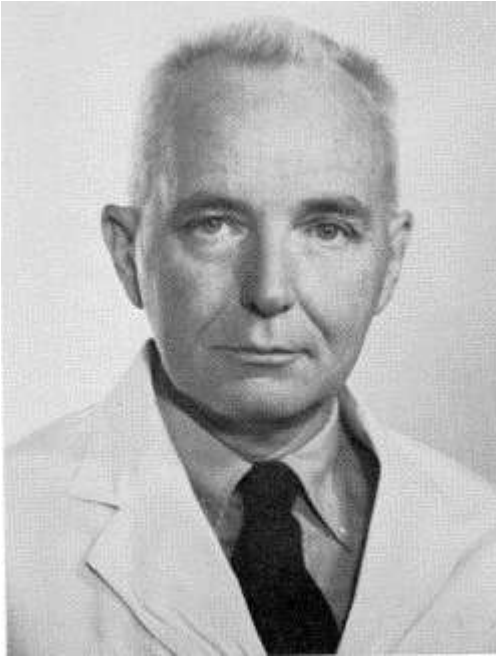
Visceral



# Treatment options



# Systemic therapies in prostate cancer

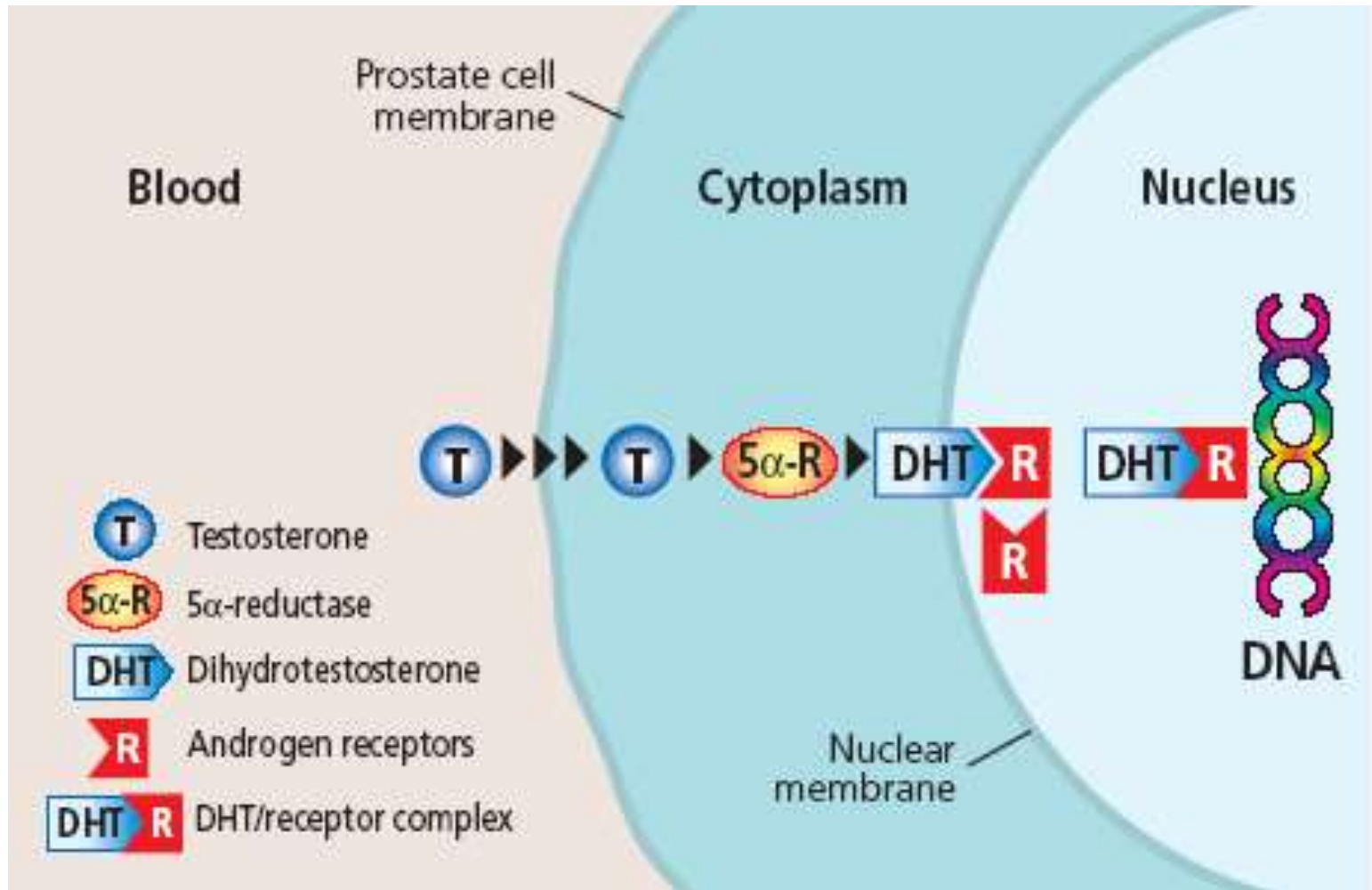


>90% PSA response  
>80% clinical response  
Response durations very variable.



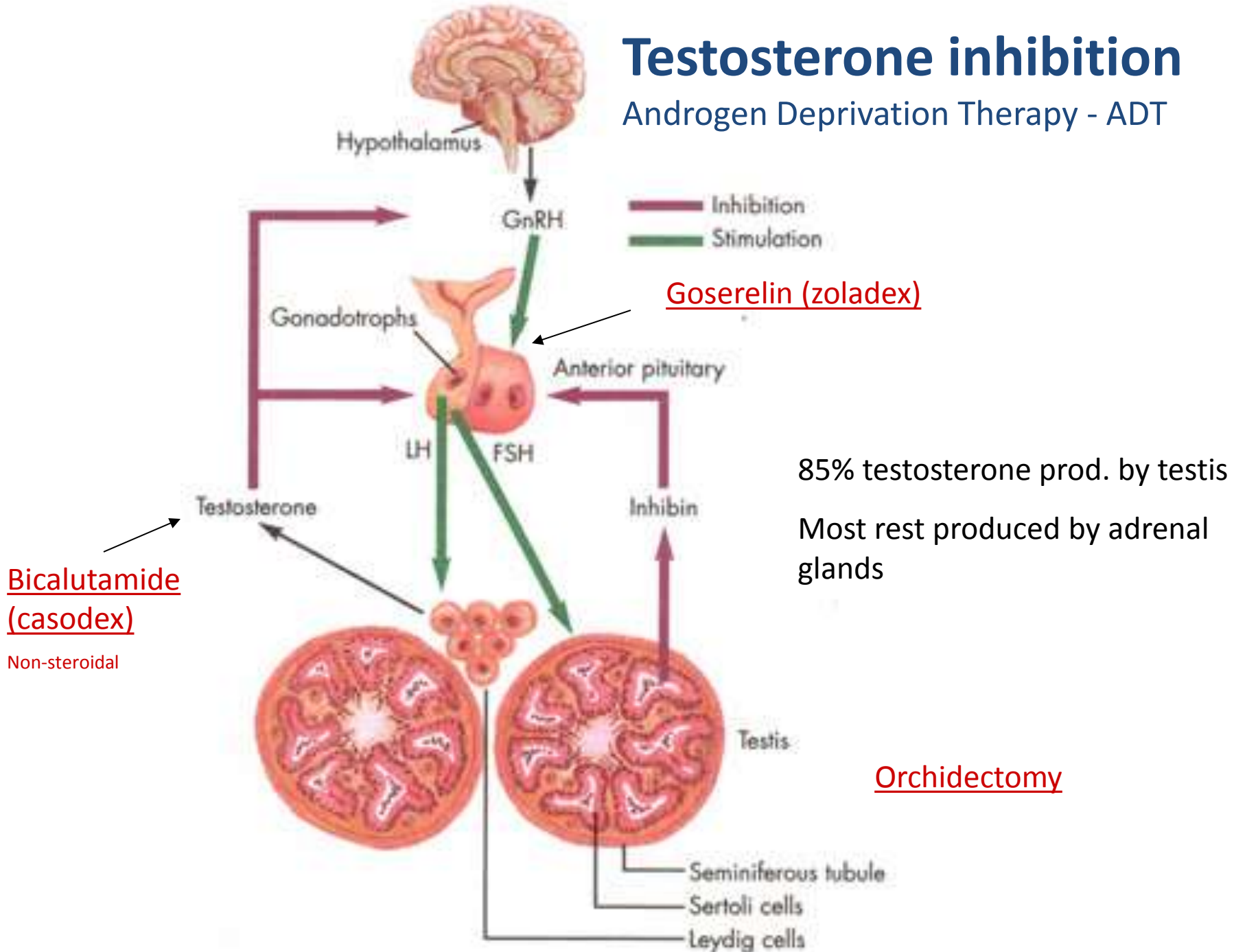
Chemo – traditionally poor results  
Lymphoma vs Colon vs lung vs prostate ca

# Testosterone and the prostate cell



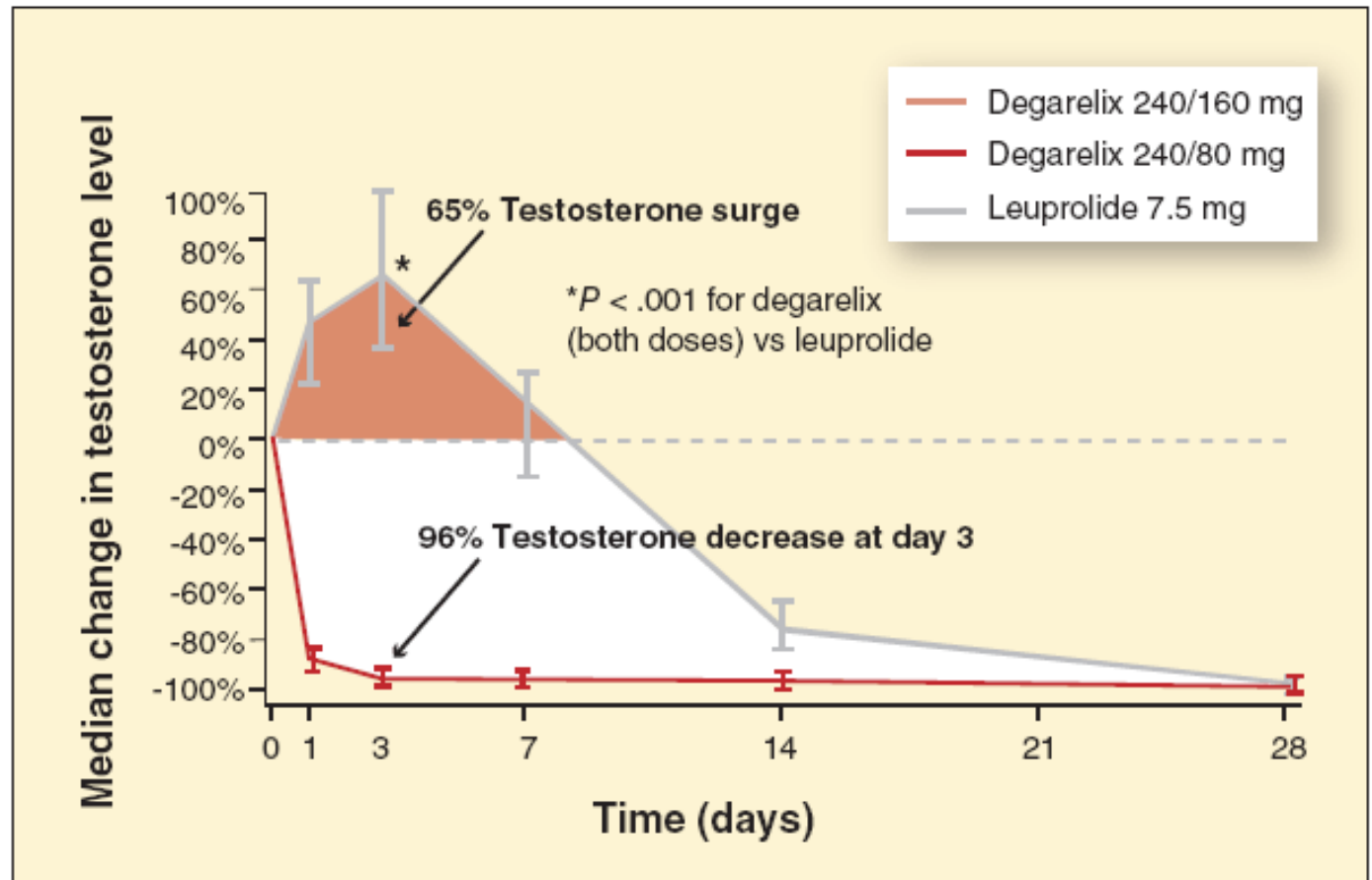
# Testosterone inhibition

Androgen Deprivation Therapy - ADT



2. GnRH blocker – Degarelix

Genitourinary Cancers Symposium 2011

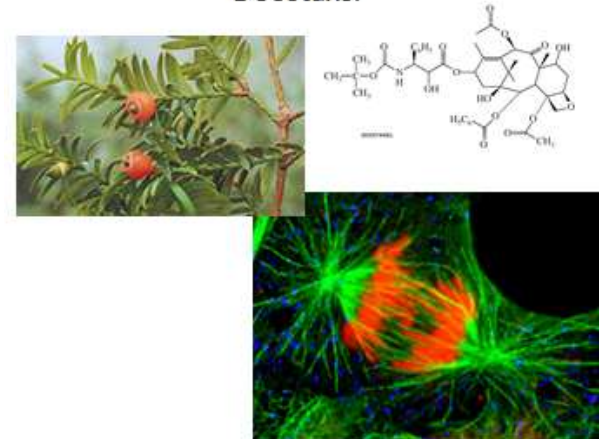




# 2005 treatment metastatic prostate cancer

- LHRH analogue
- Add in bicalutamide (total androgen blockade)
- Stop bicalutamide trial –
  - Steroid i.e. dexamethasone
  - Oestrogen i.e. diethylstilboesterol
  - ?? Mitoxantrone – no OS benefit
- Palliative radiotherapy or strontium

Docetaxel



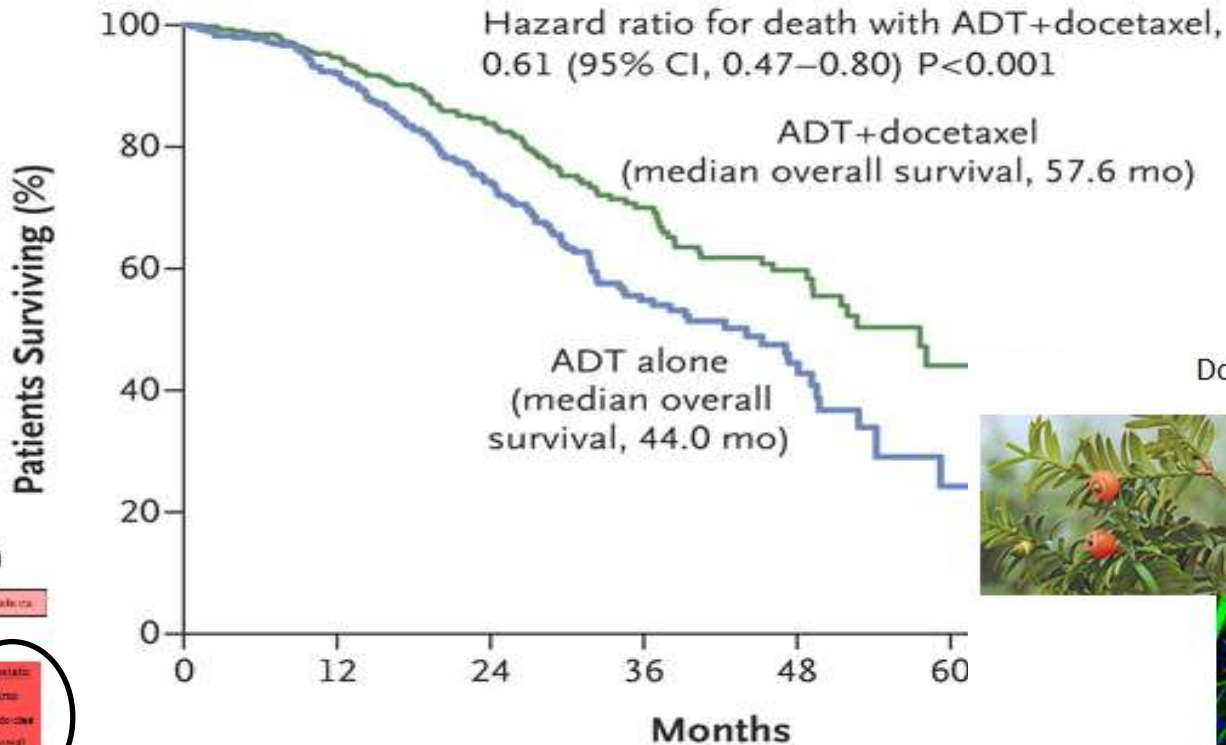
# Treatment for newly diagnosed metastatic prostate cancer M1+

73yr old G4+5 PSA 113 M1b  
Hypertension PS 0

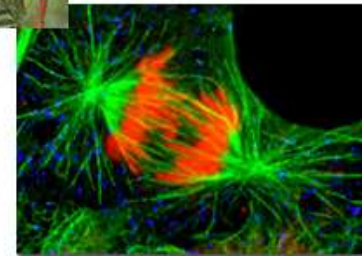
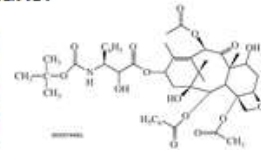
69 G4+3 PSA 89 M1b  
Mod – COPD, IHD, AF, NIDDM PS 2

- LHRH or LHRH + Docetaxel
- LHRH alone

A All Patients



Docetaxel



Prostate ca staging 2016  
(MRI prostate + pelvis and bone scan)

Localised prostate ca.				Metastatic prostate ca.	
Low	Inter-	High	Very High	N1	Metastatic
<10	10-20	>20	≥15 High + PSA>40	Tany	Bone
G1	G2	G3-4	PSA>40	M0	Nodules
T1-2a	T1-2c	T3-4			Naxial
AS	IHR SP	HRHone Naxial	HRHone Axial/ST	EDRT (Pain) Prostate (No ADT)	Prostate Bone

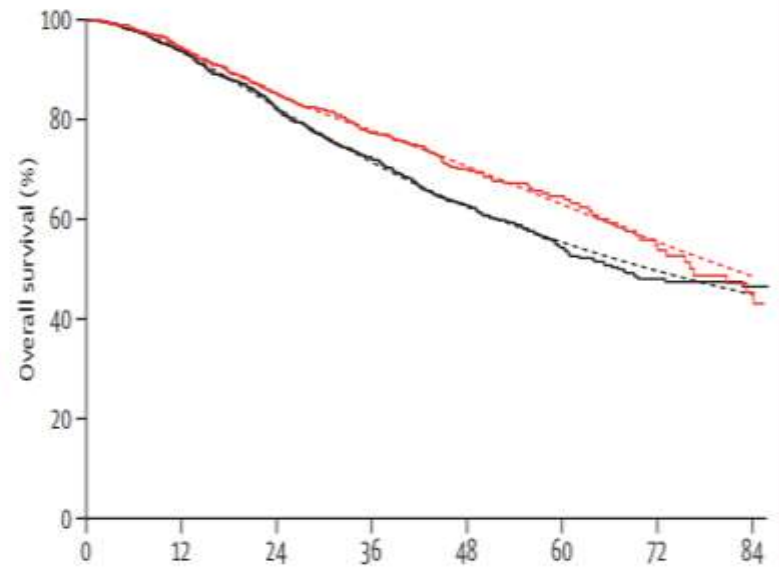
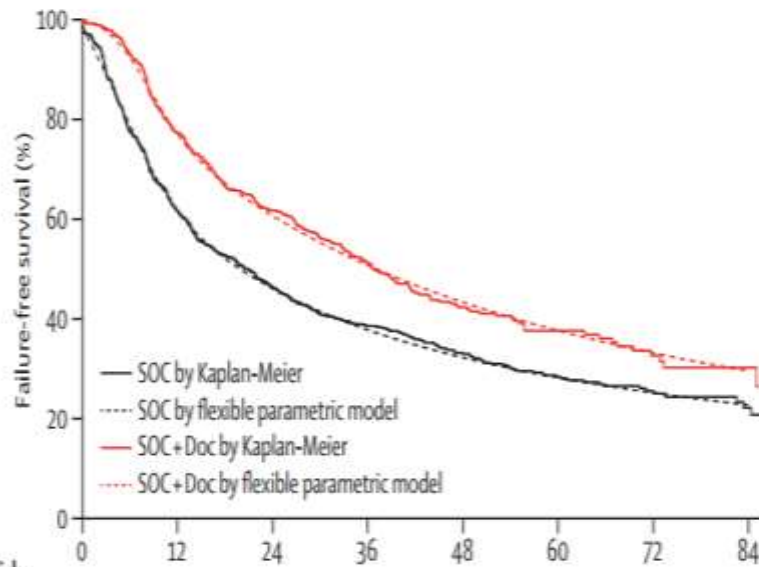


# Metastatic prostate cancer - STAMPEDE

V.High risk localised  
 N1M0  
 M1 (60%)

Prostate ca staging 2016  
 (MRI prostate + pelvis and bone scan)

Localised prostate ca				Metastatic prostate ca	
Low	Inter	High	Very High	N1	Metastatic
<10	10-20	>20	≥75 ng/ml	Tany	Bony
G6	G7	G8	T3a+b	M0	N1 absolute
T1-2a	T2b-c	T3-a			Mets
AS	108 EP BEST AS	PROSPER 42pASO 37/1/2507	PROSPER 43pASO 1500	SWOG (Pilot) Prostate for M1	PROSPER 36 307 + 180mg 7AS



Number at risk (events)

	0	12	24	36	48	60	72	84
SOC	1184 (449)	712 (174)	493 (73)	291 (33)	162 (20)	88 (7)	46 (4)	19
OC+Doc	592 (131)	441 (88)	324 (48)	189 (28)	106 (10)	57 (6)	30 (2)	11

	0	12	24	36	48	60	72	84
SOC	1184 (73)	1093 (134)	876 (92)	538 (60)	322 (35)	166 (17)	87 (2)	43
OC+Doc	592 (33)	545 (52)	447 (35)	290 (22)	181 (12)	93 (13)	51 (6)	20

**61 yr old 2015 T3b G8 PSA 8 EBRT 2015  
On LHRH analogues told “problem with  
bone scan”**

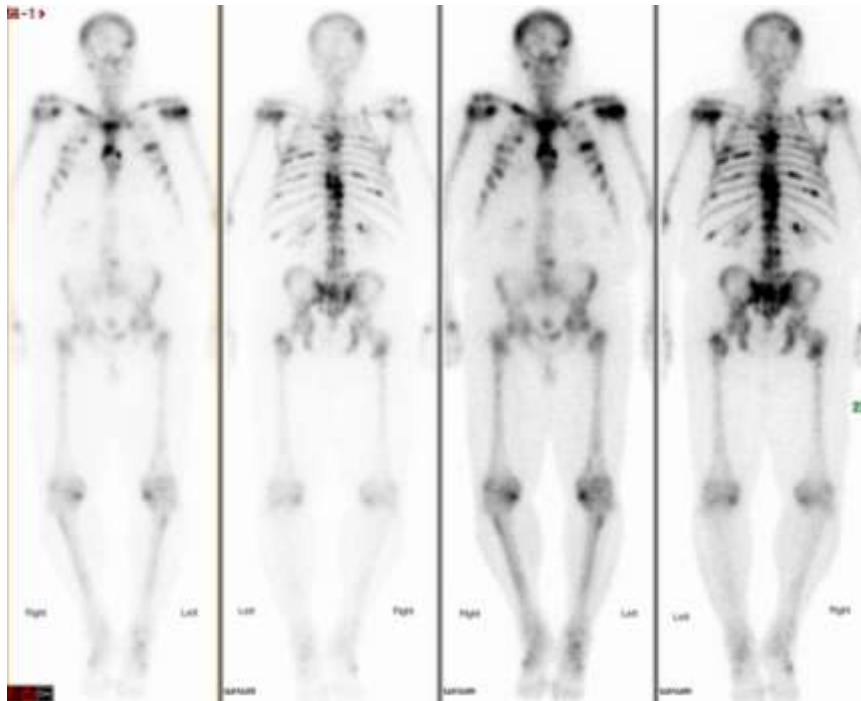
Hb 87

Platelets 107

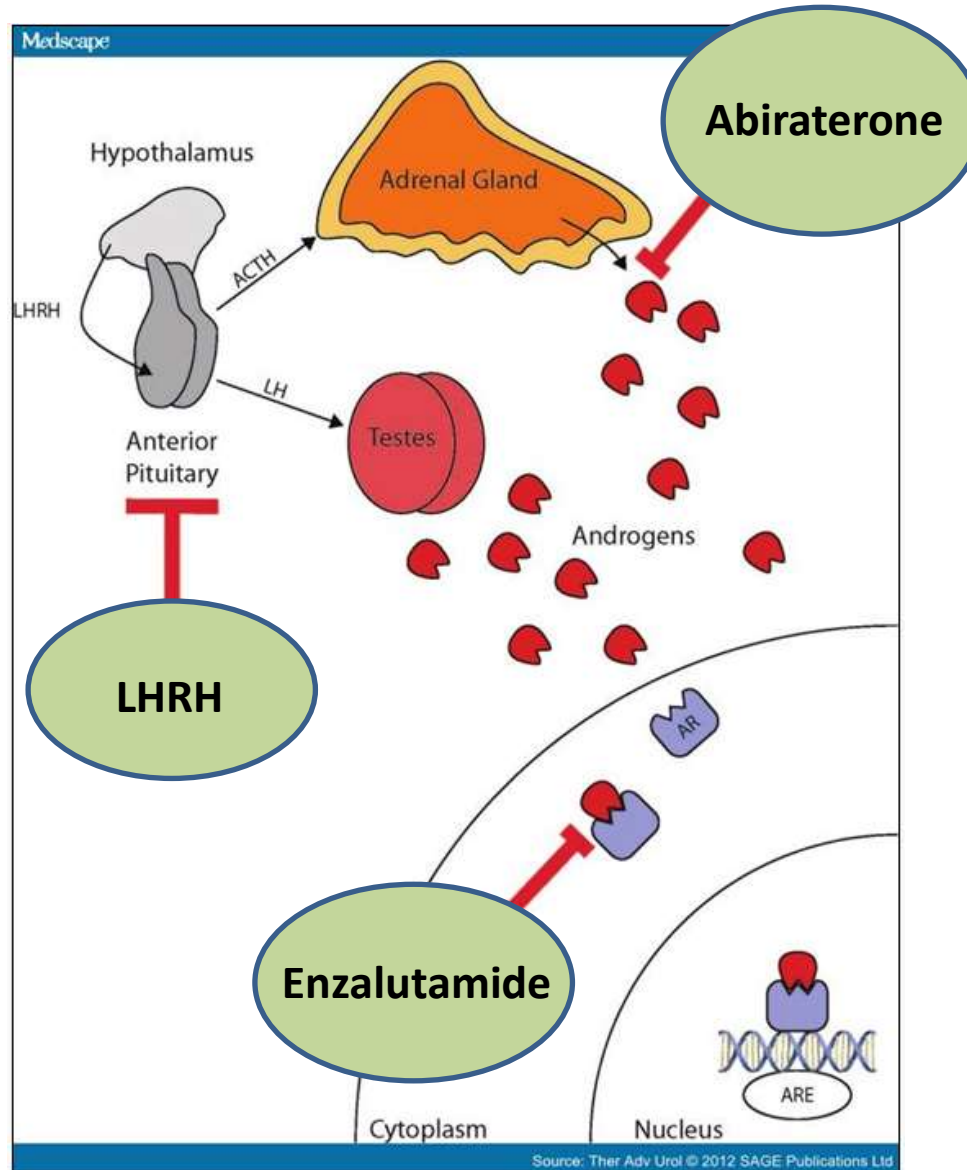
PSA 79

ALP 1400

Enzalutamide



# Novel Hormones

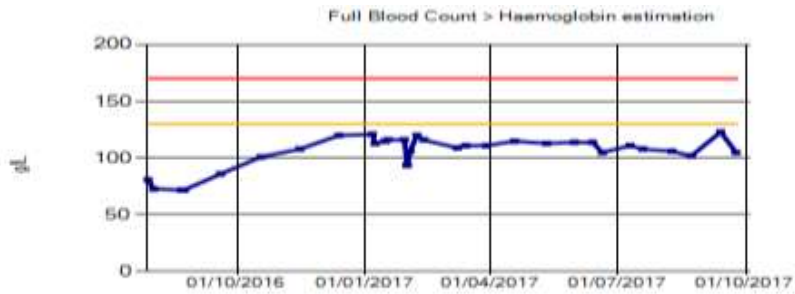




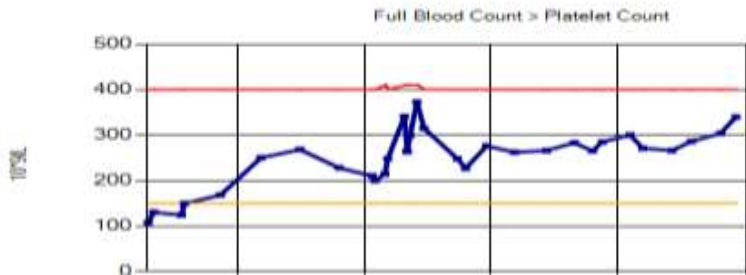
Enz

Docetaxel

### Prostate specific antigen

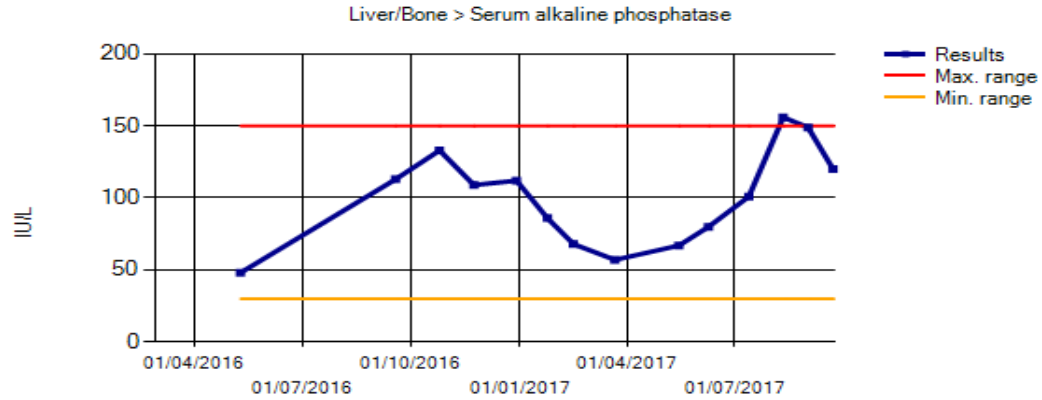


### Platelet Count

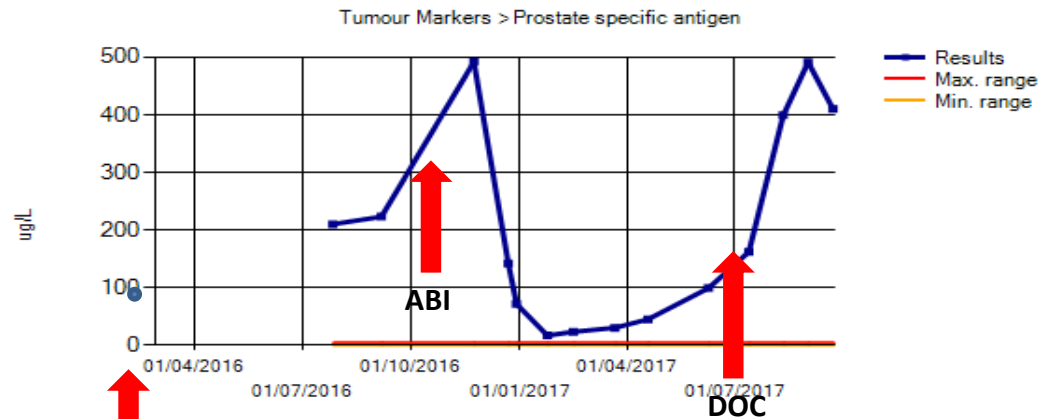


# Mr PC - T4N0M1 March 2015 LHRH (longer doubling times)

## Serum alkaline phosphatase



## Prostate specific antigen



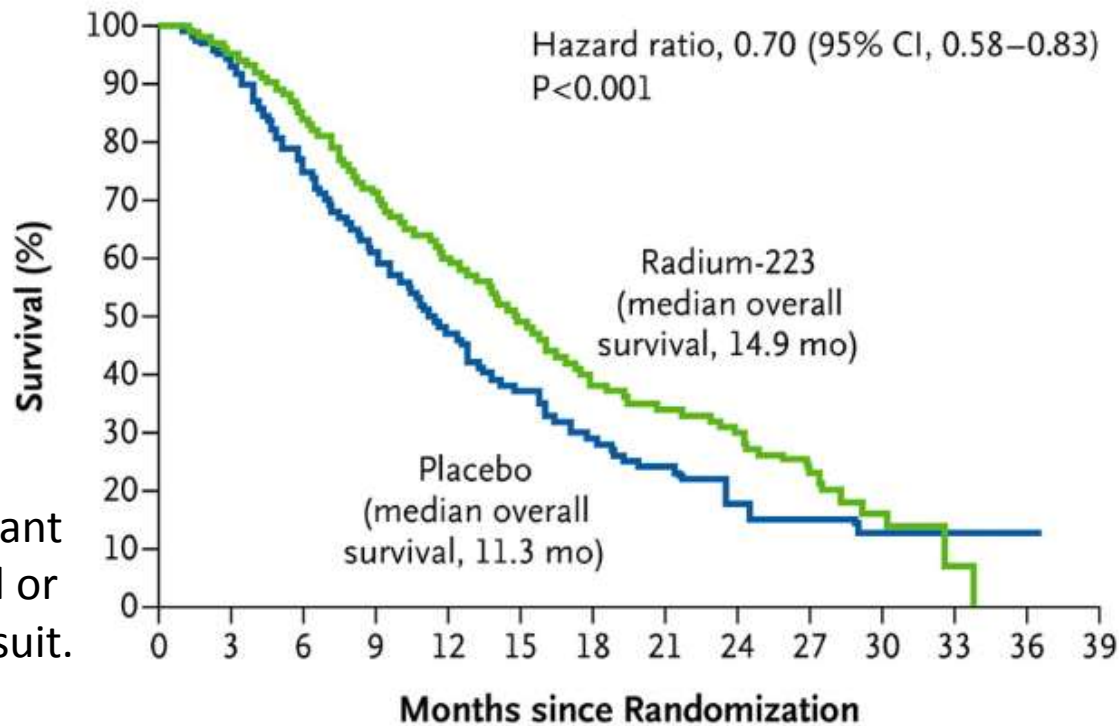
Bical.

DOC

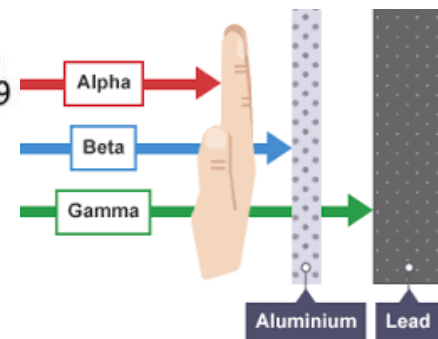
# Radium 223 trial NEJM 2013

Mr GH 73 bone only mets LHRH + 2 cycles Docetaxol.  
18months later aches + PSA rise not keen on hospital visits doesn't want chemo.

A Overall Survival

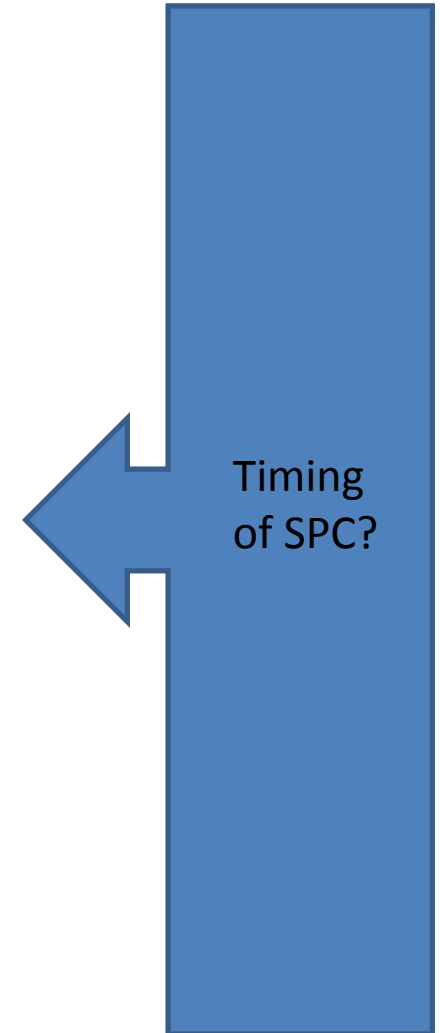


Castrate resistant  
Post docetaxel or  
Declined/not suit.



# Options in M1 disease

- LHRH + Docetaxel if good PS
- Progression
  - Abiraterone/Enzalutamide
  - Docetaxel
  - Radium 223
  - Carbazitaxel
  - ?diethylstilboesterol or dexamethasone
- Symptomatic Mx
  - Bone radiotherapy
  - Zoledronic acid
  - Dexamethasone appetite/well being





# The Future

- Radical treatment of prostate even with M1?
- Early Abiraterone instead of Docetaxel?
- Early Abi or Enz or Abi+Enz with Docetaxel?
- Early Radium223 with any of above?
- Immunotherapies?
  - Sipuleucel-T (autologous APC)
  - Newer PD-1 and PDL-1 Ab

