Prostate Cancer - Managing side effects of ADT

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Disclosures

Jennifer Locke

- None

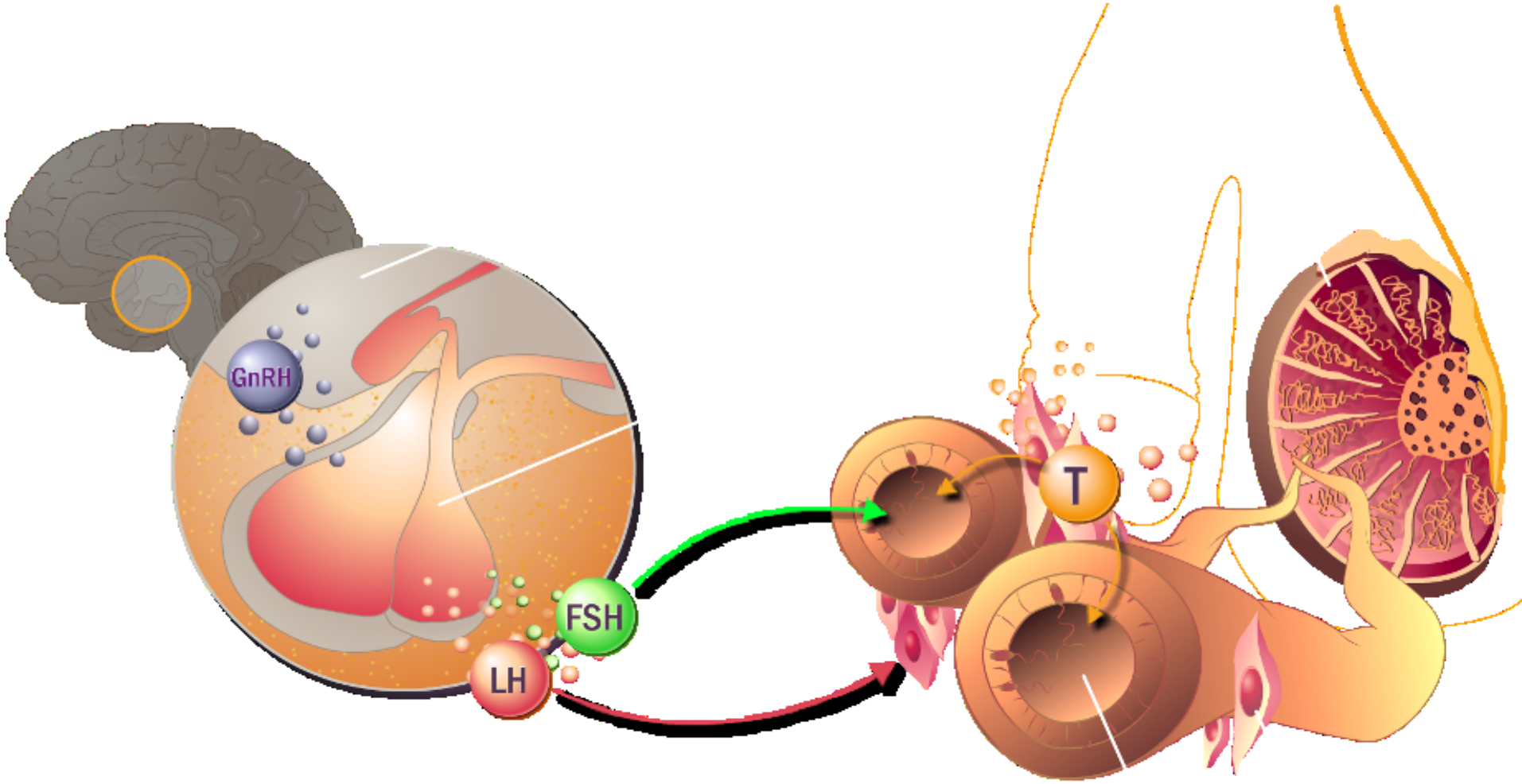
Stacy Elliott

- CME developer, lecturer, Advisory Board Member for Abbott, Lilly
- No financial interest

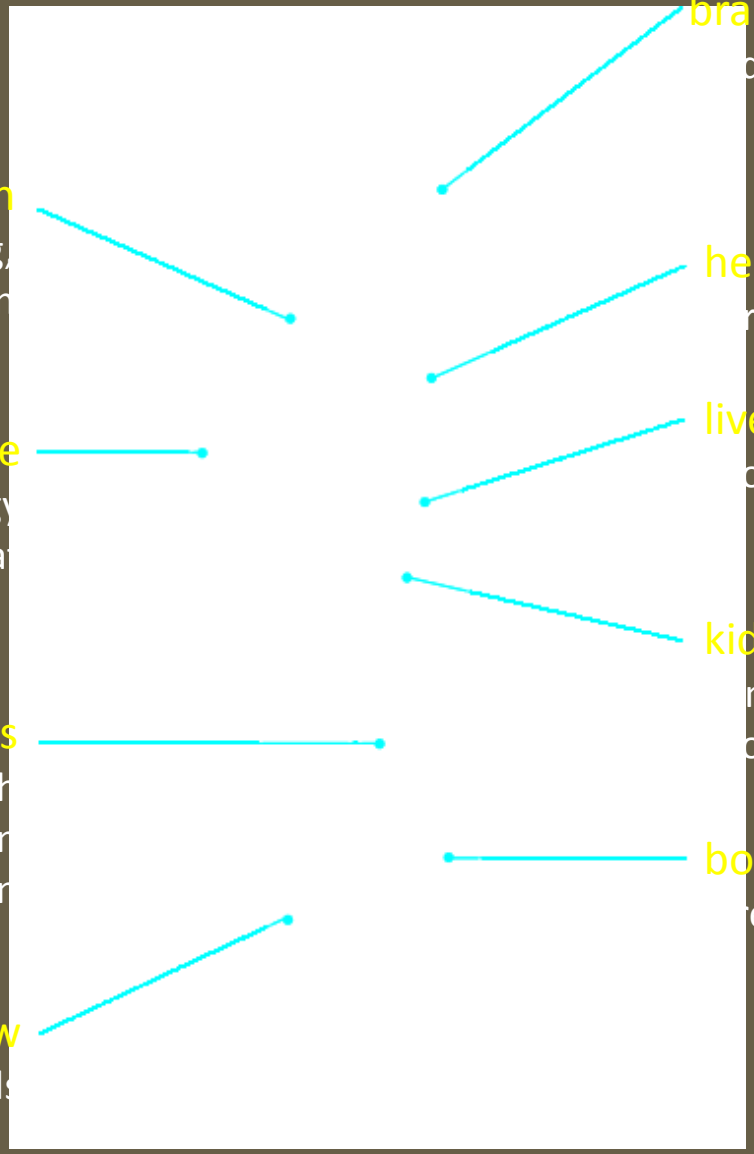
Objectives

1. Discuss the history of androgen axis based agents in prostate cancer
2. Discuss current androgen axis agents and their mechanisms of action
3. Identify side effects associated with these therapies
4. Highlight methods to reduce the burden of these side effects for patients
5. Highlight implementation of these methods in a busy office

Testosterone Biosynthesis



Testosterone: Target Organs



brain
do, mood, cognition

skin
hair growth, balding,
sebum production

heart
rdiovascular health

muscle
strength, volume, energy
reduction in visceral fa

liver
otein synthesis

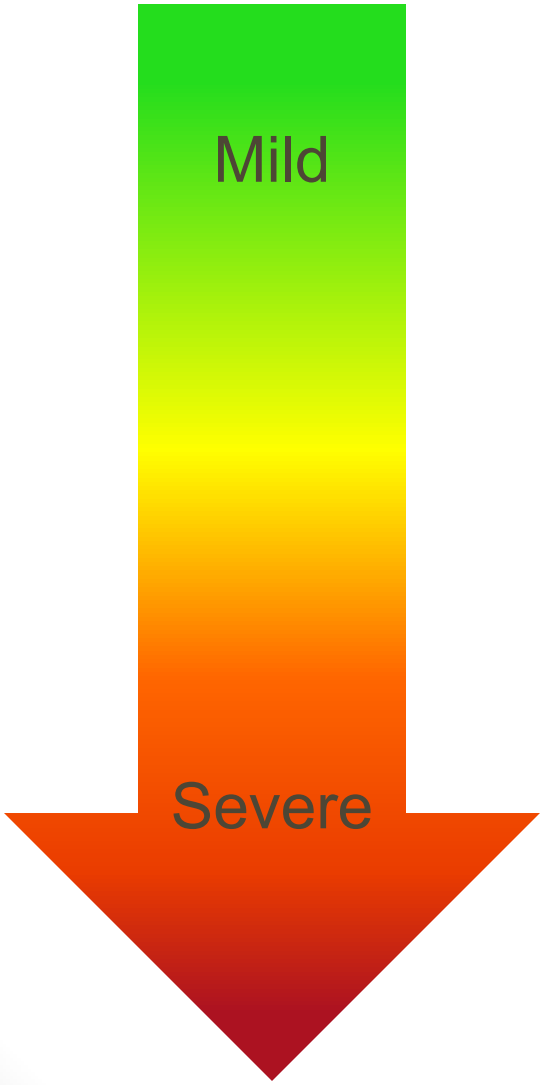
kidney
mulation of erythropoietin
oduction

male sexual organs
penile growth
spermatogenesis, erection
prostate growth and function

bone
rength and density

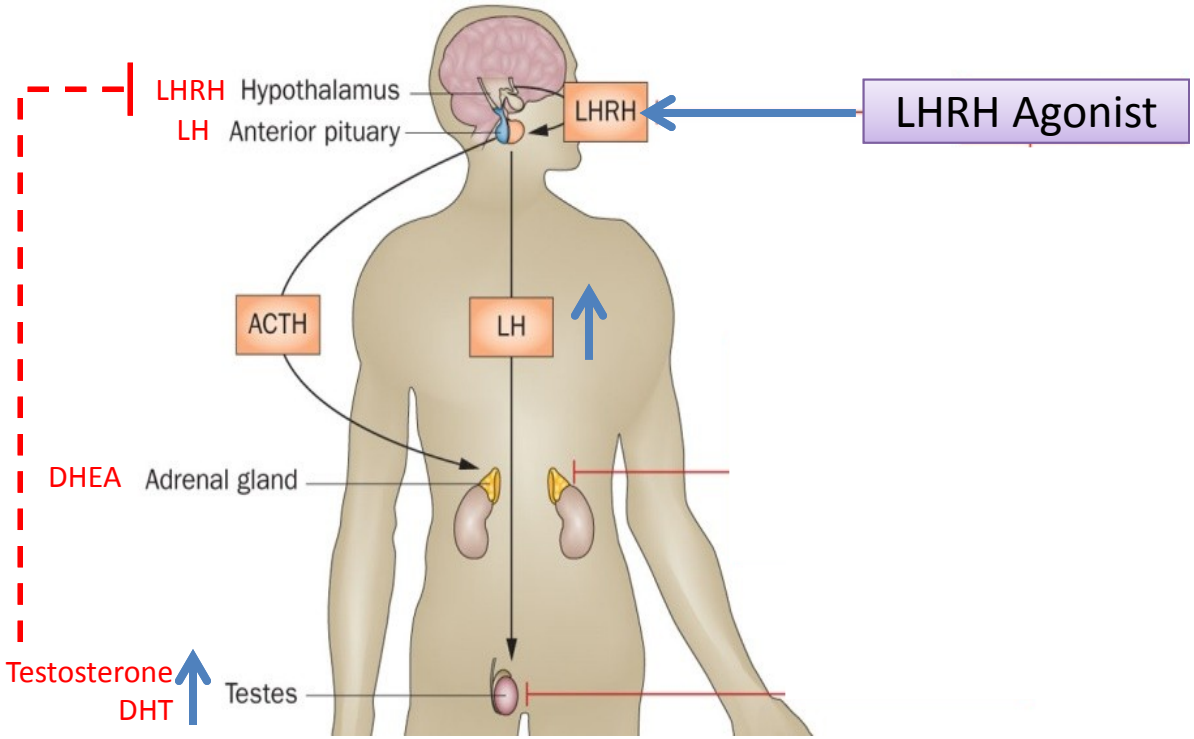
bone marrow
stimulation of stem cells

Order of appearance of signs and symptoms as testosterone levels fall



- **Decreased libido**
- Decreased vitality
- Fatigue
- Mood changes
- Insomnia
- Anemia
- Delayed ejaculation
- Flushes
- **Erectile dysfunction**
- Decreased muscle mass
- Increased visceral body fat
- Testicular atrophy
- Weakness
- Osteopenia/osteoporosis
- Thinning of facial hair, loss of axillary and pubic hair

Androgen Deprivation Therapy (ADT)



- Agonists

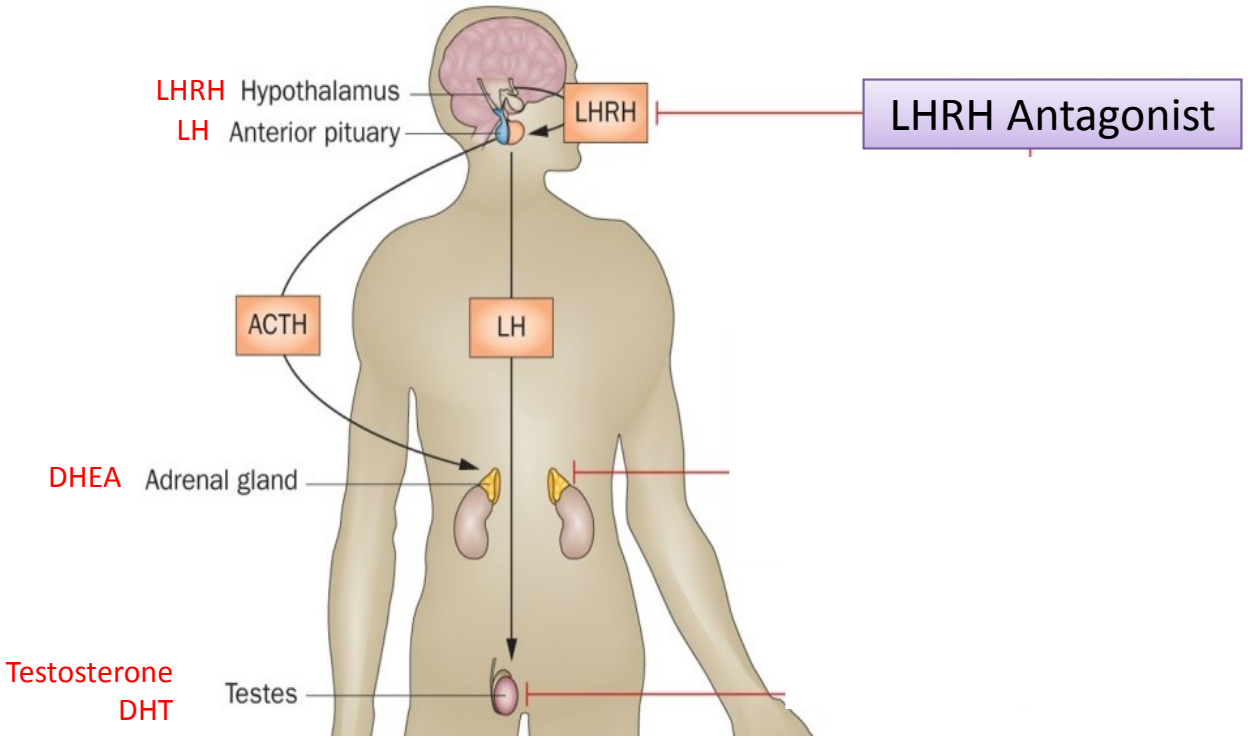
  -Over-stimulate the hypothalamus-pituitary-adrenal-testes axis stopping the production of testosterone and DHT via a feedback loop

  -**Goserelin, Leuprolide**

  -Flare phenomenon

Wong, Y. N. S. et al. (2014) Nat. Rev. Clin. Oncol

Androgen Deprivation Therapy (ADT)

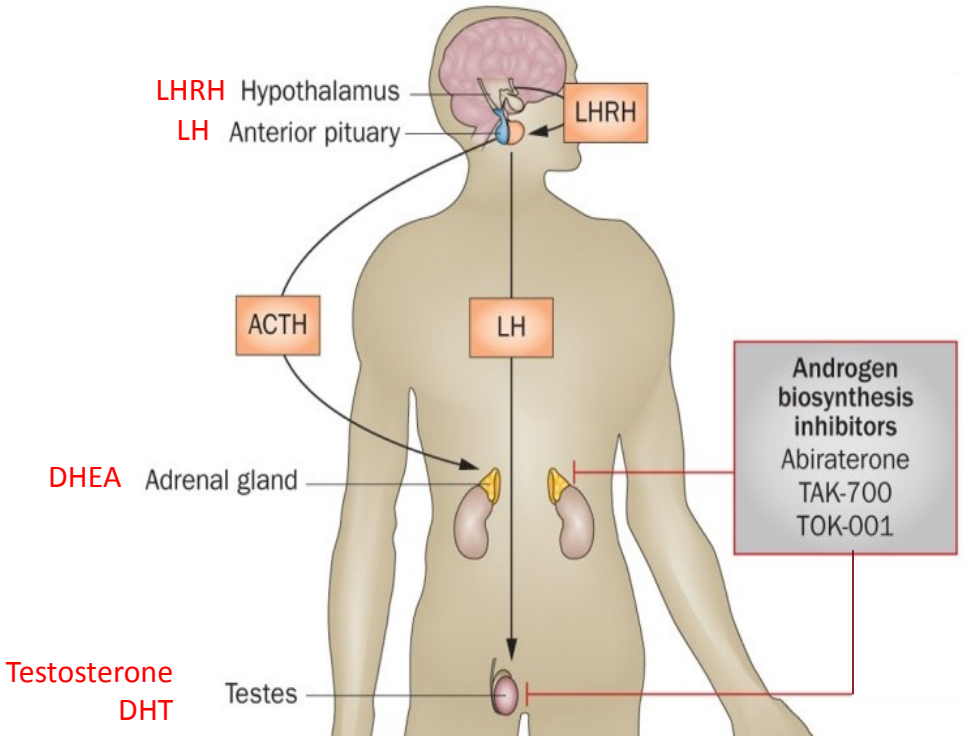


- Antagonists

  -Inhibit activation of the entire axis reducing the production of testosterone and DHT

  -**Degarelix**

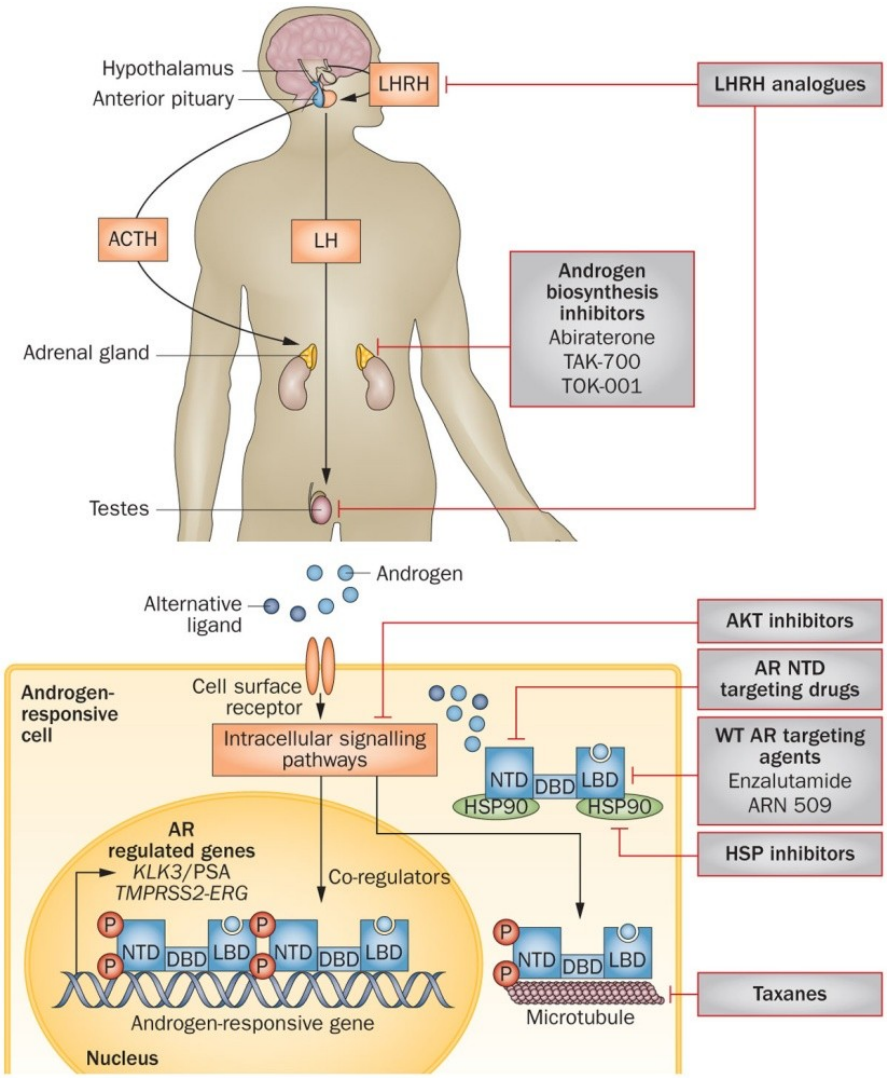
Androgen Deprivation Therapy (ADT) Adjuncts



- Androgen biosynthesis inhibitors
  - **Ketoconazole, Abiraterone, TAK-700, TOK-001**

Wong, Y. N. S. et al. (2014) Nat. Rev. Clin. Oncol

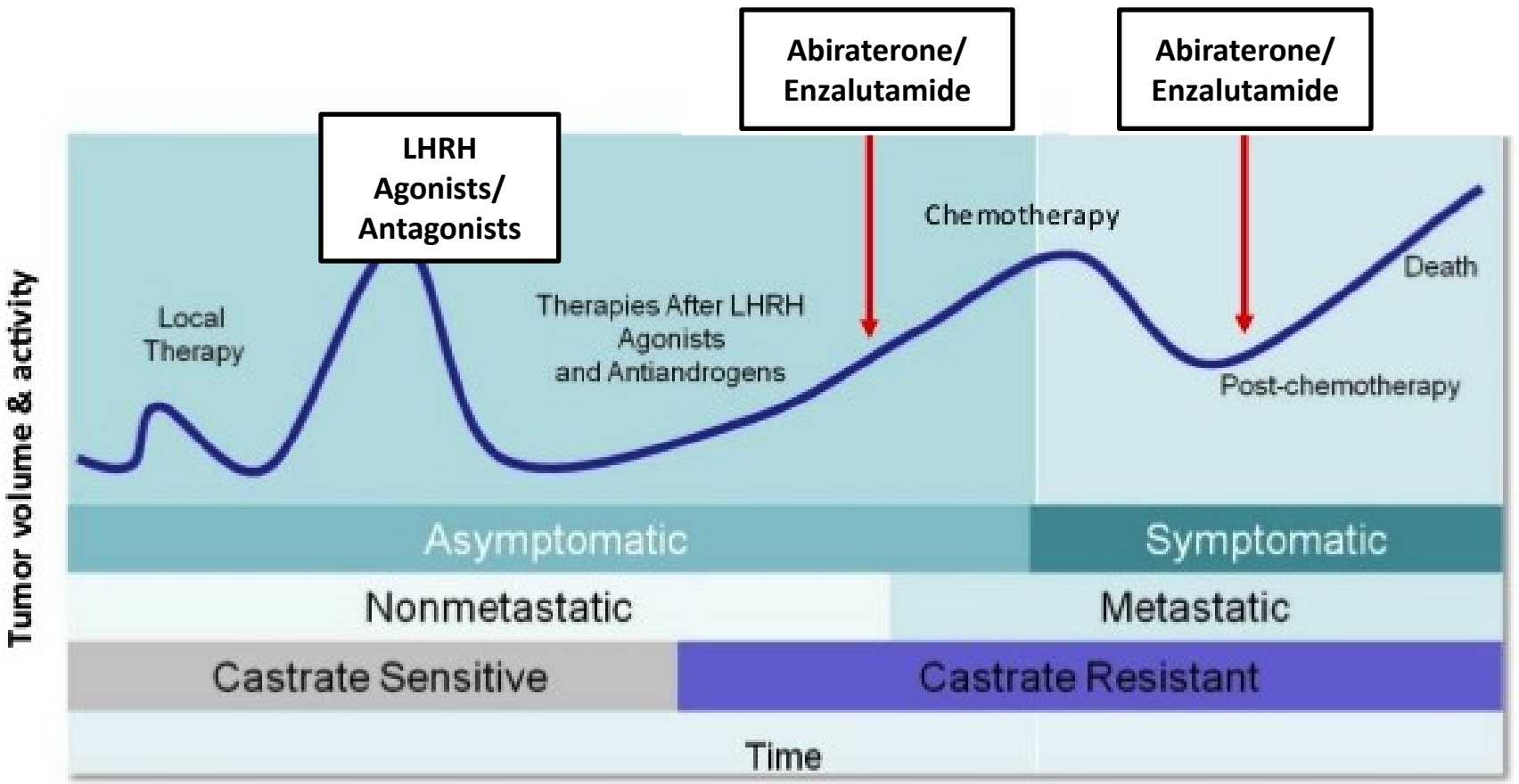
Androgen Deprivation Therapy (ADT) Adjuncts



- Androgen receptor inhibitors
  - **Bicalutamide, Nilutamide, Flutamide Enzalutamide**

Wong, Y. N. S. et al. (2014) Nat. Rev. Clin. Oncol

Timeline for agent use in prostate cancer progression



Summary of ADT and adjuncts

Category	Examples	Mechanism of action	When to use	Coverage in Canada
LHRH agonists	Buserelin, Goserelin, Histrelin, Leuprolide, Triptorelin	Over-stimulate the hypothalamus-pituitary-adrenal-testes axis stopping the production of testosterone and DHT via a feedback loop	Rising PSA despite local therapy; CaP that cannot be treated with local therapy	Buserelin-yes Goserelin-yes Histrelin- no in BC Leuprolide-yes Triptorelin-no in BC
LHRH antagonists	Degarelix, Cetrorelix, Ganirelix, Abarelix	Inhibit activation of the entire axis reducing the production of testosterone and DHT	Rising PSA despite local therapy; CaP that cannot be treated with local therapy	Degarelix-yes Cetrorelix unknown Ganirelix unknown Abarelix unknown
Androgen biosynthesis	Abiraterone, Ketoconazole, Cyprotereone acetate, TAK-700,TOK-001	Inhibit the production of adrenal and intra-tumoral synthesis of testosterone	CRPC with evidence of metastasis or rising PSA on ADT	Abiraterone- yes Ketoconazole- yes Cyprotereone acetate- yes
Androgen receptor	Bicalutamide, Flutamide, Nilutamide, Enzalutamide	Inhibit the activation of the androgen receptor	CRPC with evidence of metatastasis or rising PSA on ADT; occasionally adjunct to ADT	Bicalutamide- yes Flutamide- yes Nilutamide- yes Enzalutamide-*yes (special authority)
5 alpha-reductase inhibitors	Dutasteride, Finasteride	Inhibit the conversion of testosterone to more potent androgen DHT via blockade of 5 alpha reductase	BPH	Dutasteride- yes Finasteride- yes
Chemotherapy	Docetaxel, Cabazitaxel, Mitoxantrone	Interferes with cell division	CRPC or rising PSA on ADT or adjunct to ADT	Docetaxol-yes; Carbazetaxol is restricted in BC Mitoxantrone unknown
Bone targeting agents	Zoledronic acid, Denosumab	Zoledronic acid is a bisphosphonate Denosumab is a RANK ligand inhibitor Treat/prevent osteoporotic fracture; Prevent or delay sketetal related events	Treat/prevent osteoporotic fracture; Prevent or delay skeletal related events	Zoledronic acid- yes (palliative) Denosumab- yes
Immunotherapies	Sipuleucel-T	Induces immune response targeted against PAP, an antigen expressed in most CaP	CRPC with metastasis and no or minimal symptoms	Sipuleucel-T-no, Health Canada approval pending
Radio-pharmaceuticals	Radium-223	Calcium mimetic that gives off alpha radiation when taken up in bone	CRPC with bone metastasis	Radium-223- no

What are the side effects of ADT drugs?

If testosterone affects…..

- Sexual function
- Mood and cognition
- Bone density
- Muscle bulk and strength
- Erythropoiesis (anemia)
- Autonomic function (sweating)
- Cardiovascular health
- Metabolic parameters
- Energy

Then side effects of castrate levels of testosterone are predictable but diverse and individualized

The %

Adverse Effects	Prevalence Rate (%)
Genital shrinkage: penile length lo	93%
Cessation of sexual activity	80-93%
Mild anemia	82%
Erectile dysfunction/impotence	73-95%
Weight gain	70%
Hyperglycemia	65%
Concern about body image	60%
Loss of libido/sexual interest/drive	58-91%
Metabolic syndrome (risk as early	55%
Hypertriglyceridemia	55%
Osteoporosis 2 years on ADT	53%
Perceived loss of masculinity	50%
Hot flashes	44-80%
Decline in executive functioning	38-48%
HDL cholesterol < 40mg/dL	35%
Fatigue or decreased energy	33-47%
Decline in spatial ability	24-47%
Breast swelling	25%
Decline in verbal memory	19-48%
Breast tenderness	19%
Average increase in arterial stiffen	17%
Osteoporosis 10 years on ADT	15-81%
Depression	14%
Bone fracture	14%
Gynecomastia	13%
Average HDL rise at 3 months	9-20%
Diabetes type II risk	9%
Night sweats	5%
Mood swings	2%

Walker et al. (2013) Clinical Genitourinary Cancer.

Potential Complications from ADT: Patient Perspective

What physicians commonly tell you	What you feel	What you see	What you don't see
Loss of libido	Fatigue or loss of energy, initiative	Weight gain	Loss of bone mineral density
Erectile dysfunction	Aches and pains	Loss of muscle mass and strength	Changes in lipids
Hot flashes	Low spirits, depression	Increased subcutaneous tissue, especially hips and thighs	Glucose intolerance, diabetes
	Emotional lability	Gynecomastia	Anemia
	Cognitive changes	Decrease in testicular size and penile length	Increased cardiovascular risk?
		Loss of body hair	

Modified from Higano C (2006) Hematol Oncol Clin North Am.

Managing your patients with ADT side effects

The common complaints

- Hot flashes
- Fatigue/weight gain
- Low libido/erectile dysfunction
- Mental and cognitive effects

The big risk factors

- Cardiovascular events
- Metabolic changes
- Bone fractures

The reality : living with a partner on ADT

ADT adverse effects on sex, weight and hot flashes

Adverse Effects	Prevalence Rate (%)
Genital shrinkage: penile length loss > 1cm	93%
Mild anemia	82%
Cessation of sexual activity	80-93%
Erectile dysfunction/impotence	73-95%
Weight gain	70%
Hot flashes	44-80%

Walter L et al. (2013) Clinical Genitourinary Cancer

"Doctor I can't keep taking this stuff…I hate the hot flashes"

Efficacy of venlafaxine, medroxyprogesterone acetate, and cyproterone acetate for the treatment of vasomotor hot flushes in men taking gonadotropin-releasing hormone analogues for prostate cancer: a double-blind, randomised trial

Jacques Irani, Laurent Salomon, Rosland Oba, Philippe Bouchard, Nicolas Mottet

Published in final edited form as:
J Support Oncol. 2010 ; 8(3): 128–132.

Gabapentin for the Management of Hot Flashes in Prostate Cancer Survivors: A Longitudinal Continuation Study – NCCTG Trial N00CB[1]

Amanda R. Moraska, M.S.[2], Pamela J. Atherton, M.S.[2], Daniel W. Szydlo[2], Debra L. Barton, Ph.D.[2], Philip J. Stella, M.D.[4], Kendrith M. Rowland Jr, M.D.[5], Paul L. Schaefer, M.D.[6], James Krook, M.D.[7], James D. Bearden III, M.D.[8], and Charles L. Loprinzi, M.D.[2]

Hot Flashes with ADT

- True incidence has not been measured (but …55% - 80%)
- Do not necessarily abate over the course of therapy
- Agents utilized:
  - gabapentin 300 mg at hs or 300 mg q 8 hrs and titrate
  - venlafaxine – helps hot flashes and depressive symptoms (Effexor 12.5 mg and 25 mg Effexor XR)

Higano, C (2003) Urology

Hot Flashes with ADT continued…

- cyproterone acetate reduces subjective symptoms related to hot flashes
- diethylstilbestrol (DES) is oral (not good) while other estrogens (compounded) gels and patches reduce thrombotic risk : best is topical estradiol*
- medroxyprogesterone acetate - 85% effective but can be associated with PSA increase (reversed with withdrawal)
- acupuncture +/- , soy – ?
- clonidine shown not to be useful as compared to placebo

ADT adverse effects on energy and fatigue

Adverse Effects	Prevalence Rate (%)
Fatigue or decreased energy	33-47%
Mild anemia	82%

Walter L et al. (2013) Clinical Genitourinary Cancer

Medications for ADT fatigue

- Use of **Amantadine** (in fatigue in MS, TBI etc. for its dopaminergic and adrenergic activity) and **Modafinil** **(**traditionally for sleep disorders) used to decrease fatigue and depression *not been studied in ADT*

- Although the single site clinical trial was closed early due to poor accrual Richard et al. demonstrated that **methylphenidate (Ritalin and Concerta)** was associated with improved fatigue as compared to placebo (p=0.0220 and also improved QOL (p=0.04)

- **Bottom Line : no useful drugs known to date**

Richard PO et al. (2014) BJU Int.

ADT fatigue: exercise works

- Cormie et al. randomized 63 men scheduled to receive ADT to a 3-month supervised exercise program or usual care and found that those in the exercise program had better preserved fatigue (p=0.042), social functioning (p=0.015) and mental health (P=0.022)

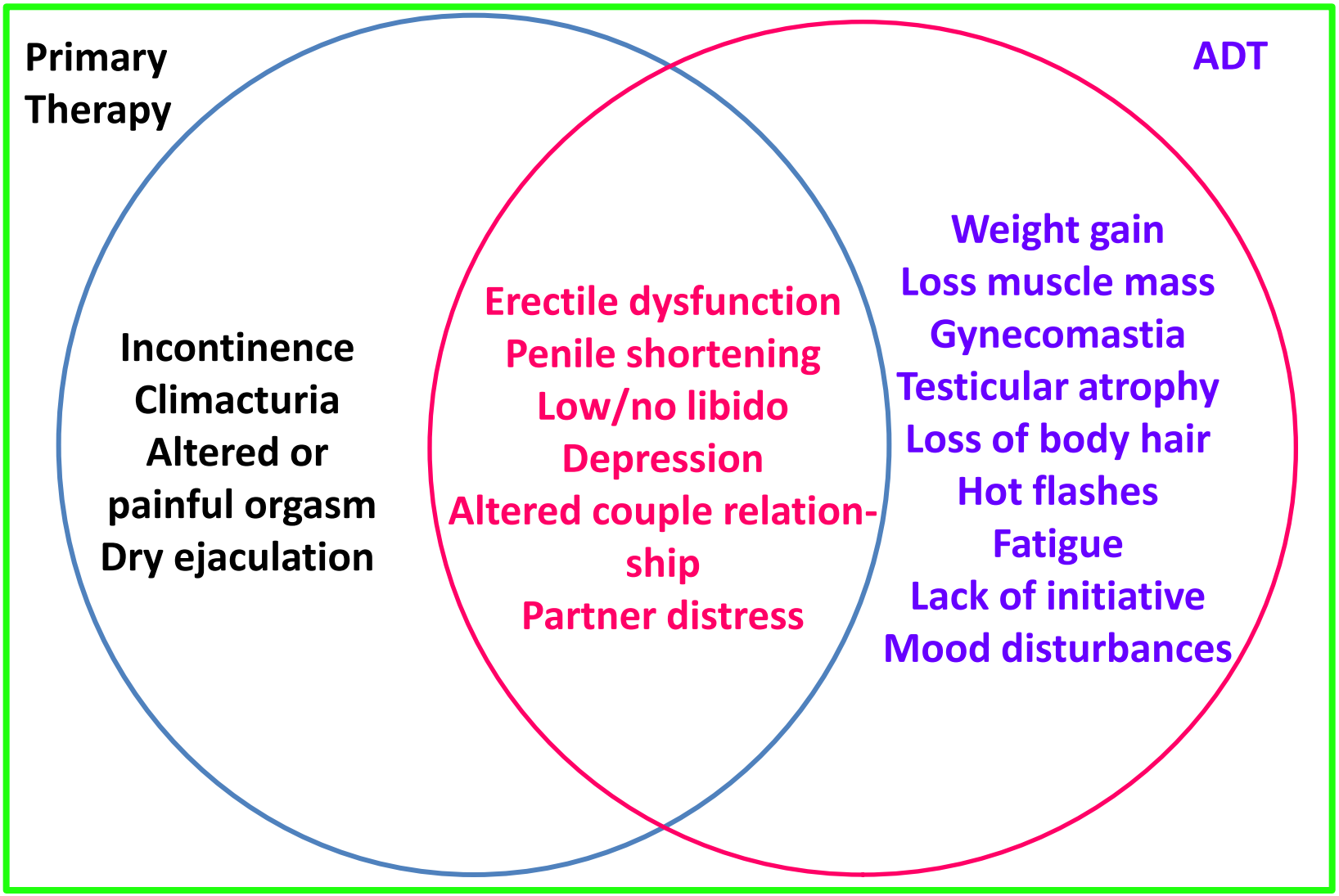
- Gardner et al. conducted a literature review of and found that exercise training demonstrated benefits in fatigue amongst other side effects of ADT

Cormie P et al. (2014) BJU Int. Gardner et al. (2014) J Clin Oncol.

Doctor I just can't have sex…

- My erection is gone..
- I don't have the old desire but I want to be intimate – I miss my partner…

Effects of primary therapy and ADT on sexuality and intimacy



Higano J (2012) J Clin Oncol.

What happens to sexual function when testosterone levels decline?

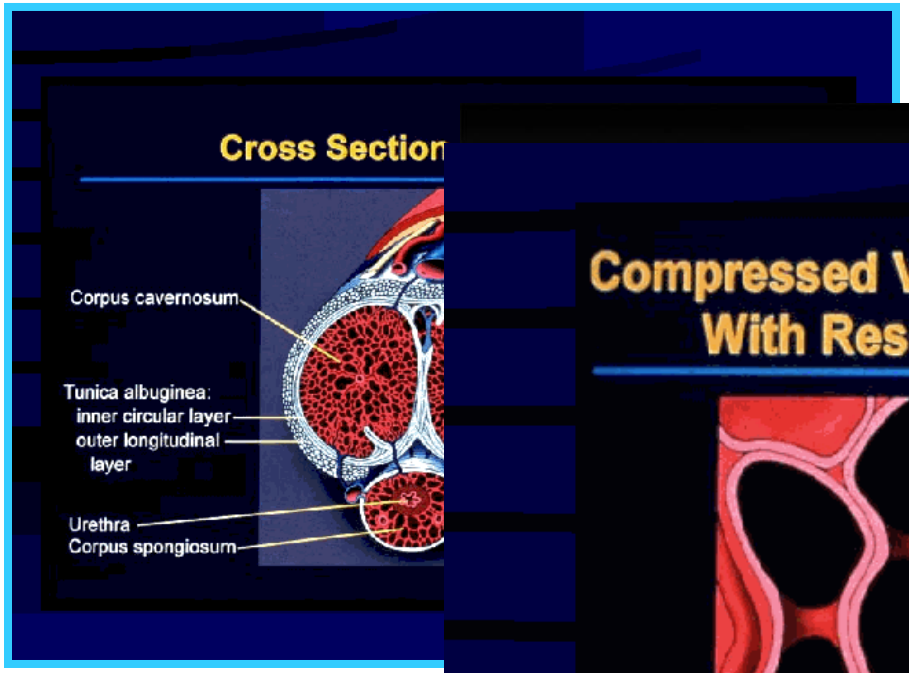
Erectile capacity in response to visual stimulation is less sensitive to androgen than is sexual interest, fantasy and cognitive sexual activities

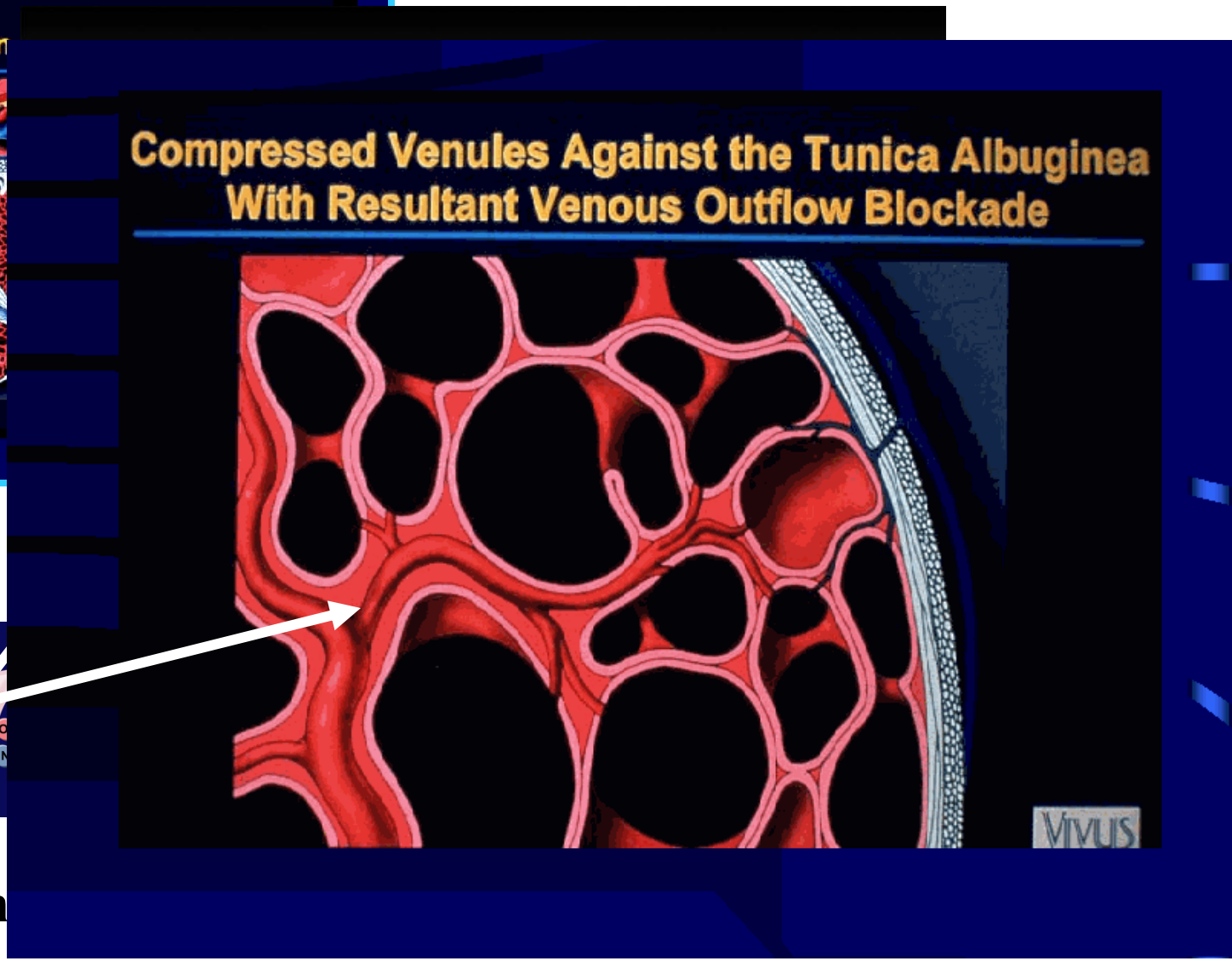
1st : sexual drive /libido changes
2nd: ejaculatory changes*
3rd: loss of nocturnal erections
4th: loss of daytime/erotic erections

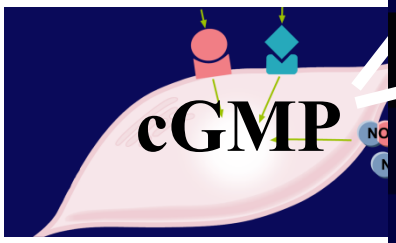
Younger verses older man

Intermittent vs continuous ADT

Bancroft and Wu (1983) Arch Sex Behaviour.







Tonic smooth muscle contraction

Smooth muscle relaxation

Castration : what happens to the genitals?

- Changes the critical balance of trabecular smooth muscle (apoptosis) and connective tissue (increase in intracellular matrix)
- Accumulation of fat containing cells just below the tunica, contributing to the impaired veno-occlusive mechanism.
- Penile fibrotic changes may be permanent: philosophy of penile rehabilitation.

Translation : loss of erectile capacity

The genitals shrink: penis length, girth and testicular volume

Penile rehabilitation plays a role in preservation

Assisting with Sexual Side Effects

- Take the *complete* sexual history (↓erection, no ejaculate, orgasmic delay, potential pain with orgasm, body image difficulties, sexual self-esteem) and not just focus on erection enhancement
- Men may not know erection not required for orgasm
- Can be a dissociation between lack of libido and the need to have an erection—don't assume men on ADT don't wish to have an erection if libido is low
- Men wish to remain sexual for intimacy purposes, just like their partners (positive affirmation of life)

Sexual decline: How can you help?

- **Exercise, lifestyle improvements** are the substrates of sexual energy and motivation
- **Medical therapies** for erection improvement
  - most often ED in older men is comorbid with vascular issues
  - below a threshold of testosterone of 10.4 nmol/L, the efficacy of PDE5i is suboptimal
  - often require penile injection therapy (PGE1 may or may not be tolerated) or vacuum erection device
  - past quality of sexual life and partner involvement best + predictors
- Deal with orgasmic problems—refer?
- Psychological and/or relationship counseling
- Access: specialized sexual health services in BC

Mental and cognitive effects of ADT

- ADT causes alterations in cognition with specific effects on memory in *some* men (conflicting studies)
- Can be described as a “brain fog” or generalized forgetfulness, lack of motivation, noted effects on visuomotor processing
- +/- improvement with estrogen*
- Can affect work and partner relationships
- Can alter self esteem, usual assertiveness and in some cases lead to depression

Beer et al. (2006) J Urol. McGinty (2014) Support Care Cancer.

Cognition effects: what to do?

- Acknowledge emotional lability is to be expected
- Cognitive workshops may have a benefit (under investigation)
- Exercise is the most important
- Utilize “brain food” and antioxidants
- Reduce alcohol and other depressants
- Lack of androgens the issue—some help in some men with other hormones (estrogens*)
- Monitor and treat for major depression

Cherrier (2013) Life Sciences.

Depression and ADT

- Known correlation with lowered testosterone, hypogonadism and depression risk
- ADT patients had higher depression rates than men with radical prostatectomy alone or non-cancer controls at initial intake (28%, 12%,5%) and 6 months later (39%, 11%, 9%)*

- ADT patients should receive particular focus in depression screening and intervention

Lee (2014) Psychooncology.

CV and Metabolic ADT Adverse Effects

Adverse Effects	Prevalence Rate (%)
Metabolic syndrome	55%
Osteoporosis 2 years on ADT	53%
Bone fracture	14%
Diabetes type II risk	9%

Walter L et al. (2013) Clinical Genitourinary Cancer

“Doctor, I can’t lose weight and my sugars are always high…”

review

Annals of Oncology 22: 2556–2560, 2011
doi:10.1093/annonc/mdr037
Published online 18 March 2011

Metformin in prostate cancer: two for the price of one

A. Clements*, B. Gao, S. H. O. Yeap, M. K. Y. Wong, S. S. Ali & H. Gurney

Department of Medical Oncology, Westmead Cancer Care Centre, Sydney, Australia

Received 24 November 2010; revised 15 January 2011; accepted 24 January 2011

BJUI
BJU INTERNATIONAL

A prospective, randomized pilot study evaluating the effects of metformin and lifestyle intervention on patients with prostate cancer receiving androgen deprivation therapy

Jenny P. Nobes, Stephen E.M. Langley, Tanya Klopper, David Russell-Jones* and Robert W. Laing

*St Luke's Cancer Centre, and *Department of Diabetes and Endocrinology, The Royal Surrey County Hospital NHS Foundation Trust, Guildford, UK*

Accepted for publication 10 June 2011

Body composition and lipid changes on ADT

- Most gain between 2.3 – 6.0 kg
- Fat increases, lean body mass decreases
- Increases appetite, insulin levels, increased visceral fat
- *Weight gain from ADT not readily lost*
- Lipids increase in unpredictable ways
- Lipid changes associated with increases in insulin levels and central arterial pressure
- Increases risk of metabolic syndrome and diabetes

- **Key**
  - **Nutritional counseling**
  - **Supervised exercise program (can also help with bone loss and fatigue)**
  - **No evidence for starting metformin in non-diabetic /non-MetS**

“Doctor what does this drug do to my heart…”

ELSEVIER

Critical Reviews in Oncology/Hematology 86 (2013) 42–51

CRITICAL REVIEWS IN
Oncology
Hematology
Incorporating Genetic Oncology

www.elsevier.com/locate/critrevonc

The cardiovascular risk of gonadotropin releasing hormone agonists in men with prostate cancer: An unresolved controversy

Vincenza Conteduca [a,*], Giuseppe Di Lorenzo [b], Alfredo Tartarone [a], Michele Aieta [a]

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journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Prostate Cancer

Editorial by Derek J. Rosario, Liam Bourke and Nancy L. Keating on pp. 574–576 of this issue

Cardiovascular Morbidity Associated with Gonadotropin Releasing Hormone Agonists and an Antagonist

Peter C. Albertsen [a,], Laurence Klotz [b], Bertrand Tombal [c], James Grady [a], Tine K. Olesen [d], Jan Nilsson [e]*

[a] University of Connecticut Health Center, Farmington, CT, USA; [b] Division of Urology, University of Toronto, ON, Canada; [c] University Clinics Saint Luc/Catholic University of Louvain, Brussels, Belgium; [d] Ferring Pharmaceuticals, Copenhagen, Denmark; [e] Department of Clinical Sciences, Lund University, Sweden

Metabolic and Cardiovascular Effects of Hypogonadism versus ADT

	Hypogonadism	ADT
Definition by T level	T < 325 ng/dL (11.3 nmol/L)	T < 50ng/dL (1.7 nmol/L) or <20 ng/dL (0.7 nmol/L)
Time to reach low T levels	years	hours to days
Metabolic syndrome	yes	metabolic abnormalities
Insulin resistance/diabetes	yes	yes, at 3 mos
Obesity	yes	yes
Lipid abnormalities	yes	triglycerides up
Hypertension	yes	no
Cardiovascular death increased[1]	yes	depends[2,3]
Increased all cause mortality[1]	yes	yes in selected high risk: Previous hx CHF, MI[4]

T, testosterone; hx, history; CHF, congestive heart failure; MI, myocardial infarction

Slide courtesy T.Higano

1. Araujo et al (2011) J Clin Endocrinol Metab, 2. Nguyen et al (2011) JAMA, 3.Tombal B, et al.(2013) EAU, 4. Nguyen et al (2012) In J Radiat Oncol Biol Phys.

ADT and cardiovascular disease 2014

- Patients with pre-existing cardiovascular disease* **are at increased risk** for CV events when treated with ADT
- GnRH antagonists may be associated with less risk than GnRH agonists
  - requires prospective evaluation
- Patients should be advised to follow lifestyle interventions to reduce risk

Higano, C (2014)

ADT and cardiovascular disease 2014

- Meta- analysis of 129,802 ADT users, and 165,605 controls* which showed ADT increased the overall cardiovascular risk
- Controversy is for who ? : pre-existing CVD is at consistently higher risk maybe due to involvement of T –lymphocytes (very prevalent in mature plaques more prone to rupture and secondly are activated by GnRH?)
- Risk primarily due to LHRH drugs (heart may have LHRH receptors?) not to antiandrogens or castration *but not proven*.

Bottom Line: starting CVD patients (i.e., prior MI or CHF) on ADT will lead to increased risk of CV events

Zhao (2014) PLoS One.

"Doctor did this drug cause my bone fracture….could it have been prevented? …"

DOI:http://dx.doi.org/10.7314/APJCP.2013.14.5.3337
Bisphosphonates for Osteoporosis in Androgen-deprivation PCa Cases

RESEARCH ARTICLE

Bisphosphonates for Osteoporosis in Nonmetastatic Prostate Cancer Patients Receiving Androgen-deprivation Therapy: A Systematic Review and Meta-analysis

Hui Ding[1], Li Yang[1], Wan Du[2], Yang Teng[3], Sheng-Jun Fu[1], Yan Tao[1], Jian-Zhong Lu[1], Zhi-Ping Wang[1,4*]

VOLUME 30 · NUMBER 30 · OCTOBER 20 2012
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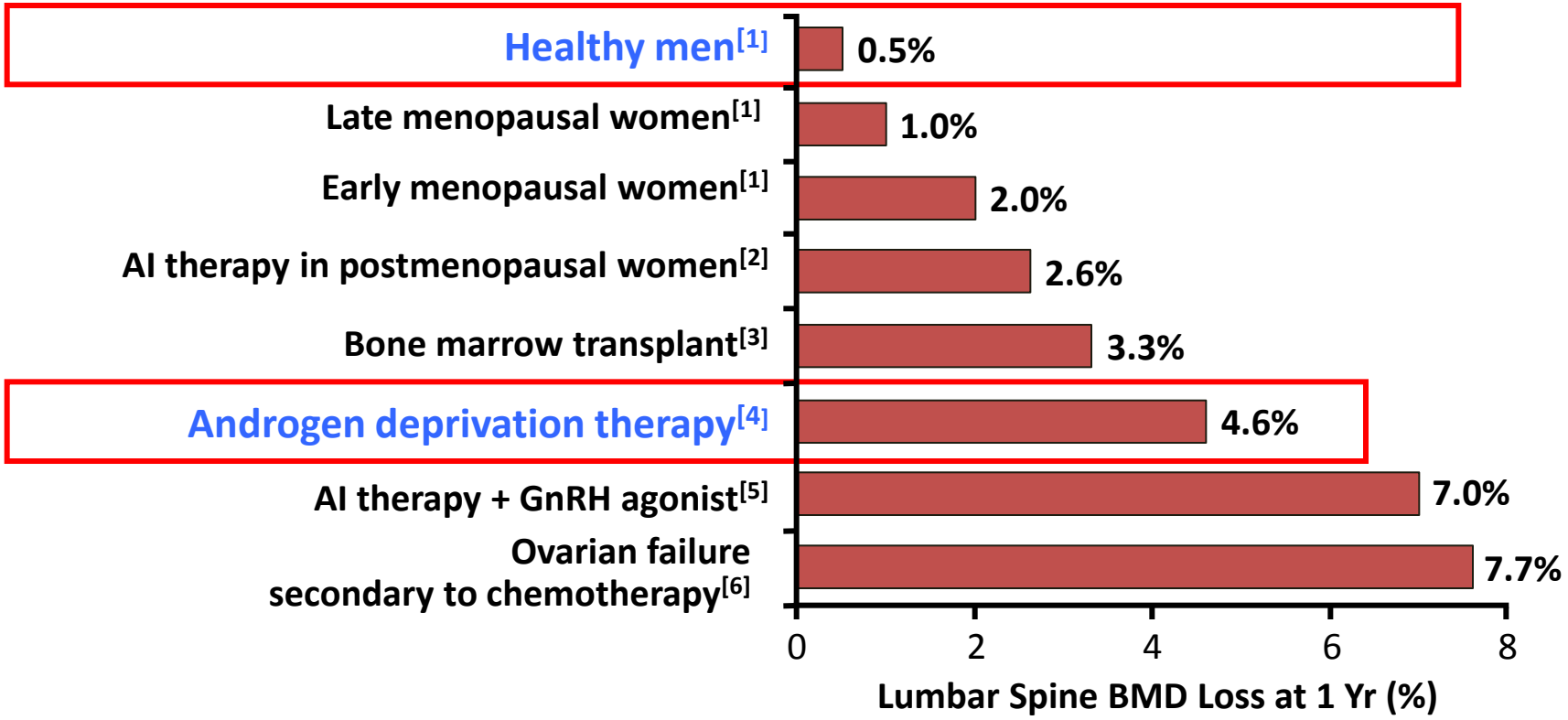
REVIEW ARTICLE

Bone Health in Adult Cancer Survivorship

Maryam B. Lustberg, Raquel E. Reinbolt, and Charles L. Shapiro

ADT-associated bone loss



1. Kanis JA. (1997) Osteoporosis. Blackwell Healthcare Communications Ltd, 2. Eastell R, et al.(2002) J Bone Mineral Res, 3. Lee WY, et al. (2002) J Clin Endocrinol Metab, 4. Maillefert JF, et al. (1999) J Urol, 5. Gnant M. (2002) Breast Cancer Res Treat, 6. Shapiro CL, et al.(2001) J Clin Oncol. (Used with permission Clinical Options Oncology)

How does ADT affect bone health?

- Loss of bone mineral density (BMD)
  - Rapid loss in first 6-12 months, slower thereafter
- Increased risk of fracture
  - 19.4% in ADT treated men versus 12.6% no ADT
- Loss of muscle mass and strength
  - Risk for fall and fracture

Shahinan et al (2005) NEJM.

Skeletal Complications: Approach is related to stage of disease

	Bone Health: non-metastatic	SRE Delay, Prevention: metastatic
Bone scan	negative	positive
Goals of evaluation and treatment	Identify men at risk for fracture, Prevent fracture, morbidity, mortality	Prevent SREs: fracture, spinal cord compression, radiation to bone
Work-up	DXA, FRAX	DXA not necessary if treating for SRE prevention
Treatment options	denosumab 60 mg q 6 mos* zoledronic acid 5 mg/year alendronatet risedronate raloxifene toremifene*	denosumab 120 mg q month zoledronic acid 4 mg q month

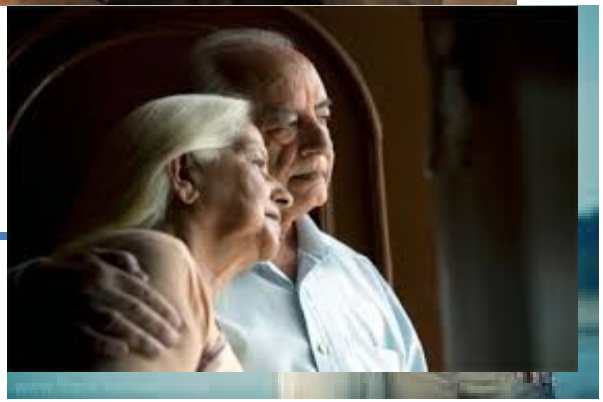
* Has been shown to reduce fracture risk

ADT and bone health

- All patients should be on calcium and vitamin D supplements
  - 1,000 mg calcium and 800 IU vitamin D per day
- Men with moderate to high risk of 10-year risk of fracture should be offered pharmacologic therapy
  - moderate to high risk defined as over 50 who have had one fragility fracture, or those with a T score of −2.5 or lower at the lumbar spine, total hip or femoral neck
  - Denosumab is better than zoledronic acid for prevention of skeletal-related events
  - Note: when starting denosumab or zoledronic acid the patient must see a dentist to assess for dental hygiene*

Datta et al. (2012) Oncologist. Fizazi K, et al. (2011) Lancet. Cheung A, et al. (2014) CUAJ. Papaioannou A, et al. (2010) CMAJ.

Psychosocial and relationship issues: The Ripple Effect



"Doctor … I love him but he's becoming hard to live with…"

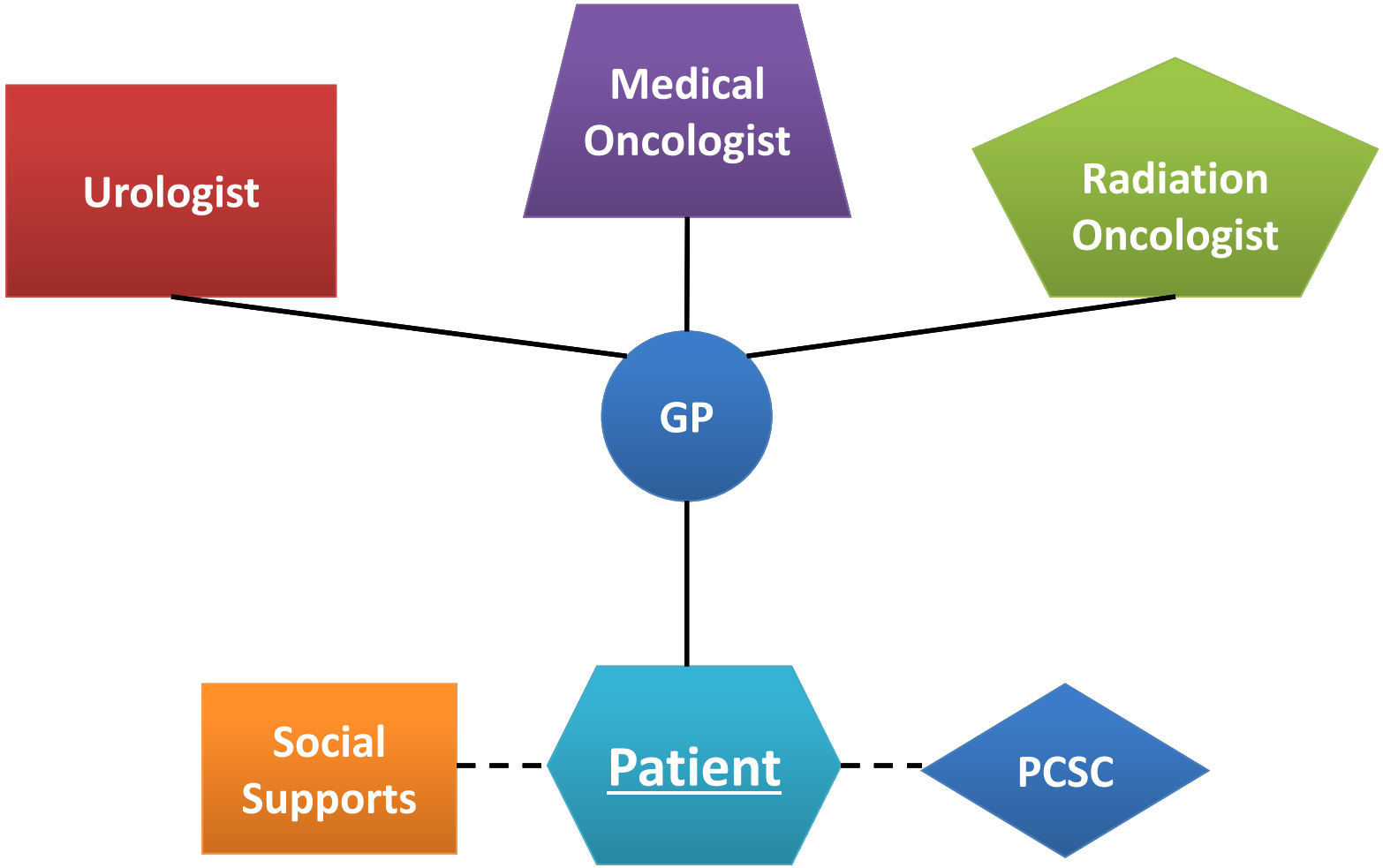
Patients may experience

- moodiness (shorter fuse)
- emotional lability (cry easily)
- depression (dysthymia or clinical depression)
- anxiety
- loss of confidence and/or assertiveness
- cognitive difficulties (esp. attention and memory)

Higher risk if history of past depression??

Large social impact for patient and partner and huge impact on quality of life

The GP in the management team



How do you manage all this?

- Don’t try to manage it all at once! Use your specialists.
- Treat it like an “ADT” work up—routine assessment of all factors (longer visit) with physical exam and associated follow up imaging or blood work.
- Shorter follow up visits to review:

  Lipids, HbA1c, Hb, total testosterone,

  DEXA, Xray or other imaging
- Coordination with medical and rad oncologists

How do you do this in a busy clinic?

- Utilize resources available to you:
  - Vancouver Prostate Centre Supportive Care Program's Module : *Androgen Deprivation Therapy: An essential guide for prostate cancer patients and their loved ones*
  - Lebret et al. created a educational tool kit for diet and physical exercise
  - Online access for patients and physicians:
    - www.cancer.org/cancer/prostatecancer/detailedguide/prostate-cancer-treating-hormone-therapy
    - www.medscape.com/viewarticle/738378
    - www.prostatecentre.com/patient-information/PCSC
    - www.Lifeonadt.com (patient blog)

VANCOUVER'S PROSTATE CANCER SUPPORTIVE CARE (PCSC) PROGRAM*

A comprehensive program designed to help both patients and their partners across the entire disease trajectory:

1. Introduction to Treatment Options
2. Managing the Impact of Prostate Cancer Treatments on Sexual Function
3. Lifestyle Management: exercise and nutrition
4. Adapting to Androgen Deprivation Therapy
5. Pelvic Floor Physiotherapy for Urinary Incontinence

* Patients or physicians : 604-875-4111, x 22946

Pearls

- **Ask** your patients about fatigue, hot flashes, sexual and intimacy issues and partner well-being
- **Discuss** the importance of quality of life and methods to achieve this such as healthy diet and exercise with your patients
- Don't forget to **screen** for bone health, cardiovascular health and metabolic syndrome
  - Investigations: DEXA, testosterone, PSA, lipids, HbA1c

How to help your patient on ADT and help yourself…

- Be proactive : do complete medical, psych history, physical and blood work prior to initiation of ADT as a baseline to identify pre-existing problems (eg hyperlipidemia, glucose intolerance, past depression) and for comparison over time

- Educate patients re: what side effects to expect from ADT and that the patient can play an active role in minimizing side effects, exercise and diet (ADT workbook, ADT educational session at the Vancouver Prostate Centre)

How to help your patient on ADT and help yourself…

- Stress the importance of exercise as the single most beneficial therapy for ADT side effects and prevent the mental and metabolic snowball effect

- Monitor at regular intervals: prevention strategies, institute appropriate therapies (learn so you are prepared!)* as needed (e.g., statins, metformin, antihypertensives)

How to help your patient on ADT and help yourself…

- Focus on QoL: watch for medical AND psychological issues; encourage attendance at prostate cancer support groups
- Listen to the patient: what is most bothersome, symptomatically
- Listen to the partner: he/she is often the thermostat to the partner's wellbeing
- Use your local and online resources to help

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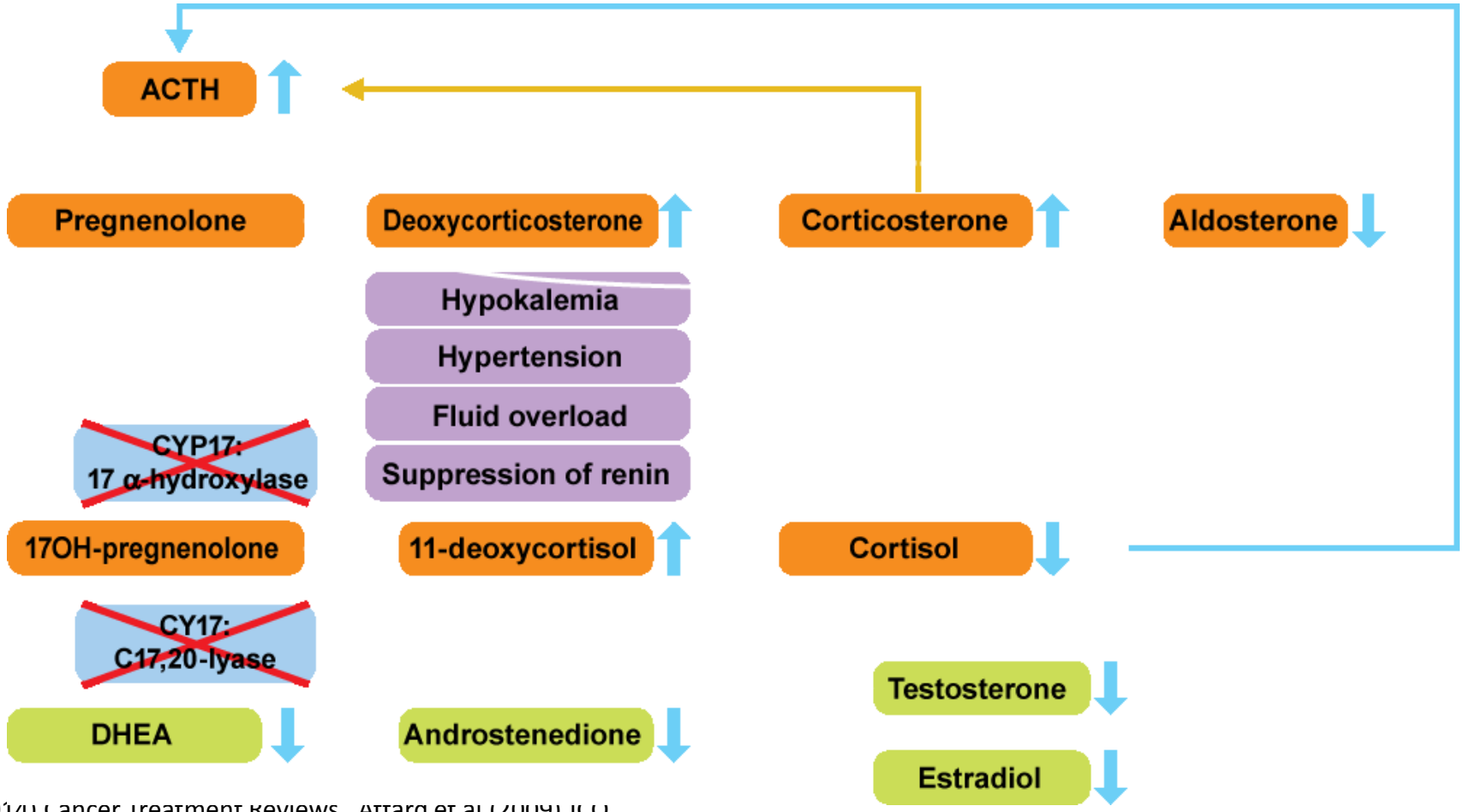
VANCOUVER PROSTATE CENTRE

AHDC & VGH Centre of Excellence

Extra slides

Abiraterone

- Order baseline CBC, liver enzymes, electrolytes, Cr, glucose
- Cycles 1-3 monitor BP, potassium, liver enzymes, bilirubin
- Do a MUGA scan or echo if cardiac history



Bahl et al. (2014) Cancer Treatment Reviews, Attard et al.(2009) JCO.

Enzalutamide

- Order baseline CBC, electrolytes, Cr, ECG (QT prolongation)
- Cycles 1-3 monitor BP

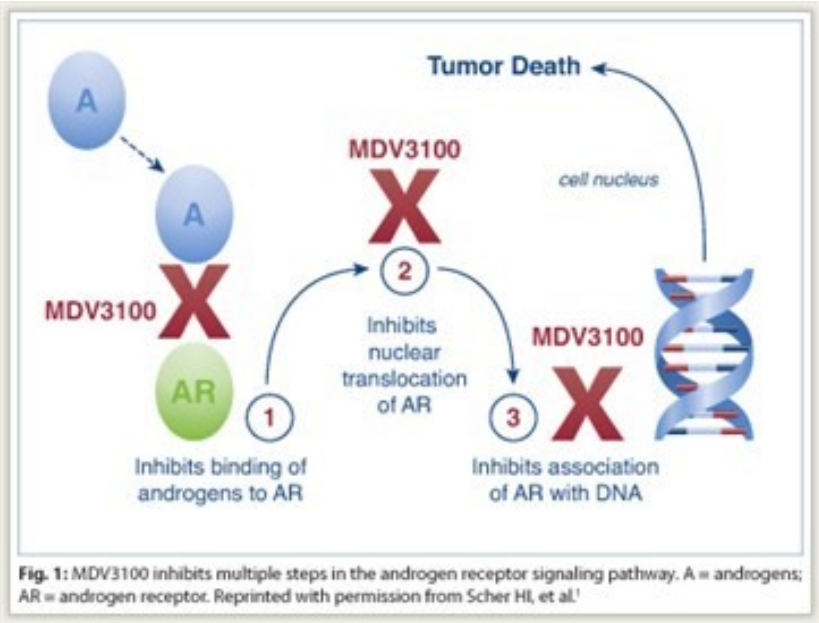


Fig. 1: MDV3100 inhibits multiple steps in the androgen receptor signaling pathway. A = androgens; AR = androgen receptor. Reprinted with permission from Scher HI, et al.[1]

DRUG INTERACTIONS	
Drugs that increase enzalutamide exposures	
CYP2C8 inhibitors	i.e. gemfibrozil
CYP3A4 inhibitors	i.e. itraconazole
Drugs that decrease enzalutamide exposures	
CYP2C8 inducers	i.e. rifampin
CYP3A4 inducers	
Drugs whose exposures may be decreased by enzalutamide	
CYP3A4, CYP2C9 and UGTAI substrates	
analgesics anticoagulants anti-epileptics anti-gout agents antipsychotics benzodiazepines B-blockers Calcium channel blockers corticosteroids anti-cancer agents HIV antivirals immune modulators macrobid statins thyroid agents	fentanyl, tramadol dabigitran, warfarin phenytoin, phenobarbitone colchicine haloperidol diazepam, mitazolam bisoprolol, propanolol diltiazem prednisone cabazitaxel indinavir, ritonavir cyclosporine levothyroxine
Drugs whose exposures may be increased by enzalutamide	
BCRP and MRP2 substrates	
Drugs that cause QT prolongation	

Bahl et al. (2014) Cancer Treatment Reviews,
Scher et al. (2012) CU Cancer Sym.