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: Target Organs

- Brain: libido, mood, cognition
- Heart: cardiovascular health
- Liver: protein synthesis
- Kidney: stimulation of erythropoietin production
- Male sexual organs: penile growth, spermatogenesis, erection, prostate growth and function
- Skin: hair growth, balding, sebum production
- Muscle: strength, volume, energy, reduction in visceral fat
- Bone marrow: stimulation of stem cells
- Bone: strength and density
- Bone:
- Testosterone:
- Target Organs:
- Brain:
- Heart:
- Liver:
- Kidney:
- Male sexual organs:
- Skin:
- Muscle:
- Bone marrow:
- Bone:
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

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
Androgen Deprivation Therapy (ADT)

Adjuncts

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

Timeline for agent use in prostate cancer progression

- **LHRH Agonists/Antagonists**
- **Abiraterone/Enzalutamide**

During the progression of prostate cancer, different agents are used at various stages:
- **Asymptomatic**
  - **Nonmetastatic**
  - **Castrate Sensitive**
- **Symptomatic**
  - **Metastatic**
  - **Castrate Resistant**

Therapies after LHRH Agonists and Antiandrogens, followed by chemotherapy and post-chemotherapy.
## Summary of ADT and adjuncts

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
<th>Mechanism of action</th>
<th>When to use</th>
<th>Coverage in Canada</th>
</tr>
</thead>
</table>
| **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, Cyproterone 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
|                           |                                           |                                                                                      |                                                                             | Cyproterone acetate- yes
| **Androgen receptor**     | Bicalutamide, Flutamide, Nilutamide, Enzalutamide | Inhibit the activation of the androgen receptor                                     | CRPC with evidence of metastasis 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; Cabazitaxol 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 skeletal 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
<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Prevalence Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genital shrinkage: penile length loss</td>
<td>93%</td>
</tr>
<tr>
<td>Cessation of sexual activity</td>
<td>80-93%</td>
</tr>
<tr>
<td>Mild anemia</td>
<td>82%</td>
</tr>
<tr>
<td>Erectile dysfunction/impotence</td>
<td>73-95%</td>
</tr>
<tr>
<td>Weight gain</td>
<td>70%</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>65%</td>
</tr>
<tr>
<td>Concern about body image</td>
<td>60%</td>
</tr>
<tr>
<td>Loss of libido/sexual interest/drive</td>
<td>58-91%</td>
</tr>
<tr>
<td>Metabolic syndrome (risk as early)</td>
<td>55%</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>55%</td>
</tr>
<tr>
<td>Osteoporosis 2 years on ADT</td>
<td>53%</td>
</tr>
<tr>
<td>Perceived loss of masculinity</td>
<td>50%</td>
</tr>
<tr>
<td>Hot flashes</td>
<td>44-80%</td>
</tr>
<tr>
<td>Decline in executive functioning</td>
<td>38-48%</td>
</tr>
<tr>
<td>HDL cholesterol &lt; 40mg/dL</td>
<td>35%</td>
</tr>
<tr>
<td>Fatigue or decreased energy</td>
<td>33-47%</td>
</tr>
<tr>
<td>Decline in spatial ability</td>
<td>24-47%</td>
</tr>
<tr>
<td>Breast swelling</td>
<td>25%</td>
</tr>
<tr>
<td>Decline in verbal memory</td>
<td>19-48%</td>
</tr>
<tr>
<td>Breast tenderness</td>
<td>19%</td>
</tr>
<tr>
<td>Average increase in arterial stiffen</td>
<td>17%</td>
</tr>
<tr>
<td>Osteoporosis 10 years on ADT</td>
<td>15-81%</td>
</tr>
<tr>
<td>Depression</td>
<td>14%</td>
</tr>
<tr>
<td>Bone fracture</td>
<td>14%</td>
</tr>
<tr>
<td>Gynecomastia</td>
<td>13%</td>
</tr>
<tr>
<td>Average HDL rise at 3 months</td>
<td>9-20%</td>
</tr>
<tr>
<td>Diabetes type II risk</td>
<td>9%</td>
</tr>
<tr>
<td>Night sweats</td>
<td>5%</td>
</tr>
<tr>
<td>Mood swings</td>
<td>2%</td>
</tr>
</tbody>
</table>

## Potential Complications from ADT: Patient Perspective

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

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

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Walter L et al. (2013) Clinical Genitourinary Cancer
“Doctor I can’t keep taking this stuff...I hate the hot flashes”
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
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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
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 and found that exercise training demonstrated benefits in fatigue amongst other side effects of ADT.
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

Primary Therapy
- Incontinence
- Climacturia
- Altered or painful orgasm
- Dry ejaculation

Erectile dysfunction
- Penile shortening
- Low/no libido
- Depression
- Altered couple relationship
- Partner distress

ADT
- Weight gain
- Loss muscle mass
- Gynecomastia
- Testicular atrophy
- Loss of body hair
- Hot flashes
- Fatigue
- Lack of initiative
- Mood disturbances

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

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

Younger verses older man
Intermittent vs continuous ADT

Tonic smooth muscle contraction

Smooth muscle relaxation

Compressed venules against the tunica albuginea with resultant venous outflow blockade

cGMP
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 $10.4 \text{ nmol/L}$, 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

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
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

## CV and Metabolic ADT Adverse Effects

<table>
<thead>
<tr>
<th>Adverse Effects</th>
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<tr>
<td>Metabolic syndrome</td>
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<tr>
<td>Osteoporosis 2 years on ADT</td>
<td>53%</td>
</tr>
<tr>
<td>Bone fracture</td>
<td>14%</td>
</tr>
<tr>
<td>Diabetes type II risk</td>
<td>9%</td>
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</tbody>
</table>
“Doctor, I can’t lose weight and my sugars are always high...”

Metformin in prostate cancer: two for the price of one

Department of Medical Oncology, Westmead Cancer Care Centre, Sydney, Australia
Received 24 November 2010; revised 15 January 2011; accepted 24 January 2011

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...”
### Metabolic and Cardiovascular Effects of Hypogonadism versus ADT

<table>
<thead>
<tr>
<th></th>
<th>Hypogonadism</th>
<th>ADT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition by T level</strong></td>
<td>$T &lt; 325 , \text{ng/dL} \ (11.3 , \text{nmol/L})$</td>
<td>$T &lt; 50, \text{ng/dL} \ (1.7 , \text{nmol/L})$ or $&lt;20 , \text{ng/dL} \ (0.7 , \text{nmol/L})$</td>
</tr>
<tr>
<td><strong>Time to reach low T levels</strong></td>
<td>years</td>
<td>hours to days</td>
</tr>
<tr>
<td><strong>Metabolic syndrome</strong></td>
<td>yes</td>
<td>metabolic abnormalities</td>
</tr>
<tr>
<td><strong>Insulin resistance/diabetes</strong></td>
<td>yes</td>
<td>yes, at 3 mos</td>
</tr>
<tr>
<td><strong>Obesity</strong></td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td><strong>Lipid abnormalities</strong></td>
<td>yes</td>
<td>triglycerides up</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td><strong>Cardiovascular death increased$^1$</strong></td>
<td>yes</td>
<td>depends$^{2,3}$</td>
</tr>
<tr>
<td><strong>Increased all cause mortality$^1$</strong></td>
<td>yes</td>
<td>yes in selected high risk: Previous hx CHF, MI$^4$</td>
</tr>
</tbody>
</table>

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

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**Slide courtesy T. Higano**
• 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

“Doctor did this drug cause my bone fracture....could it have been prevented? ...”
ADT-associated bone loss

Healthy men\textsuperscript{[1]}: 0.5%

Late menopausal women\textsuperscript{[1]}: 1.0%

Early menopausal women\textsuperscript{[1]}: 2.0%

Al therapy in postmenopausal women\textsuperscript{[2]}: 2.6%

Bone marrow transplant\textsuperscript{[3]}: 3.3%

Androgen deprivation therapy\textsuperscript{[4]}:
- Al therapy + GnRH agonist\textsuperscript{[5]}: 4.6%
- Ovarian failure secondary to chemotherapy\textsuperscript{[6]}: 7.0%

Lumbar Spine BMD Loss at 1 Yr (%)

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

<table>
<thead>
<tr>
<th>Bone scan</th>
<th>Bone Health: non-metastatic</th>
<th>SRE Delay, Prevention: metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>negative</td>
<td>positive</td>
<td>Prevent SREs: fracture, spinal cord compression, radiation to bone</td>
</tr>
</tbody>
</table>

**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  
  - alendronate  
  - 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*

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

- Urologist
- Medical Oncologist
- Radiation Oncologist
- Social Supports
- Patient
- PCSC
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.prostatecentre.com/patient-information/PCSC](http://www.prostatecentre.com/patient-information/PCSC)  
    • [www.Lifeonadt.com](http://www.Lifeonadt.com) (patient blog)
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.
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
Acknowledgements

- Dr. Tia Higano
- Dr. Larry Goldenberg
- Ms. Christine Zarowski
- Dr. Richard Wassersug
- Dr. Lauren Walker, Dr. John Robinson, Dr. Tony Soeyonggo, Dr. Padraig Warde, Mr. Phil Pollock
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

**DRUG INTERACTIONS**

<table>
<thead>
<tr>
<th>Drugs that increase enzalutamide exposures</th>
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<tbody>
<tr>
<td>CYP2C8 inhibitors</td>
<td>i.e. gemfibrozil</td>
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<td>CYP3A4 inhibitors</td>
<td>i.e. itraconazole</td>
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<th>Drugs that decrease enzalutamide exposures</th>
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<tbody>
<tr>
<td>CYP2C8 inducers</td>
<td>i.e. rifampin</td>
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<th>Drugs whose exposures may be decreased by enzalutamide</th>
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<tr>
<td>CYP3A4, CYP2C9 and UGTAI substrates</td>
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<tr>
<td>analgesics</td>
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<tr>
<td>anticoagulants</td>
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<tr>
<td>anti-epileptics</td>
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<td>anti-gout agents</td>
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<td>antipsychotics benzodiazipines</td>
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<td>B-blockers</td>
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<td>Calcium channel blockers</td>
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<td>macrobid</td>
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<td>statins</td>
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<td>fentanyl, tramadol</td>
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<td>dabigitran, warfarin</td>
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<tr>
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<td>cyclosporine</td>
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<tr>
<td>BCRP and MRP2 substrates</td>
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