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# ADT Management

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# Speaker Disclosures | Alan So

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- Advisory Boards: None

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Potential for conflict(s) of interest:

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# Mitigating Potential Bias

The scientific planning committee of this program have complete control over the content of this program.

There has been no influence from the sponsors on the content.

# Learning Objectives

Upon completion of this program, participants will be able to:

- 1. Discuss the adverse side effects of ADT for the treatment of prostate cancer
- 2. Understand treatments to mitigate the adverse side effects of ADT
- 3. Develop a role for family physicians in the multi-disciplinary team to treat prostate cancer in ADT

CUA GUIDELINE

# *UPDATE* – Canadian Urological Association guideline on androgen deprivation therapy: Adverse events and management strategies

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# Androgen deprivation therapy (ADT)

- ADT is the removal of serum testosterone either through medications or surgical castration
- Used across various stages of the disease
- Considered the "*back-bone*" to all systemic therapies in the management of advanced prostate cancer
- ADT is associated with significant adverse events that span across multiple organ systems

# Domains affected by ADT

- Cardiometabolic health
- Bone health
- Hot flashes
- Breast events
- Cognitive function
- Fatigue and anemia
- Sexual function
- Overall health-related quality of life

# Goals of ADT

**1. In a multidisciplinary approach, the overall goal of ADT in prostate cancer is to optimize oncological outcomes while maintaining acceptable health-related quality of life.**

**2. The family physician is a key member of the team.**

CV cancer survivorship issues begin at the time of diagnosis… not years after completion of treatment.

# Cardiometabolic health

**1. Cardiometabolic health refers to the effects of ADT on cardiovascular disease (CVD), body composition and metabolic parameters**

**2. ADT impacts multiple domains of cardiometabolic health**

**3. Medical optimization of risk factors is critical to mitigating ADT-related complications**

# Cardiometabolic health: Adverse events

- ADT may increase the risk of **cardiac complications**, especially in patients with pre-existing CVD or a history of major adverse cardiac events (MACE), which includes stroke, myocardial infarction and unstable angina
- ADT may also increase the risk of **venous thromboembolism**
- ADT is associated with **changes in body composition**, including increased body weight and fat mass, decreased lean body mass and decreased muscle mass
- **The risk of cardiac complications increase the longer men are on ADT…unfortunately many men are on ADT for the rest of their lives**

# Cardiometabolic health: Adverse events (cont'd)

- The **metabolic complications** of ADT include insulin resistance, glucose intolerance, and changes in lipid profile
- ADT is associated with increased risk of incident **diabetes** and may worsen glycemic control in men with a pre-existing diagnosis
- Men receiving ADT may be at risk for developing **metabolic syndrome**

# Cardiometabolic health: CUA Recommendations

- The patient's **primary care provider** should be informed that the patient has been initiated on ADT and that there may be adverse events associated with this therapy *(Expert opinion)*

- Providers should obtain a **comprehensive baseline physical examination** prior to ADT initiation that includes blood pressure, weight, waist circumference, and calculation of body mass index (BMI) *(Expert opinion)*

# Cardiometabolic health: CUA Recommendations (cont'd)

- Patients should have their blood pressure monitored and **hypertension should be treated** *(Expert opinion)*
- **Dyslipidemia should be treated according to current best practice guidelines *(Expert opinion)***
- Metabolic assessments should be continued at 6–12-month intervals throughout treatment duration *(Expert opinion)*
  - *Lipid assessment (Cholesterol profile)*
  - *Diabetic risk assessment (HgB A1c, serum glucose)*
  - *Cardiac risk assessment (CRP, BNP, and ECG if indicated)*

# Cardiometabolic health: CUA Recommendations (cont'd)

- **Lifestyle modifications (smoking cessation, dietary modifications, exercise) should be strongly encouraged *(Expert opinion)***
- Patients should be encouraged to attend **supervised exercise programs** using a combination of resistance and aerobic training *(Level of evidence [LE] 2, strong recommendation)*
  - *Can be offered in local cancer centre, Canadian Cancer Society, Prostate Cancer Foundation Canada*

# Cardiometabolic health: CUA Recommendations (cont'd)

- In patients with a history of myocardial infarction or stroke should be **referred to a cardiologist or cardio-oncologist** for assessment and medical optimization at the time of initiating ADT *(Expert opinion)*
- All patients receiving ADT should undergo a baseline cardiovascular risk assessment and be monitored for cardiovascular complications while receiving therapy *(Expert opinion)*

# Bone health

**Use of ADT in men with PCa has detrimental effects on bone health, including decreased bone mineral density (BMD), osteoporosis, and increased risk for clinical fractures**

# Bone health: CUA Recommendations

- A comprehensive **history and physical examination** to include fall risk and height measurement should be performed prior to initiating ADT *(Expert opinion)*
- Providers should obtain baseline calcium and 25-hydroxyvitamin D levels at the start of ADT *(Expert opinion)*

# Bone health:
# CUA Recommendations (cont'd)

- Patients should be counselled regarding **smoking and alcohol cessation** *(Expert opinion*)
- Patients should be encouraged to participate in **exercise therapy** using a combination of resistance and aerobic training, preferably in a supervised setting *(LE 2, strong recommendation)*

# Bone health: CUA Recommendations (cont'd)

- Providers should screen men initiating long-term ADT for osteoporosis using **BMD testing** with dual energy x-ray absorptiometry (DXA) (as per the 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada) *(Expert opinion)*
- A 10-year major **osteoporotic fracture risk** using a validated tool should be calculated *(Expert opinion)*
  - *FRAX score*
  - *CAROC score*

# Bone health: CUA Recommendations (cont'd)

- Men diagnosed with osteoporosis, those with history of fragility fractures in the hip or spine, those with a history of multiple fragility fractures, or those with a moderate or high 10-year fracture risk should be treated with a **bisphosphonate or denosumab at doses recommended for the general population** *(LE 1, strong recommendation)*
- DXA should be repeated every 2–3 years in men at low risk for fractures receiving ADT. In men with osteopenia or those at moderate or high risk for fractures, DXA should be repeated every 1–2 years until treatment cessation. Patients started on pharmacological therapy should have followup DXA to assess for treatment response *(Expert opinion)*

# Hot Flashes

- 80% of men on ADT have hot flashes (vasomotor symptoms)
- Similar to menopausal hot flashes, these symptoms include an intense heat sensation, flushing and diaphoresis that usually involve the face and trunk
- Episodes may occur early after initiation of ADT, and may occur repeatedly
- Can last for a few to several minutes
- Although the severity is variable, this can be impactful on the patient's quality of life

# Hot Flash - treatments

- Avoid triggers:
  - EtOH, caffeine, spicy foods
- Pharmacologic therapy may be helpful:
  - SSRI/ SNRI
  - Gabapentin
  - Oxybutinin
  - Novel medications such as NK-3 antagonists (fezolinetant) being studied and efficacy still unknown
- Acupuncture, exercise and cognitive therapy have also be shown to have some benefit

Qin, Mertens, et al. Translational Andrology and Urology , 2024

# ADT - Other adverse events

| | |
|---|---|
| **Breast events** | • Uncommon in men receiving GnRH agonists, antagonists or orchiectomy. Treatment with tamoxifen is most effective |
| **Cognitive function** | • Monitor for cognitive decline and depression |
| **Fatigue and anemia** | • Encourage exercise therapy |
| **Sexual function** | • Referral to sex therapists and medical management. Use of intermittent ADT may be considered |
| **Health-related quality of life** | • Encourage exercise therapy and consider intermittent ADT |

# Conclusions

- ADT improves survival in men with PC and is a mainstay of treatment
- ADT is associated with AEs that span multiple organ systems and should be reserved for those who are likely to derive an oncological benefit
- Patients require appropriate counselling regarding adverse events
- Multidisciplinary approach is needed to manage potential complications of ADT

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