Urology CHEAT SHEETS

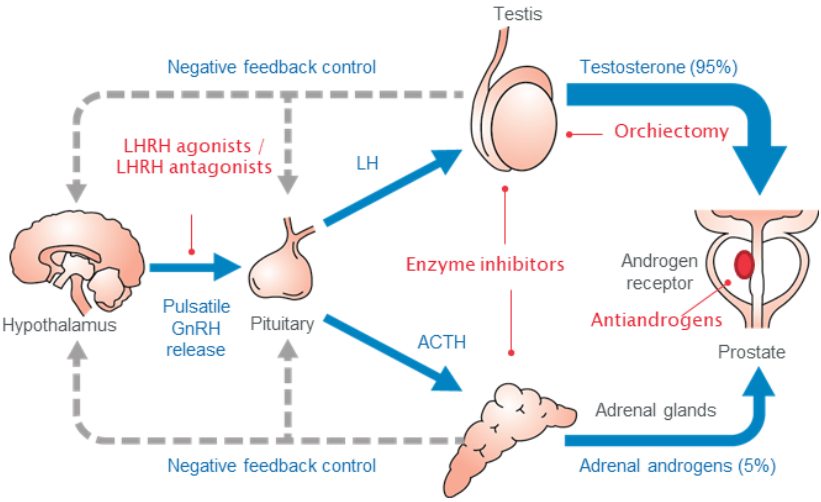
HORMONE THERAPY IN PROSTATE CANCER

WHAT IS HORMONE THERAPY OR ANDROGEN DEPRIVATION THERAPY (ADT)?

ADT reduces circulating testosterone levels to castration levels and blocks androgen stimulation of prostate cancer (PCa) cells. Due to androgen dependence of prostate tumour cells, the goal of this treatment is to reduce levels of androgens or to inhibit its union to androgen receptor (AR) in tumour cells.

Castration concentration is defined as a testosterone concentration below 50 ng/dl (1.7 nmol/l). The blood testosterone level after surgical castration is approximately 15 ng/dl therefore, it is currently accepted that the testosterone level at castration should be less than 20 ng/dl (1 nmol/l).

TYPES OF ADT:



Modified from Drudge-Coates. Int J Urol Nurs 2009;3:85-92

1. ORCHIECTOMY:

Bilateral subalbugineal orchiectomy is an alternative to medical androgen deprivation therapy to reduce androgen production as quickly as possible.

2. LHRH ANTAGONISTS:

Block the **LHRH receptor**, reducing LH synthesis, which reduces testosterone production. **Degarelix.**

3. LHRH AGONISTS:

Over-stimulate the pituitary to negatively regulate the LHRH receptor, reducing LH synthesis, which reduces testosterone production. **Leuprolide, Goserelin, Triptorelin.**

4. ENZYME INHIBITORS:

Selective CYP17 enzyme inhibitor (enzyme expressed in testicular, adrenal, and prostatic tumor tissue).
Used in castration sensitive and resistant metastatic PCa in combination with ADT. **Abiraterone acetate.**

5. ANTIANDROGENS:

- **FIRST-GENERATION:**

Prevent androgens from mediating their biological effects, blocking the androgen receptor (AR) and/or inhibiting or suppressing androgen production. **Cyproterone acetate (steroidal), bicalutamide, nilutamide, and flutamide (non-steroidal)**

- **APALUTAMIDE: Selective AR antagonist.**

Indicated for non-metastatic castration-resistant PCa and metastatic castration-sensitive PCa in combination with ADT.

- **ENZALUTAMIDE: Selective AR antagonist.**

Inhibitor of AR signalling and AR antagonist. Indicated for metastatic castration-resistant PCa, non-metastatic castration-resistant PCa and metastatic castration-sensitive PCa in combination with ADT.

- **DAROLUTAMIDE: Selective AR antagonist**

It competitively inhibits androgen binding, nuclear translocation of the AR and AR-mediated transcription.
Indicated in non-metastatic castration-resistant PCa in combination with ADT.

INDICATIONS OF ADT:

1. MONOTHERAPY AS INITIAL TREATMENT:
Patient not suitable for other local or systemic treatment, not suitable for active surveillance or watchful waiting and patients with the following characteristics: high-risk tumour, PSA Doubling Time (PSA-DT) ≤12 months and: PSA≥50ng/mL or poorly differentiated tumours.

2. ADJUVANT TO RADIOTHERAPY: Intermediate-risk local PCa: 4-6 months adjuvant ADT. High-risk local PCa: 2-3 years adjuvant ADT.

3. ADJUVANT TO SALVAGE RADIOTHERAPY AFTER RADICAL PROSTATECTOMY: pT3b-pT4, Gleason Score ≥8 and pre-salvage PSA ≥ 5 ng/mL.

4. MONOTHERAPY IN BIOCHEMICAL RECURRENCE AFTER RADICAL TREATMENT: Patient with long life expectancy and PSA-DT ≤ 6-12 months or initial ISUP grade ≥2-3.

5. ADJUVANT TO RADICAL PROSTATECTOMY WITH POSITIVE LYMPH NODES: 2 of 3 of the following: ISUP 4-5, pT3 or positive margins.

6. INTENSIVE ANDROGEN DEPRIVATION THERAPY: Different combinations of enzyme inhibitors or new antiandrogens, plus classic androgen deprivation therapy. Advanced prostate cancer (castration resistant or metastatic prostate cancer).