Vyuhpharma

PROSTATE CANCER

ONCOLOGY

Novel & emerging therapies in prostate cancer - current & future outlook

Hormonal therapy continues to be a mainstay in early disease, but nevertheless many pts progress to advanced stages with poor prognosis

Prostate cancer is a hormone driven cancer

Prostate cancer is primarily regulated through androgen receptor (AR) signaling for its maintenance and progression. Inhibition of androgen synthesis to drive testosterone to low levels either through hormonal therapies (ADT) or orchidectomy is the SoC in prostate cancer

Androgen deprivation

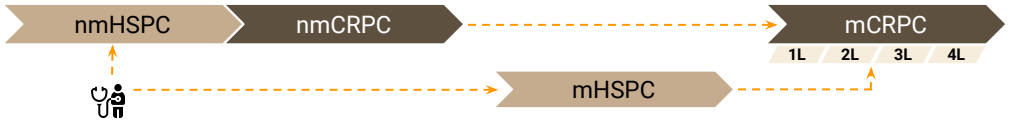
Systemic Tx

ADTs

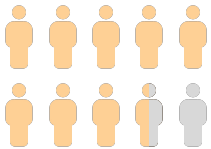
Surgical

Orchidectomy

Depending on the hormonal sensitivity/response shown to ADTs, they are mainly classified into **HSPC & CRPC stage** and further subdivided based on metastases



20% of men advance to castration-resistant prostate cancer (CRPC)



30%–78%

~24 months

No longer respond to hormonal treatment

Of CRPC patients, ~84% have metastatic disease

Only 30-70% of patients with mCRPC may respond to therapies

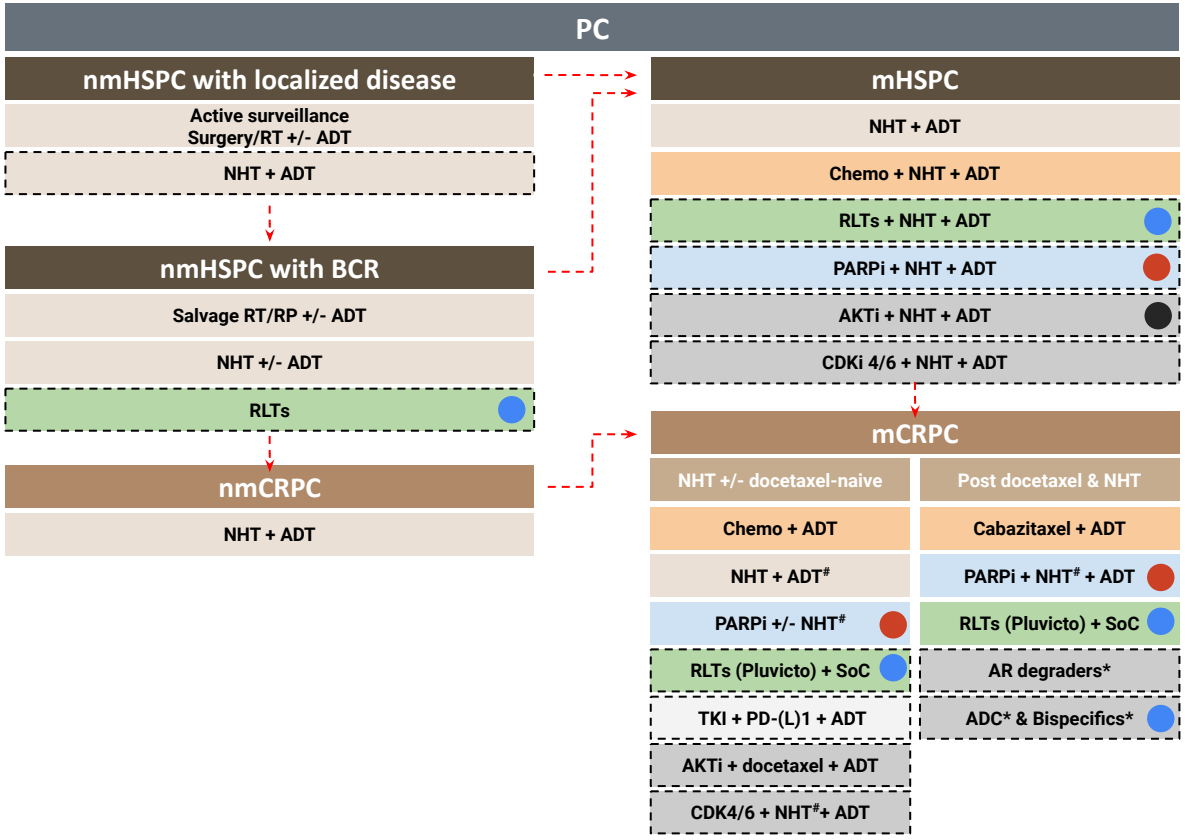
Survival progression to mCRPC

PSA & biopsies remain the gold standard for initial diagnosis. Approval of advanced imaging techniques like PSMA PET is replacing conventional scans (like MRI)

PSMA has became a validated diagnostic & therapeutic target. 6+ PSMA targeting PSMA PET and 1 RLT (therapeutic) have been approved

PSMA is a transmembrane protein highly expressed in prostate cancer and is associated with poor prognosis. Higher expression of >80% in prostate tumor and low expression in other non-prostate cells allow selective targeting for diagnostic & therapeutic modalities

NHTs are now in BCR; PARPi & RLTs are approved newer class treatments in mCRPC while many others are in Ph 3; similar trends expected in mHSPC



KEY TAKEAWAYS

Early PC: Definite therapy (surgery & RT) +/- ADT used. NHTs have started receiving approval in nmHSPC with BCR. Ph 3 investigation ongoing in localized setting with NHTs

nmCRPC: Lower interest due to declining expected incidence. NHTs are preferred in high-risk patients

mHSPC: Increased diagnosis due to lower utilization of PSA screening & higher use of PSMA-PET. ADT Tx intensification with NHT (double) or with chemo+NHT (triplets) are the current SoC NHT + ADT + chemo triplet is a recommended SoC for high burden disease. Other key MoAs, RLTs (Pluvicto), AKTi, PARPi, CDK4/6i still in clinical stages

mCRPC: The space is crowded. The PSMA+ve space is occupied by Novartis Pluvicto. Many pts are already exposed to both NHT & chemo in pre-mCRPC lines. PARPi limited to small subset (HRRm) while AKTi is delayed. AR degraders/ inhibitors and ADCs are emerging therapies in this space, but possibility of approvals in 2027 & beyond

Chemotherapy is mainstay for NEPC #Regimens Applicable for NHT-naive pts *Approvals in 2027 and beyond

Hormone sensitive Hormone resistant PSMA+ve HRRm AKTi Patients flow Upcoming approvals

Current *vs.* future: Use of novel imaging technique like PSMA PET increasing mHSPC & 1L mCRPC diagnoses; nmCRPC shrinking

	Current	Future
Screening & Diagnosis 	• **PSA & biopsies remain gold standard** for initial diagnosis; MRI widely used, but PSMA PET not widely available • **Decreasing diagnosis of PC** due to fewer PSA screening tests (and consequently lower number of biopsies) • Increase in biomarker testing for HRRm since the approval of Cdx for PARPi in 2020. Both tissue- and liquid-based testing available	• **Biopsies remain important**; PSA scores remain important for diagnosis/prognosis, but not screening • **PSMA-PET scans to become gold standard for imaging but availability still an issue** • HRRm remains standard test during initial diagnosis workup to identify eligibility for targeted therapies
Disease characteristics 	• **Decrease in the** number of **PC patients diagnosed at localized stage** due to fewer PSA screenings • Increasing incidence of M1 mHSPC and declining BCR & **M0 nmCRPC pts (due to increasing detection of metastasis by PSMA imaging)** • In mCRPC, numbers are relatively stable • Increasing rate of NHT resistance, even in early mCRPC	• **Locally advanced to further shrink** because of decrease in PSA-based screening assays • **Strong increase in M1 and 1L mCRPC** (due to PSMA PET scans & later diagnosis) • In mCRPC, almost all patients are NHT exposed and higher chemo-refractory patients (due to triplet usage in mHSPC) • Growing NHT resistance population, even in mHSPC
Pricing & Reimbursement 	• Abiraterone **generics have only impacted ZYTIGA U.S. revenues** • **Pricing for NHTs remains stable**, despite expansion into earlier/larger populations • **No indication specific or value-based** pricing yet • Increasing divergence between approved and reimbursed indications	• **Generic competition** causes decline in pricing conditions for all therapies • PSMA RLTs being challenged by other PSMA modalities, but penetration limited to richer markets • Value-based pricing common across all lines • Strong **competition within NHT & PARPi class** • **Cost of diagnostic assays becomes important**

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