Metastatic castration-naive and castration-sensitive prostate cancer

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Conflicts of interest

Dr. So has been an advisory board member for Abbvie, Amgen, Astellas, Bayer, Janssen, Ferring, and TerSera; and has participated in clinical trials supported by Astellas, Ferring, and Janssen.

Dr. Chi has received honoraria from Astellas, Bayer, Janssen, and Sanofi; and has participated in clinical trials supported by Astellas, AstraZeneca, Bayer, Eli Lilly, Essa, Janssen, Merck, Novartis, Pfizer, Roche, and Sanofi.

Dr. Danielson has received advisory board honoraria and speaker fees from Amgen, Astellas, Bayer, and Janssen.

Dr. Fleshner has been a consultant or advisory board member for Abbvie, Amgen, Astellas, Bayer, Ferring, Hybridyne Health, Janssen, and Sanofi; and has participated in clinical trials supported by Astellas, Bavarian Nordic, Bayer, Ferring, Janssen, Medivalion, Nucleix, Progenics Pharmaceutical, Sanofi, and Spectracure AB.

Dr. Kapoor has been an advisory board member for BMS, Eisai, Ipsen, Merck, Novartis, Pfizer, and Roche; a speakers' bureau member for Eisai, Ipsen, Novartis, and Roche; and has received grants/honoraria from BMS, Eisai, Ipsen, Merck, Novartis, Pfizer, and Roche.

Dr. Niazi has received research grants and honoraria from Abbvie, Amgen, Astellas, Astra Zeneca, Bayer, Janssen, and Sanofi; and has participated in clinical trials supported by Astellas, Ferring, Janssen, and Sanofi.

Dr. Pouliot has been an advisory board member for Amgen, Astellas, Bayer, and Janssen; has received payment from Abbott, Amgen, Astellas, Astra Zeneca, Bayer, Ferring, Janssen, and Sanofi; has received grants from Astra Zeneca and Sanofi; and has participated in clinical trials supported by Astellas, Bayer, Ferring, and Janssen.

Dr. Rendon has been an advisory board and speakers' bureau member for, and has received honoraria from Abbvie, Amgen, Astellas, Astra Zeneca, Bayer, Ferring, Jansen, and Sanofi.

Dr. Shayegan has been an advisory board member for Astellas, Bayer, and Janssen; and has received a research grant from Janssen.

Dr. Sridhar has been an advisory board member for Astellas, AstraZeneca, Bayer, Janssen, Merck, and Roche; and has participated in several pharma-supported clinical trials. Dr. Vigneault has been an advisory board member for Abbvie, Bayer, Ferring, and Sanofi.

Dr. Saad has been an advisory board member for and has received payment/honoraria from Abbvie, Amgen, Astellas, Bayer, Janssen, and Sanofi; and has participated in clinical trials supported by Amgen, Astellas, Bayer, Janssen, and Sanofi.

Background

- Metastatic prostate cancer remains an incurable disease
- In Canada, approximately 8% of men with prostate cancer are diagnosed de novo with metastatic disease
- Men with de novo metastatic PC have a poor prognosis, with an estimated median overall survival of approximately 3–4 years
- Compared to PC that develops metastases after diagnosis, de novo metastatic PC has been shown to have a worse prognosis

PC: prostate cancer

Methods

- MEDLINE and Embase were searched from January 2000 to August 2019
- An expert panel comprised of urologists, medical oncologists, and radiation oncologists with significant experience managing mCNPC/mCSPC was used to develop the recommendations
- Levels of evidence and grades of recommendation employ the ICUD/WHO modified Oxford Center for Evidence-Based Medicine grading system
  - Wherever Level 1 evidence is lacking, the guideline provides expert opinion
- The strength of each recommendation is represented by the words STRONG or WEAK

ICUD: International Consultation on Urologic Diseases; mCNPC: metastatic castration-naive prostate cancer; mCSPC: metastatic castration-sensitive prostate cancer; WHO: World Health Organization

Staging and prognosis

- For newly diagnosed PC with any high-risk features, staging with CT scan of the abdomen and pelvis and bone scan (99mTc-MDP) should be performed (*Level 3, Strong recommendation*)
  - High risk features: PSA>20 ng/mL, Gleason score >7, cT3 or greater
- Patients diagnosed with metastatic PC should be classified as high-volume/high-risk or low-volume/low-risk based on conventional imaging and prostate cancer biopsy for prognostication (*Level 2, Weak recommendation*)

CT: computed tomography; PC: prostate cancer; PSA: prostate-specific antigen

ADT

- ADT should be started on men newly diagnosed with metastatic PC (*Level 1, Strong recommendation*)
- Continuous ADT is the standard of care for metastatic PC, while intermittent may be considered in select patients

ADT: androgen-deprivation therapy; PC: prostate cancer

Treatment of the primary cancer in mCNPC

- Patients with low-volume metastatic disease burden should be considered for external beam radiation to the prostate (*Level 2, Strong recommendation*)
- Radical prostatectomy should only be performed in a clinical trial setting (*Expert opinion, Strong recommendation*)

mCNPC: metastatic castration-naive prostate cancer

Systemic therapies: Chemotherapy

- Docetaxel (75 mg/m^2 every three weeks for six cycles) plus ADT is an option for men with good performance status and high-volume metastatic disease (*Level 1, Strong recommendation*)
- Docetaxel plus ADT may also be an option in patients with good performance status with low-volume disease (*Level 2, Weak recommendation*)
- “High-risk” patients with good performance status can also be considered for docetaxel chemotherapy (*Level 1, Strong recommendation*)

ADT: androgen-deprivation therapy

Systemic therapies: Abiraterone acetate

- Abiraterone acetate (1000 mg daily) with prednisone (5 mg daily) plus ADT is an option for patients with at least two of three of:
  - Gleason score of ≥8, presence of three or more lesions on bone scan, or presence of measurable visceral metastasis (*Level 1, Strong recommendation*)
- Abiraterone acetate (1000 mg daily) with prednisone (5 mg daily) plus ADT may be considered for patients with low-volume mCNPC (*Level 3, Weak recommendation*)

ADT: androgen-deprivation therapy; mCNPC: metastatic castration-naive prostate cancer

Systemic therapies: Enzalutamide

- Enzalutamide (160 mg/day) is a treatment option regardless of volume of disease (*Level 1, Strong recommendation*)
- Enzalutamide should not be used *in combination with* docetaxel (*Level 2, Strong recommendation*)
- Enzalutamide may be considered in mCSPC patients *previously treated* with docetaxel chemotherapy (*Level 1, Weak recommendation*)

mCSPC: metastatic castration-sensitive prostate cancer

Systemic therapies: Apalutamide

- Apalutamide (240 mg) is a treatment option regardless of volume of disease (*Level 1, Strong recommendation*)

Prevention of osteoporosis

- All men with mCNPC/mCSPC treated with ADT should be assessed for fracture risk
- All men treated with ADT require vitamin D supplementation (800–1200 IU daily) and calcium supplementation (800–1000 mg total intake daily)
- Those at high risk of fractures should be treated (zoledronic acid 5 mg once a year, alendronate 70 mg weekly, denosumab 60 mg every six months)

ADT: androgen-deprivation therapy; mCNPC: metastatic castration-naive prostate cancer; mCSPC: metastatic castration-sensitive prostate cancer

Other considerations

- There is evolving evidence of the role of radiation to treat asymptomatic distant metastases, especially in low-burden “oligometastatic” disease
- Men with mCNPC/mCSPC should be assessed in a multidisciplinary manner whenever possible (*Level 3, Strong recommendation*)

mCNPC: metastatic castration-naive prostate cancer; mCSPC: metastatic castration-sensitive prostate cancer

Conclusions

- The last five years has seen a significant change in the treatment landscape for patients with mCNPC/mCSPC
  - These new treatments are life-extending
- All men with mCNPC should be considered for treatments that are combined with ADT:
  - Those with high-risk/high-volume disease should be given systemic therapy
  - Those with low-risk/low-volume should be strongly considered for prostate radiation therapy and/or systemic therapy

ADT: androgen-deprivation therapy; mCNPC: metastatic castration-naive prostate cancer; mCSPC: metastatic castration-sensitive prostate cancer