PROSTATE CANCER: 
METASTATIC CASTRATE-SENSITIVE PROSTATE CANCER (mCSPC)

10 QUESTIONS TO ASK YOUR DOCTOR ABOUT METASTATIC CASTRATE-SENSITIVE PROSTATE CANCER (mCSPC)

1. What is metastatic Castrate-Sensitive Prostate Cancer (mCSPC)?
Metastatic Castrate-Sensitive Prostate Cancer (mCSPC) is an advanced form of cancer in which cancer cells have spread from the prostate to other areas of the body, but the patient is still sensitive to androgen deprivation therapy (ADT). (Some mCSPC patients have never had ADT, while others may have had ADT but have recovered testicular function.)

2. Does mCSPC include metastatic disease at initial diagnosis (de novo) as well as metastatic castrate-sensitive disease that develops after prior therapy with curative intent?
Most metastatic Castrate-Sensitive Prostate Cancer patients have already received prior treatment for localized disease; only a small percentage are mCSPC at diagnosis (“de novo”).

3. What is high-volume mCSPC disease and what is low-volume mCSPC?
High-volume mCSPC involves visceral (soft tissue) metastases and/or at least 4 bone metastases, with at least 1 bone metastasis outside of the spine and pelvis. Low-volume mCSPC means metastatic disease that does not meet the criteria for high-volume disease.

4. Should mCSPC be treated systemically (affecting the whole body)?
Yes, because metastatic disease involves the whole body. Standard care for mCSPC includes systemic therapy of: ADT plus either chemotherapy (docetaxel) or one of several newer agents, called ARIs. Selection of therapy depends upon personal tumor biology, volume of the patient’s disease, and patient preferences.

5. What are the most effective systemic treatments for mCSPC?
The mainstay of treatment for mCSPC has always been ADT. Now standard of care for mCSPC includes either ADT plus docetaxel (chemotherapy), or ADT plus a 2nd generation anti-androgen (ARI) of either abiraterone, enzalutamide or apalutamide. Clinical trials have evaluated these agents, leading to their approval.

6. How is treatment personalized on the basis of clinical groups?
In some of the clinical trials evaluating abiraterone, enzalutamide, and apalutamide, patients had different results depending upon their disease burden, meaning in some trials patients with high-volume disease derived different benefit from the drug. Your physician will recommend therapy in part based upon his assessment of your disease volume.

7. What is the role of metastasis-directed (focal) therapy in the setting of effective systemic therapy?
In patients with “oligometastatic disease” (5 or fewer metastases) or low-volume disease, there has been some success in “metastasis-directed radiotherapy”, whereby the metastatic lesions are targeted with radiation, while the patient also receives systemic therapy. This is believed to create an immune response, leading to an improved outcome.

8. What is the role of local therapy to the prostate in mCSPC?
Currently, surgical removal of the prostate in mCSPC is considered only in the context of a clinical trial. However, in some studies radiation therapy (RT) to the prostate has been found to improve overall survival for low-volume disease patients willing to undergo local therapy.

9. What are the quality of life (QOL) issues that should be considered in mCSPC?
Although ADT, chemotherapy and ARIs have known side effects, they are generally well-tolerated. Studies evaluating some of these agents found that overall, patient-reported QOL did not decline with their use. However, treatment must always take into account the patient’s own treatment goals, as well as factors such as age, co-morbidities, time commitment, preference for oral/IV meds, insurance coverage and cost reimbursement.

10. Is PSA monitoring used in mCSPC?
Yes. Sometimes mCSPC transitions into metastatic castrate-resistant disease, and one such indication may be a continuous rise in PSA. The physician should check PSA at intervals in order to identify this transition before it becomes symptomatic or visible on imaging. He can then start the patient on new therapies to delay the effects of castrate-resistant disease.

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Prostate cancer growth is dependent upon testosterone, resulting in the common use of Androgen Deprivation Therapy (ADT), typically LHRH Agonists (leuprolide, goserelin) or GnRH Antagonists (degarelix, relugolix). The development of metastases while the cancer is still sensitive and responsive to ADT is called Metastatic Castrate-Sensitive Prostate Cancer (mCSPC).

Although most prostate cancer cases present without metastases, approximately 1/3 of patients will eventually develop metastatic disease. Most men who develop metastatic castrate-sensitive prostate cancer (mCSPC) do so after failure of curative-intent therapy. The castrate-sensitive phase often transitions to castrate-resistant disease, so the aim is to prolong the castrate-sensitive phase by intensifying treatment with approved new agents, and thereby increase Overall Survival (OS).

The physician should assess the extent of metastatic disease using conventional imaging. “High-volume disease”, used in the mCSPC setting, was first defined in the CHAARTED Trial as the presence of visceral metastases and/or ≥ four bone metastases with at least one outside of the vertebral column and pelvis. “Low-volume” disease is metastases not meeting high-volume definition. auanet.org/guidelines/advanced-prostate-cancer. In some trials that evaluated the 4 agents (4,5), only “high-volume” patients derived benefit; in others there was benefit across all sub-types.

Yes. The standard of care is to add one of the 4 agents (docetaxel, abiraterone, enzalutamide, and apalutamide) to ADT. The focus is on the biological basis of each patient’s disease, volume of disease, and patient preferences (6).

The major clinical trials evaluating the new agents to add to ADT were CHAARTED (docetaxel), STAMPEDE - ARM C (docetaxel plus prednisolone) and G (abiraterone plus prednisolone), GETUG-AFU15 (docetaxel), LATITUDE (abiraterone plus prednisolone), ARCHES and ENZAMET (enzalutamide), and TITAN (apalutamide). These agents have not yet been evaluated one against another, but have similar efficacy. Decisions about an agent to add to ADT for mCSPC patients should be based upon the patient’s disease burden and his preferences (6).

New ASCO Guidelines offer directions about using docetaxel, abiraterone, enzalutamide, and apalutamide, each combined with ADT, and represent separate standards of care for mCSPC. ascopubs.org/doi/10.1200/JCO.20.03256. The Guidelines can also help patients better understand their options and consider their personal preferences. Patients may want early treatment, or prefer oral medication. Other factors include frequency of visits, cost, and existing co-morbidities. Genetic counseling and germline testing may be helpful in considering a PARP inhibitor or I-O therapy.

Radiation to metastases Metastasis Directed Therapy, mostly SBRT), in oligometastatic disease (up to 5 extraprostatic lesions) may prolong life and delay disease progression, and may also create an immune response. A goal of MDT is to delay the initiation of ADT rather than improve OS. (Trials: STOMP with next-gen imaging, ORIOLE with conventional imaging).

Definitive radiation therapy to the prostate (with systemic therapy) may be considered in low-volume disease as it may prolong OS. Two trials : SWOG 1802 [US], and TRoMbone [UK], are investigating. Also, STAMPEDE (Arm H) and HORRAD found that adding RT to the prostate meant better failure-free survival. Those with low-volume disease had an improved OS. ascopubs.org/doi/full/10.1200/JCO.19.01595

Patients should know the potential side effects of ADT, chemotherapy, and the other ARI’s, which have a strong impact on quality of life. Existing co-morbidities play an important part in treatment selection. Studies show that improvements in survival from treatment intensification correlate with improvements in QOL.

Yes. Clinicians should obtain a baseline PSA and then a PSA every 3-6 months after initiation of ADT, and consider periodic conventional imaging. Guideline 12, auanet.org/guidelines/advanced-prostate-cancer; nccn.org/professionals/physician_gls/pdf/prostate.pdf.

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