



Treatment Options in Metastatic Castration-Sensitive Prostate Cancer



Expert Interview With
Atish D. Choudhury, MD, PhD
Dana-Farber Cancer Institute
Boston, Massachusetts



For more information, watch the full program, scan the QR code.

During a *Clinical Consult* presentation, **Atish D. Choudhury, MD, PhD**, spoke with CancerNetwork@ about long-term safety and efficacy data for agents related to metastatic castration-sensitive prostate cancer (mCSPC) as well as several unmet needs for this patient population.

“We have been seeing an increase in men who are presenting initially with metastatic disease,” explained Choudhury, co-director of the Prostate Cancer Center at the Dana-Farber/Brigham and Women’s Cancer Center and assistant professor of medicine at Harvard Medical School. “It means that more men are presenting in a space and we’re getting some increasing data around how to optimally manage them.”

Choudhury expanded on those unmet needs for patients with mCSPC and the various treatment options that are considered for each individual patient.

Clinical Research Supporting Treatment Options for mCSPC

“The backbone of all treatment is androgen deprivation therapy [ADT]. These medications suppress the level of testosterone in the body, since testosterone is the fuel for prostate cancer to grow and spread,” Choudhury explained.

Although ADT remains a key component of treating patients with mCSPC,

Choudhury emphasized that ADT alone works only for a few patients. He explained that intensifying ADT with different treatment modalities has been linked with prolonged survival.

Specifically, Choudhury mentioned docetaxel chemotherapy; androgen receptor (AR)–targeted agents, including abiraterone acetate (Zytiga), apalutamide (Erleada), and enzalutamide (Xtandi); and radiation as viable modalities to intensify therapy.

“It’s not clear from [completed] studies that any one of those agents is superior to any other in terms of overall survival,” Choudhury explained. “We can conclude only that they are all superior to ADT alone.”

Choudhury mentioned 2 studies—ARCHES (NCT02677896), examining enzalutamide plus ADT, and TITAN (NCT02489318), of apalutamide plus ADT—as research that confirmed positive survival data with these drugs in mCSPC.^{1,2} Additionally, both trials led to FDA approvals of their respective agents for patients in this setting.^{3,4}

ARCHES built on previously reported results from the phase 3 ENZAMET trial (NCT02446405), which investigated enzalutamide for metastatic prostate cancer. A significant reduction in the risk of death or progression was noted in the ARCHES cohort of patients who received

“It’s clear from the studies presented [to date] that even patients with low-volume metastatic disease benefit from intensification of treatment. Quality-of-life data from these studies also suggest that patients will benefit from earlier treatment with [androgen deprivation therapy].”

enzalutamide plus ADT compared with placebo plus ADT (HR, 0.39; 95% CI, 0.30-0.50; $P < .001$).¹ In TITAN, the combination of apalutamide plus ADT reduced the risk of death by 35% compared with matched placebo (HR, 0.65; 95% CI, 0.53-0.79; $P < .0001$) and by 48% after adjusting for treatment crossover (HR, 0.52; 95% CI, 0.42-0.64; $P < .0001$).²

“These data confirm findings from previous studies that all demonstrated a prolongation of overall survival when adding an AR pathway inhibitor to initial ADT,” Choudhury explained.

Further, triplet therapies—with abiraterone plus docetaxel/ADT in the PEACE-1 trial (NCT01957436)⁵ and darolutamide (Nubeqa) plus docetaxel/ADT in the ARASENS trial (NCT02799602)⁶—have shown a benefit over docetaxel plus ADT alone for patients with mCSPC.

“It’s clear from the studies presented [to date] that even patients with low-volume metastatic disease benefit from intensification of treatment,” Choudhury explained. “Quality-of-life [QOL] data from these studies also suggest that patients will benefit from earlier treatment with these agents.”

Choudhury further explained the QOL benefits that emerge from intensification of therapy.

“Even though there are [toxicities, these agents] clearly decrease adverse effects associated with the cancer itself,”

Choudhury said. “The QOL with these agents is superior [to that of] patients who are treated with ADT alone.”

Overall, Choudhury emphasized the importance of starting therapy earlier in the process. Unless a contraindication exists for patients, he suggested that the survival and QOL data support the early integration of intensified therapy into mCSPC treatment.

“There’s no cancer-related or QOL reason to not consider these agents earlier in the process,” Choudhury said.

Unmet Needs for mCSPC

“There are a variety of unmet needs to understand how to best manage each individual patient,” Choudhury acknowledged. These include determining optimal treatment for patients with localized disease; the role of androgen receptor therapy intensification for patients treated in the neoadjuvant or adjuvant setting; using molecular diagnostics to determine if a patient should escalate or deescalate treatment; and who should receive salvage radiation and when it should be initiated. Of note, Choudhury mentioned that the US Preventive Services Task Force recommendations in 2012 played a key role in changing the diagnosis and management of patients with mCSPC and specifically cited decreased prostate-specific antigen (PSA) screenings in this setting.⁷

“Where novel imaging comes into play is unclear,” Choudhury explained.

“Should all patients who have a PSA less than 0.2 get a [prostate-specific membrane antigen]/PET scan as part of the radiation planning? I don’t think that answer has been developed yet.”

Concluding Thoughts

“So many advances have been made in hormone-sensitive prostate cancer that survival has been prolonged quite a bit,” Choudhury explained. “Some patients may discontinue treatment and still retain benefit. It’s a constantly changing space and we need to be adaptive on a patient-to-patient [basis] and make sure that our recommendations are individualized.”

Despite the evident need to individualize treatment, Choudhury said the benefit of intensification is clear. “[That] all patients would benefit from some form of intensification is the most important lesson that we’ve learned over the past year,” he said. “The data that have been presented recently justify that patients’ QOL is better with the addition of these other agents, even though many providers are concerned about their toxicities.” ■

REFERENCES

1. Armstrong AJ, Szmulewitz RZ, Petrylak DP, et al. ARCHES: a randomized, phase III study of androgen deprivation therapy with enzalutamide or placebo in men with metastatic hormone-sensitive prostate cancer. *J Clin Oncol*. 2019;37(32):2974-2986. doi:10.1200/JCO.19.00799
2. Chi KN, Chowdhury S, Bjartell A, et al. Apalutamide in patients with metastatic castration-sensitive prostate cancer: final survival analysis of the randomized, double-blind, phase III TITAN study. *J Clin Oncol*. 2021;39(20):2294-2303. doi:10.1200/JCO.20.03488
3. FDA approves enzalutamide for metastatic castration-sensitive prostate cancer. FDA. December 17, 2019. Accessed February 16, 2022. <https://bit.ly/3oPHoov>
4. FDA approves apalutamide for metastatic castration-sensitive prostate cancer. FDA. September 18, 2019. Accessed February 16, 2022. <https://bit.ly/3rRHZYL>
5. Fizazi K, Galceran JC, Foulon S, et al. A phase III trial with a 2x2 factorial design in men with de novo metastatic castration-sensitive prostate cancer: overall survival with abiraterone acetate plus prednisone in PEACE-1. *Ann Oncol*. 2021;32(suppl 5):S1283-S1346. doi:10.1016/annonc/annonc741
6. Smith MR, Hussain M, Saad F, et al. Overall survival with darolutamide versus placebo in combination with androgen-deprivation therapy and docetaxel for metastatic hormone-sensitive prostate cancer in the phase 3 ARASENS trial. *J Clin Oncol*. 2022;40(suppl 6):13. doi:10.1200/JCO.2022.40.6_suppl.013
7. Prostate cancer: screening. U.S. Preventive Services Task Force. May 8, 2018. Accessed February 16, 2022. <https://bit.ly/3uVCv1d>



Interested in more content like this?

SUBSCRIBE TODAY!