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Commentary

Androgen Deprivation Therapy for Advanced Prostate Cancer in the Contemporary Era: Are We Aligning What We Offer to What Our Patients Prefer?

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DESCRIPTION

Developed regions are seeing increasing incidences of Prostate Cancer (PCa). With widening adoption of opportunistic screening and worldwide effect in health advocacy, a substantial amount of patients were diagnosed at early stages. Subsequently, up to one in five patients could progress to recurrent disease, advanced disease or metastatic Hormone Sensitive Prostate Cancer (mHSPC) in 5 years [1]. Meanwhile, a nonneglible portion of patients were still diagnosed with mHSPC at presentation [2]. Aside from Androgen Deprivation Therapy (ADT) which had remained the backbone of treatment, the current standard of care for mHSPC also includes novel hormonal therapy and chemotherapy [3]. With the anticipated long term commitment to these treatments, assessing patient preference has gained traction in the process of shared decision making during consultation [4]. This aims to ensure long term compliance and patient satisfaction [5]. Certain factors were investigated and highlighted to identify patient perspectives in treatment selection.

Side effects profile

Differential side effect profiles in ADT options play a role in guiding physician choice of treatment. When our patients are in face of the different options, its relative importance compared to other factors still remained not fully known. Our group of investigators in Hong Kong conducted a survey-based cross-sectional study in 2022 to assess the impact of patient perception of side effects on ADT preference. 100 Asian mHSPC patients were recruited and given the hypothetical choices of 6-monthly injection, 1-monthly injection and daily oral prescription. They were asked to rate their options separately in the conditions of 1) the treatments have identical efficacy and side effects and 2) the oral prescription and the 1-monthly injection had relatively less risk of Major Adverse Cardiac and Cerebrovascular Events (MACCE). We noted that their preference did not differ significantly given the different side effect profile, with a considerable 56%-61% preferring the 6 month formulary while 38%-39% choosing the oral regimen. This suggested that some other factors may come into play, aside from treatment side effects [6].

Treatment frequency

Traditionally, Gonadotrophin Releasing Hormone (GnRH) agonists were prescribed every 3 or 6 months in the form of injection, and GnRH antagonist being injected every month. Recently, the oral GnRH antagonist given in daily fashion was also available commercially [7]. From healthcare administrative standpoint, infrequent prescriptions aided delivery convenience, and was assumed often to translate to better quality of life for patients with reduced clinical visit [8]. The validity of this assumption in the care of advanced cancer remained unproven.

A Danish study in 2014 attempted to identify the preferred treatment frequency and their reasoning behind. They recruited a group of 1776 PCa patients receiving ADT with mixed indication including relapse after primary treatment and metastatic disease. In the cohort, 38.1% patients preferred frequent treatment of every month or every 3 months. Another 32.4% preferred every 6 or 12 months while the remaining subjects had no preference. This challenged the common assumption that patients would seek to space out follow-ups for better quality of life. The authors reported that the feeling of security was the most common reason why the patients preferred a frequent treatment. On the other hand, wanting less hospital visit and avoiding long journey to hospital were the most common reasons why the rest of the cohort preferred less frequent treatment. They also reported that disease progression was the sole predictor for the cohort's preference, with advanced stage patients being increasingly favour of frequent treatments (Odds ratio=4.4). Contrastingly, age, comorbidities, indication of ADT or side effects were not predictor of their choice [9].

Cost of treatment

While healthcare system patient strategies are vastly heterogeneous and could have significant implication in patient

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preferences, examining the effect of treatment cost could still bring meaningful insight. Presented in the 2023 American Urological Association Annual Meeting, Collins and colleagues conducted a discrete choice experiment for 304 self-reported prostate cancer patients of different stages with history of receiving ADT. Cost was identified as the most important attribute in choosing between ADT options. They reported that reducing out-of-pocket costs from 350 to 5 US dollars per month for ADT scored the highest Relative Importance (RI) of 32.7 out of 100. The preference still stood with patients either receiving ADT for local or metastatic disease, and regardless of their races. Switching from injection to oral formulary ranked the second most important factor (RI=21.6). Both were significantly deemed more important than cardiovascular side effects (RI=7.4) or impact on sexual activity (RI=17.5) [10]. The conclusion may not apply to every region, whose healthcare financing would be substantially different.

Concurrent therapies and the efficacy of treatment

As the treatment spectrum of advanced PCa widened, upfront combinatory options had been incorporated into international guidelines for treatment of mHSPC [3].

Gonzalez and colleagues developed a discrete choice experiments instrument and recruited 550 mHSPC or high risked localised PCa patients due for ADT to examine their preference. From 2021 to 2022, patients in United Kingdom, Canada and the United States of America were asked to choose between ADT alone and combinatory treatment alternatives with hypothetically designed profiles that differ in efficacy, tolerability and convenience. Treatment efficacy was valued most out of the attributes, with more than 75% respondents choosing combination therapies based on improved survival compared to ADT alone, and up to 39% respondents commenting it as the most important factor. Compared to treatment side-effects, the study population reported that efficacy was valued 50-100%more important. Convenience factors (frequency of visits, blood investigation, administration) weigh similar as tolerability factors (nausea, skin rash and tiredness) according their study [11]. With treatment efficacy being ranked the most important attribute, it could extrapolate that ADT monotherapy would be considered inadequate by our patients, even if combinatory options bring along additional side effects and administration or monitoring challenges.

Summary

With changing landscape in the treatment of advanced PCa and evolving evidences in concurrent therapies, patient preferences remain to be an important aspect in the shared decision making and should not be overlooked.

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