Case report

Apalutamid for treatment of nonmetastatic castration-resistant prostate cancer – case study

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ABSTRACT

A special form of prostate cancer is non-metastatic castration-resistant prostate cancer. Patients with this form have rising prostate-specific antigen and castrate testosterone levels, with no radiological findings of metastatic disease on computed tomography and bone scan. The phase III trials demonstrated apalutamide, darolutamide or enzalutamide to be associated with a significantly longer median metastasis-free survival. The featured description presents one case of man with non-metastatic castration-resistant prostate cancer who was treated with apalutamide.

Key words: non-metastatic castration-resistant prostate cancer, nmCRPC, androgen receptor targeted agents, ARTA, apalutamide, darolutamide, enzalutamide

INTRODUCTION

Prostate cancer is one of the most frequent malignant cancers in the male population. Recently, there has been significant progress both in the area of biological understanding and treatment of metastatic prostate cancer. Several breakthrough phase 3 studies have led to approval of new drugs, and thus to changes in therapeutic procedures [1].

Treatments initially assessed in more advanced stages of the disease (metastatic castration-resistant prostate cancer [mCRPC]) have begun appearing also at earlier stages.

A special condition involves non-metastatic castration-resistant prostate cancer (nmCRPC) [2]. This group of patients is characterised with continuously growing prostate-specific antigen (PSA) levels despite castrate blood testosterone level. Unless treatment is modified, most patients in the nmCRPC stage record metastases, which significantly affects the quality of life and survival rates. It is currently known that the shorter PSA doubling time (PSADT) ≤ 10 months involves a risk of metastases occurring [3].

The main treatment objective in this group of patients is to prevent the occurrence of metastases and to maintain optimal quality of life. In the event of PSADT progression ≤ 10 months in prostate cancer patients at the nmCRPC stage undergoing androgen deprivation therapy (ADT), the standard procedure is to qualify them for state-of-the-art antiandrogens from the ARTA group (androgen receptor-targeted agents): apalutamide, darolutamide, or enzalutamide [4].

CASE STUDY

In February 2002, a patient aged 78 started diagnostics for prostate cancer due to PSA level elevated to 25 ng/mL. In March 2002, transrectal ultrasound (TRUS) was performed, as well as core biopsy. Histopathology test revealed prostate cancer in both lobes, Gleason score 7 (3+4). Imaging scans did not reveal any metastases. Disease progression baseline was determined according to TNM (tumour, node, metastasis) classification as T2cN0M0. The patient was qualified for combination therapy of androgen deprivation and radiotherapy. Radical radiotherapy was performed in the prostate area, total dose: 65 Gy/g. Next, the patient continued hormonal therapy for 3 years. He reported for control visits and titrated PSA levels with nadir of 0.02 ng/ml. Due to prevailing low PSA levels after 5 years from completing the radical treatment, the patient was referred for further observation in the regional health centre.

In September 2014, the patient was hospitalised due to urinary retention, at which time urethral calibration procedure was performed. In February 2015, PSA levels increased to 4.86 ng/mL. TRUS was performed, which did not reveal any pathologies. Furthermore, imaging scans were requested: bone scintigraphy and computed tomography (CT) of the chest, abdominal cavity and pelvis. Imaging scans did not reveal any metastases. Due to further PSA increase, ADT was introduced in April 2015. During hormonotherapy, significant decrease to PSA levels was achieved (PSA nadir 0.368 ng/mL in June 2017). The patient continued hormonal treatment. In August 2017, urinary retention recurred; the patient was hospitalized for this reason and had the transurethral resection of the prostate (TURP) procedure performed. No material was sampled for histopathological test during the procedure. After TURP, incontinence appeared. The patient remained under urological care.

In November 2021, PSA levels further increased reaching 1.2 ng/mL, despite the ADT. Therefore, the patient was again referred for imaging scans, which did not reveal any metastases. In further tests, PSA levels totalled: 2.2 ng/mL (December 2021), 3.2 ng/mL (January 2022), and 4.1 ng/mL (February 2022). PSA doubling time was assessed, which amounted to 1.3 months. Current disease progression: nmCRPC. Due to biochemical progression, the patient was qualified, within the B56 drug programme, to treatment of non-metastatic castration-resistant prostate cancer. In April 2022, the patient started treatment with apalutamide at the dose of 240 mg once daily, simultaneously with LHRH (luteinizing hormone-releasing hormone) analogue. During the first 3 months of treatment, PSA level reduction to 0.06 ng/mL was achieved. In the sixth month of treatment, imaging scans did not reveal any metastases. The patient did not report any adverse events related to the treatment. He is currently continuing the treatment.

DISCUSSION

Patients at the nmCRPC stage form a special group of patients. This is when we observe constantly growing PSA levels, which often causes patient anxiety. Patients usually have no symptoms of the disease, which additionally enhances the will to introduce treatment that would result in lowering of PSA levels. We know that, at the CRPC stage, approx. 33% patients develop metastases in 2 years [4]. Therefore, in the case of nmCRPC patients, decisions are necessary to modify the treatment and supplement ADT with state-of-the-art drugs from ARTA group to delay the inevitable development of mCRPC.

According to current guidelines, the administration of ARTA drugs should be considered in nmCRPC patients with PSA doubling time ≤ 10 months. Currently, this indication offers three available drugs: apalutamide, darolutamide, and enzalutamide. They all significantly improve the metastasis-free survival (MFS), PSA response, and overall survival. The decision on drug selection must be on case-by-case basis and depend on the risk-to-benefit ration, considering tolerance and treatment safety, as well as other factors, such as interactions among drugs and comorbidities.

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Author declare to have no conflict of interest.

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Ethics:
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