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Original Research

Efficacy of cabazitaxel rechallenge in heavily treated patients with metastatic castration-resistant prostate cancer

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Abstract ***Background:*** Treatment option in patients with metastatic castration-resistant prostate cancer (mCRPC) previously treated with docetaxel (DOC), cabazitaxel (CABA)

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Metastatic castration-resistant prostate cancer;
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Overall survival;
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Safety

and new hormone therapy (NHT) is limited. Rechallenge with DOC is limited because of cumulative toxicities. This study investigated the activity and safety of CABA rechallenge in mCRPC.

Patients and methods: Clinical data were collected retrospectively in 17 centres in Europe. Eligible patients had undergone rechallenge with cabazitaxel after three previous lines of treatment (DOC, NHT and CABA, in any order). Overall survival (OS) and progression-free survival (PFS) were estimated by the Kaplan–Meier method. Data on toxicities were collected.

Results: A total of 69 of 562 patients (Eastern Cooperative Oncology Group performance status 0–1 69%) were rechallenged with CABA (25 mg/m^2 q3w, 58%; 20 mg/m^2 q3w, 27.5%; other, 14.5%) for 1–10 (median 6) cycles; 76.8% received prophylactic granulocyte colony-stimulating factor. Median radiological or clinical PFS with CABA rechallenge was 7.8 months and 11.9 months with initial CABA therapy. OS was 13.7 months (95% confidence interval [CI]: 9.3–15.7) from the first CABA rechallenge cycle, 59.9 months (47.8–67.1) from the first life-extending therapy in mCRPC and 78.3 months (66.4–90.7) from mCRPC diagnosis. Best clinical benefit was improved (34.3%) or stable (47.8%). Lack of response to rechallenge occurred in 17.9% of patients (3.1% with initial CABA). The level of prostate-specific antigen decreased by $\geq$ 50% in 24% of patients at rechallenge (71% with initial CABA). There was no grade $\geq$III peripheral neuropathy or nail disorders.

Conclusions: CABA rechallenge may be a treatment option without cumulative toxicity in heavily pretreated patients with mCRPC who are still fit and had a progression >3 months after the last CABA injections.

1. Introduction

Docetaxel (DOC) was the first agent shown to improve overall survival (OS) in metastatic castration-resistant prostate cancer (mCRPC) and received US Food and Drug Administration and European Medicines Agency (EMA) approval for this indication in 2004 and 2005, respectively [1]. Since 2004, several new agents with different mechanisms of action have become available for the treatment of mCRPC contributing to further improve OS in patients with mCRPC [2]. These agents include the new hormonal therapies (NHT) such as abiraterone acetate (AA) and enzalutamide (ENZA), cabazitaxel (CABA), a next-generation taxane effective in resistant tumours [1], the radiopharmaceutical radium-223 and immunotherapy with sipuleucel-T.

Although the optimal sequence of these agents is unknown, retrospective studies suggest that OS increases with the number of life-extending therapies received and sequential use of DOC, CABA and one NHT, showing a particularly long OS, whatever the order of administration [3,4]. However, once these three life-extending therapies have been exhausted, treatment options are limited, and there is a lack of clinical studies in this area.

Rechallenge with a previously used agent is one approach to the management of patients with disease relapse after all options have been used. However, there are several potential issues with this approach. First, prospective studies have evidenced cross-resistance in most patients between NHTs [5,6]; second, reuse of docetaxel may lose some activity after androgen receptor (AR)-targeted agents [7–10] and is associated with cumulative toxicity especially neurological toxicity [11]. Conversely, CABA, associated with less peripheral neuropathy than DOC [12], does not seem to be associated with cumulative toxicity [13] and retains its activity in patients with primary resistance to DOC [14] and those progressing with NHT [15]. Rechallenge with CABA may thus represent an interesting option in patients still fit to receive it.

This multicentre, retrospective study investigated the efficacy and safety of rechallenge with cabazitaxel in heavily pretreated patients with mCRPC previously treated with DOC, CABA and NHT.

2. Material and methods

2.1. Study design

Data from patients with mCRPC consecutively rechallenged with CABA were retrospectively collected (using an electronic case report form) between December 2013 and September 2016 at 17 centres in France, Italy, UK and Austria. To be eligible, all patients had to be previously treated with three life-extending therapies (DOC, one NHT and CABA) in any order. Patient clinical characteristics and activity of the first CABA treatment and CABA rechallenge were described. Efficacy assessments included prostate-specific antigen (PSA) response (confirmed PSA decrease of $\geq$50% from baseline), best clinical benefit (according to investigator

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