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How the CARD trial has changed the cards on the table for metastatic castration resistant prostate cancer

Dear Editor,

The CARD trial[1] has the aim to show if cabazitaxel – which is known for having lower incidence of side effects than docetaxel when administered to the 20 mg/m^2 dose[2] would be superior to an androgen signaling targeted inhibitors (abiraterone acetate or enzalutamide) in patients who had already undergone docetaxel treatment and had a disease progression within 12 months while receiving abiraterone acetate or enzalutamide.

The eligible patients (255) were randomly assigned in 1:1 ratio to receive either cabazitaxel (25 mg/daily) or an androgen signaling targeted inhibitors (abiraterone acetate 1000 mg or enzalutamide 160 mg) and, after a median follow-up of 9.2 months, the primary endpoint (the imaging-based progression) and the secondary endpoints were evaluated.

The median imaging-based progression-free survival was 8.0 months in the cabazitaxel group vs 3.7 months in the androgen signaling targeted inhibitors group. Also, all key secondary endpoints were in favor of cabazitaxel and post hoc analyses confirmed all the results obtained in the first place.

In the earlier stages of prostate cancer and among patients with metastatic castration-resistant prostate cancer (CRPC), androgen signaling targeted inhibitors and taxanes are likely used as medical treatment, unfortunately, the best sequence among all these treatments remains unknown[3,4] and is mainly guided by drug toxicities or small retrospective experiences.[5,6] In our opinion, data from the CARD trial might suggest a treatment flowchart as reported in Fig. 1. Based on COU-AA-302 and PREVAIL trials[7,8] that have respectively evaluated the efficacy of abiraterone acetate and enzalutamide in patients with metastatic CRPC with no symptoms or mild symptoms and a small number of patients with visceral metastases, we might consider the use of docetaxel as first-line of therapy for patients with symptoms, high volume disease or visceral metastases, followed by an androgen signaling targeted inhibitors and then cabazitaxel, to avoid the subsequent use of the two approved androgen signaling targeted inhibitors. In the scenario of patients suitable for androgen signaling targeted inhibitors, the second line of treatment is docetaxel and as suggested by the data from the CARD trial, the third line of treatment should be cabazitaxel that has improved a number of clinical outcomes, as compared with the alternative androgen-signaling–targeted inhibitor.[1]

In conclusion, although the issue about the optimal sequence of treatment in the CRPC scenario is still unclear, we think that the CARD trial suggested a therapy guideline for metastatic CRPC.

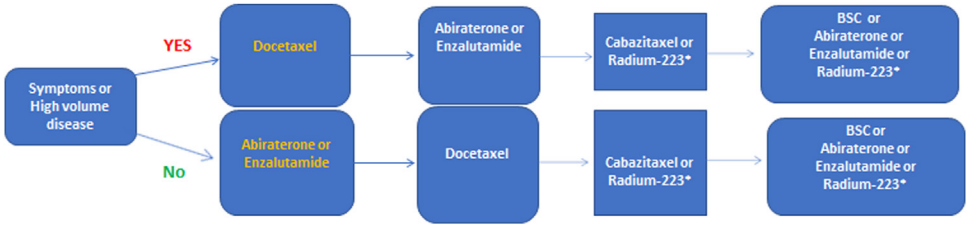

Fig. 1. Proposed flowchart for treatment of CRPC. *Symptomatic bone metastases and no known visceral metastatic disease. BSC: Best Supportive Care.

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Conflict of interest

The authors declare that there are no conflicts of interest

Financial disclosure

The authors declare that there are financial interest

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