Sequencing cabazitaxel and new generation hormonal treatments in metastatic castration resistant prostate cancer patients after first line docetaxel: a retrospective analysis

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Background: In recent years, several new drugs, such as cabazitaxel (CAB), abiraterone (AA) and enzalutamide (ENZ), demonstrated a survival improvement in metastatic castration-resistant prostate cancer (mCRPC). Nevertheless, it is not clear if a specific therapeutic sequence could be associated to a better outcome. The aim of this analysis was to describe clinical characteristics and outcome of mCRPC patients treated with different sequences in a "real-world" clinical setting after docetaxel failure.

Material and methods: We retrospectively reviewed the clinical records of mCRPC patients treated with CAB and at least one new generation hormonal therapy after docetaxel failure between 2010 and 2016 at our Institution. Patients were divided in 2 groups according to treatment sequence: AA or ENZ followed at disease progression by CAB; CAB followed at disease progression by AA or ENZ. For each group, cumulative overall survival (OS) was calculated from the start of the first treatment after docetaxel failure. Outcomes of each line of treatment (proportion of PSA response, progression-free survival [PFS] and OS) were described.

Results: Overall, 37 patients were eligible: 24 received AA or ENZ followed by CAB and 13 were treated with CAB followed by AA or ENZ. Median age was 68 years (range 55-81): pts starting with CAB were significantly younger than those starting with AA or ENZ (median 67 vs 71, p = 0.02). Baseline PSA value was significantly higher in pts starting with CAB (median 373 vs 62, p = 0.006). Proportion of pts with visceral metastases was higher in pts starting with CAB (23% vs 4%, p = 0.08). In patients treated with AA or ENZ followed by CAB, median OS was 46.8 months (95%CI 36.1 – NA). In those who received CAB followed by AA or ENZ, median OS was 21.7 months (95%CI 14.7 – NA). In those who received CAB followed by AA or ENZ, median OS was 21.7 months (95%CI 14.7 – NA). When used after AA or ENZ failure, CAB produced a PSA response in 15/24 pts (62.5%), a median PFS of 9.0 months and a median OS of 20.7 months. When used after CAB failure, AA or ENZ produced a PSA response in 6/13 pts (46%) (6/13), a median PFS of 5.0 months and a median OS of 13.2 months.

Conclusions: Both AA or ENZ after CAB and CAB after AA or ENZ are associated with clinical activity. However, due to differences in clinical characteristics of patients treated with chemotherapy followed by hormonal treatment vs. the opposite sequence, retrospective analysis do not allow the identification of the optimal strategy. Randomized trials are needed to obtain this kind of evidence.