

Efficacy of Abiraterone Acetate plus Prednisone and Enzalutamide sequences in men with metastatic castration-resistant prostate cancer: systematic review and meta-analysis

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Introduction & Objectives

Abiraterone acetate plus prednisone (AAP) and enzalutamide (ENZ) are oral hormonal agents for the treatment of prostate cancer¹⁻⁴. The way both treatments should be sequenced within the prostate cancer patient pathway, it has been a hot topic at the forefront of discussion among different scientific communities. Whether we are referring to prioritize the use of abiraterone or enzalutamide, it's obvious that both are worth having within the prostate cancer armamentarium. Hence, the main question is: which one should be used first, considering the lack of studies that show clinical outcomes regarding the optimal sequence of AAP and ENZ therapies in mCRPC patients⁵⁻⁶?

Therefore, the aim of this study is to evaluate and compare the efficacy between two sequences involving AAP and ENZ, both in the chemo-naïve and post-chemo setting, using PSA-progression-free-survival (PSA-PFS) and overall survival (OS) as efficacy variables.

Materials & Methods

A systematic review was conducted in MEDLINE and EMBASE databases. It included clinical trials and observational studies published from January 2013 to September 2017, reporting PSA-PFS and OS of sequential AAP and ENZ therapies in mCRPC patients. The Grading of Recommendations, Assessment, Development and Evaluation guide (GRADE)⁷ was used to determine the quality of the publications in scope. Publications having a GRADE equal or greater than 2 are carried out for meta-analysis. In the meta-analysis, the heterogeneity between studies was assessed by I^2 and Q test⁸. Moreover, to compare PSA-PFS and OS between therapeutic sequences, AAP-ENZ and ENZ-AAP, the Hazard Ratio (HR) for each event was estimated. The effect size measurements were summarized with fixed effects model. R statistical software version 3.2.3 (2015) was used, applying a significance level of 0.05 for hypothesis testing.

Results

The PSA-PFS of the AAP-ENZ sequence is statistically significantly longer (pooled HR: 0.54; 95%IC, 0.36-0.82, $p < 0.05$) than that observe in the ENZ-AAP sequence (Figure 1), in both, chemotherapy-naïve and post-chemotherapy mCRPC patients. The heterogeneity between studies is $I^2 = 0\%$, $p = 0.58$, meaning that the results from the compared studies are highly consistent (Figure 1). In addition, OS data was in favor of the sequence AAP-ENZ (Figure 2), although a statistically significant difference between sequences is not reached. The pooled-HR for OS in AAP-ENZ sequence vs. ENZ-AAP is 0.75 (95%IC, 0.45-1.26). The heterogeneity between studies is $I^2 = 0\%$; $p = 0.91$, supporting again highly consistent results (Figure 2).

Figure 1. Forest Plot PSA-PFS

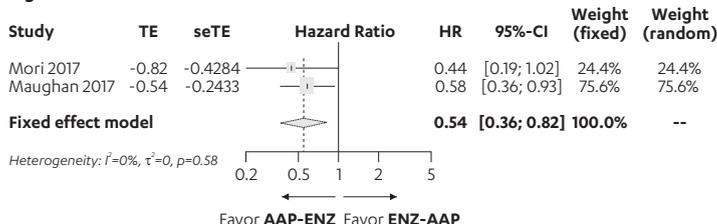
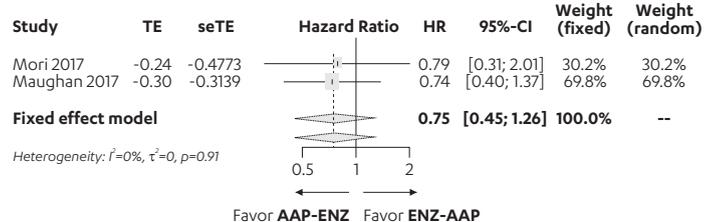


Figure 2. Forest Plot OS



Conclusions

These results lead us to conclude that, abiraterone acetate plus prednisone as a first option in the sequence of treatments for mCRPC patients, shows a statistically significant higher efficacy delaying disease progression comparing to treat with enzalutamide as a first option, with a trend towards improving patient's overall survival.

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