Clinical outcomes after combined therapy with 5alpha-reductase inhibitors and alpha-blockers or either monotherapy in men with benign prostatic hyperplasia: 4-year results from a record-linkage analysis

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Introduction First-line pharmacological treatment options for men with moderate to severe LUTS include alpha-adrenoceptor antagonists (AB) and 5 alpha-reductase inhibitors (5ARIs). The combination therapy (CT) seems to be superior to monotherapy.

Objectives To evaluate the association between treatment of BPH with AB and/or 5ARI and major clinical outcomes (BPH-related hospitalization and BPH-related surgery); to evaluate the effect of BPH medical therapy on the new onset of prostate cancer (PCa); to compare the effectiveness of 5ARI monotherapy vs AB monotherapy as well as CT vs AB monotherapy in reduction of the major clinical events and of the PCa detection.

Materials and methods. Retrospective study based on information coming from a record-linkage analysis (cross link between prescription databases, hospital records and Italian civil registry). Patients’ demographics, clinical and therapeutic characteristics were recorded. Crude incidence rates (IRs) according to pharmacological treatment were calculated. Poisson regression model was used to calculate incidence rate ratios (IRR). The association between treatment and outcomes was assessed by Cox model. Propensity score (PS) matched analysis was performed. Since PS methodology addresses only imbalances due to measured confounders, a sensitivity analysis was performed to
account for potential residual confounders from an unmeasured binary covariate. P-values <0.05 were considered significant. The analyses were done by SAS Statistical Package Release 9.2 (SAS Institute, Cary, USA).

Results. 72943 patients were identified. Patients under 5ARI or CT had a statistically lower rate of hospitalizations for BPH and PCa detection vs patients under AB (respectively IRR 0.44; p<0.0001 and 0.71; p<0.0001).

The results of the matched paired analyses were done on 10,636 patients treated with 5-ARI matched 1:1 with the same number of patients treated with AB and 9090 treated with CT matched with the same number of patients treated with AB alpha-blockers. No significant differences were observed (well balanced groups). According to the adjusted propensity score matched Cox model, the 5ARI monotherapy in comparison with AB monotherapy was associated with a significant reduction of all the outcomes. Moreover, in comparison with AB the CT significantly reduced the risk of PCa (HR 0.67 p<0.0001).

The Adjusted analyses and the Sensitivity analyses confirmed the positive effect of the 5ARI treatment on the main outcomes.

Conclusions: The results of this analysis show the protective effect of 5ARI monotherapy in comparison of AB monotherapy for reduction of BPH-related hospitalizations and prostate cancer detection. The CT compared to AB monotherapy does not appear to significantly reduce the risk of hospitalization for BPH (both medical and surgical), but seems to have a significative effect on the prevention of PCa. The propensity score matching Cox model analysis confirm the results.