Reviewer’s report

**Title:** Meta-Analysis of the Efficacy and Safety of Combination of Tamsulosin plus Dutasteride compared with Tamsulosin Monotherapy in treating Benign Prostatic Hyperplasia

**Version:** 0  **Date:** 05 Jan 2019

**Reviewer:** Maria Angela Cerruto

**Reviewer's report:**

The Authors conducted a meta-analysis to confirm the efficacy and safety of the combination of tamsulosin plus dutasteride compared with tamsulosin monotherapy in treating benign prostatic hyperplasia (BPH) during a treatment period of at least 1 year.

This meta-analysis involved five RCTs and the quality of each RCT was high. The Authors found that the combination of tamsulosin plus dutasteride provides a preferable therapeutic effect for BPH with a higher incidence of sexual side effects, but the combination therapy can markedly reduce risk of BPH-related symptom progression and 2 acute urinary retention relative to tamsulosin.

This conclusion is already present in several urological guidelines for the management of male LUTS. However this meta-analysis corroborates data already present in the urological literature.

Actually it is well known that several studies have investigated the efficacy of combination therapy against an α1-blocker, 5-ARI or placebo alone. Long-term data (four years) from Combination of Avodart and Tamsulosin (CombAT) study showed that combination treatment is superior to monotherapy for symptoms and Qmax, and superior to α-blocker alone in reducing the risk of AUR or need for surgery. The CombAT study demonstrated that combination treatment is superior to either monotherapy regarding symptoms and flow rate starting from month nine, and superior to α1-blocker for AUR and the need for surgery after eight months. combination therapy was superior to monotherapy in preventing clinical progression as defined by an IPSS increase of at least four points, AUR, UTI, incontinence, or an increase in creatinine > 50%.

In the CombAT study, combination therapy reduced the relative risks of AUR by 68%, BPH-related surgery by 71%, and symptom deterioration by 41% compared with tamsulosin, after four years. To prevent one case of urinary retention and/or surgical treatment thirteen patients need to be treated for four years with dutasteride and tamsulosin combination therapy compared to tamsulosin monotherapy while the absolute risk reduction (risk difference) was 7.7%.
The adverse events observed during combination treatment were typical of α1-blockers and 5-ARIs. The frequency of adverse events was significantly higher for combination therapy.

EAU guidelines recommend to offer combination treatment with an α1-blocker and a 5α-reductase inhibitor to men with moderate-to-severe LUTS and an increased risk of disease progression (e.g. prostate volume > 40 mL).

Carrying out the meta-analysis, the Authors could not infer the long-term efficacy and tolerance of combination therapy, and selection bias, subjective factors and publication bias may also affect the final results of their study. Thus they stated that it still needs a lot of RCTs including sufficient sample size and statistics to confirm our findings. More high-quality RCTs with suitable study cohorts are needed to ascertain the efficacy and tolerance of combination of tamsulosin plus dutasteride and tamsulosin monotherapy in treating BPH.

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