ANDROGEN RECEPTOR INHIBITORS FOR THE TREATMENT OF NON-METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

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BACKGROUND

Prostate cancer is the second most common type of cancer in men worldwide. Androgen deprivation therapy (ADT) is usually used as a first-line treatment for advanced prostate cancer. A subset of these individuals have an increase in serum prostate-specific antigen (PSA), which suggests progression of prostate cancer. This state is called castration-resistant prostate cancer (CRPC). Multiple therapeutic options have emerged for the treatment of patients with this condition. Recent data suggest the use of enzalutamide, apalutamide, and darolutamide in patients with non-metastatic CRPC (nmCRPC) on the basis of a metastasis-free survival benefit. These drugs belong to the androgen receptor antagonist class. With the publication of the final analysis of overall survival of the patients in the three main randomized controlled trials that evaluated these drugs, a systematic analysis of their benefits and risks is once again necessary.

OBJECTIVE

The aim of this study is to conduct a meta-analysis of the efficacy and safety of ARIs for the treatment of nmCRPC.

METHODS

A direct meta-analysis was conducted to evaluate the efficacy and safety of the ARIs for the treatment of nmCRPC. An indirect meta-analysis was conducted to compare the drugs against each other. The results of the random-effects model adjusted by the DerSimonian and Laird method were presented. All analyses were conducted in R.

RESULTS

The ARIs were considered efficacious in terms of overall survival (HR=0.74, 95%CI=0.65-0.83, **Figure 1**), metastasis-free survival (HR=0.32, IC95%=0.25-0.41, **Figure 2**), and PSA progression-free survival (HR=0.09, IC95%=0.06-0.13) when compared to the standard-of-care (SOC). They were, though, associated with an increased incidence of serious adverse events (RR=1.21, IC95%=1.07-1.37) and GRADE 3 or 4 adverse events (HR=1.31, IC95%=1.18-1.45).

The network meta-analysis showed no difference between the drugs in terms of overall survival (**Figure 3**), but metastasis-free survival (**Figure 4**) and PSA progression-free survival were significantly higher with apalutamide and enzalutamide than with darolutamide. No difference between the drugs in terms of the serious or GRADE 3 and 4 adverse events was observed.

CONCLUSION

The ARIs are efficacious and relatively safe for the treatment of nmCRPC. The three drugs are similar in terms of efficacy and safety with minor differences in intermediate outcomes.

Figure 1. Direct meta-analysis of overall survival comparing the ARIs with SOC.

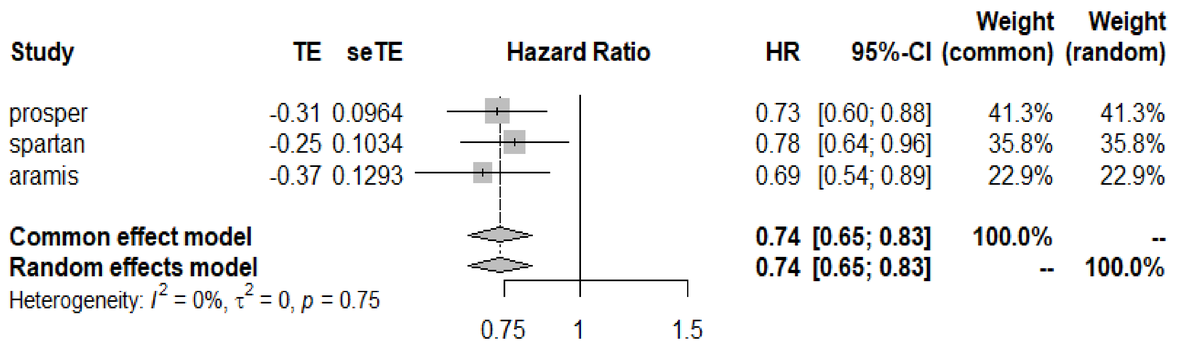


Figure 2. Direct meta-analysis of metastasis-free survival comparing the ARIs with SOC.

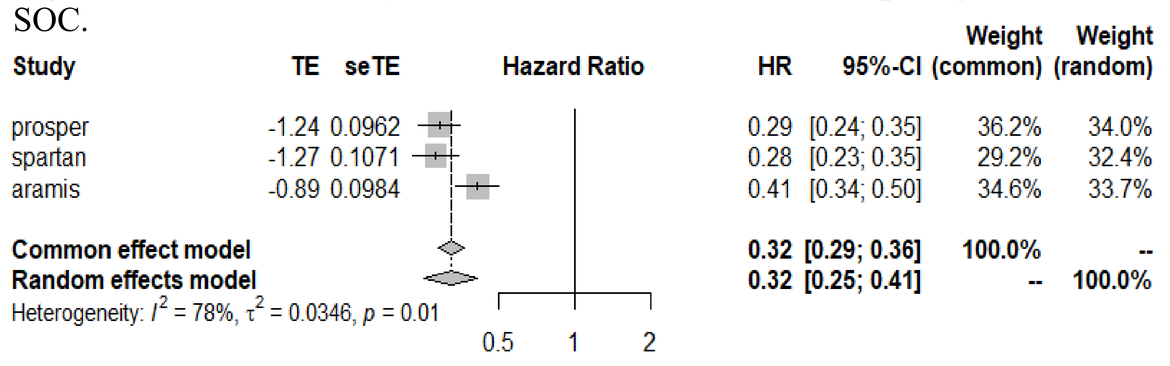


Figure 3. Network meta-analysis of overall survival.

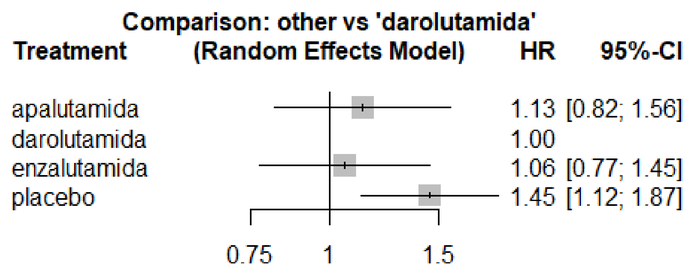
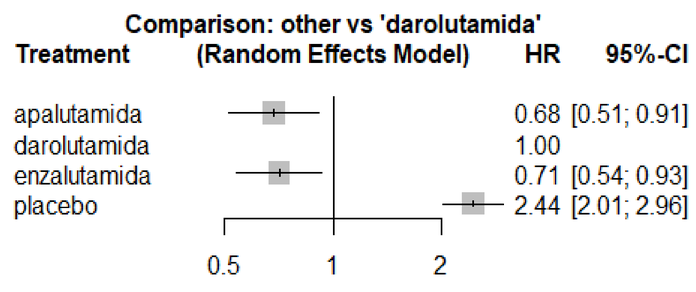


Figure 4. Network meta-analysis of metastasis-free survival.



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