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Safety profile of darolutamide versus placebo: a systematic review and meta-analysis
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Abstract
Background: Darolutamide is an androgen receptor pathway inhibitor (ARPI) used in patients with prostate cancer (PC). In pivotal trials, it has demonstrated a favorable toxicity profile. There are no head-to-head comparison studies between the different ARPIs, but the efficacy of these drugs seems to be similar making the toxicity profile a key element for treatment selection. Methods: We conducted a systematic review of all clinical trials assessing treatment with darolutamide for patients with PC using placebo as the control using the PubMed/Medline and Cochrane library databases. We also performed a meta-analysis to compare the safety of darolutamide versus placebo evaluating adverse events (AE) leading to treatment discontinuation and the rate of the AE reported as “AE of interest” in the ARAMIS trial. The comparison among darolutamide and the placebo group in terms of safety and tolerability was performed using odds ratio (OR) as meta-analytic outcome. Results: We identified three articles comprising 2902 patients for the systematic review and meta-analysis (1652 treated with darolutamide and 1250 with placebo). Darolutamide did not increase AE leading to treatment discontinuation compared to placebo (pooled OR: 1.176, 95% CI 0.918–1.507, p = 0.633). Regarding the “AE of interest” there was no difference between darolutamide and placebo in terms of asthenia, cardiac arrhythmia, cardiac disorder, coronary artery disorder, depression mood disorder, falls, fatigue, heart failure, hot flushes, hypertension, mental-impairment disorder, rash, seizure and weight loss. The only “AE of interest” with a statistically significant difference in favor of placebo was bone fractures (pooled OR: 1.523, 95% CI 1.081–2.146). Conclusions: In our systematic review and meta-analysis, darolutamide showed a toxicity profile comparable to placebo with the exception of bone fractures. In the absence of head-to-head comparison studies between the different ARPIs, the results of our research suggest a preferred use of darolutamide in the approved settings.

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