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LOWER URINARY TRACT SYMPTOMS AS ADVERSE EVENTS OF ANDROGEN AXIS BLOCKADE IN PROSTATE CANCER PATIENTS: DATA MINING OF THE PUBLIC VERSION OF THE FDA ADVERSE EVENT REPORTING SYSTEM

Hypothesis / aims of study
Although androgen axis blockade is widely used for prostate cancer, the impact of this treatment on lower urinary tract symptoms (LUTSs) is not fully understood. The adverse event (AE) profiles of each type of androgen blockade, such as antiandrogens, luteinising hormone releasing hormone (LHRH) agonists, and combined androgen blockade, may differ from each other. In this study, we reviewed the AE reports submitted to the US FDA to confirm the occurrence of LUTSs associated with androgen blockade.

Study design, materials and methods
After the deletion of duplicated submissions and revisions of arbitrary drug names, we analysed AE reports for patients with prostate cancer treated with androgen blockade, that is, bicartamide, fultamide, goserelin, leuprorelin and combination of antiandrogen and LHRH analogues. The reporting odds ratio, one of the standardised official pharmacovigilance tools, was used for quantitative detection of signals, namely, drug-associated AEs. We analysed the association of drugs with urinary incontinence (enuresis, mixed incontinence, incontinence, urge incontinence, urinary incontinence, and stress urinary incontinence), voiding symptom (dysurina, urinary hesitation, terminal dribbling, urinary retention, urinary flow decreased, urinary straining, psychogenic dysuria), storage symptom (pollakisuria, nocturia, micturition urgency, urge incontinence, and mixed incontinence), and pain-related symptom (urethral syndrome, urethral pain, strangury, bladder pain, bladder discomfort, pelvic pain, pelvic discomfort, prostatism, and urinary tract pain).

Results
A total of 188,3921 co-occurrence on male patients were analysed, and the numbers of LUTS-related co-occurrence observed were 250 for bicartamide, 43 for flutamide, 130 for goserelin, and 443 for leuprorelin. For the LUTS analysed, signals were similarly detected for antiandrogen monotherapy, LHRH analogue monotherapy, and combined androgen blockade. The signals were strongest for pain-related symptom, next for storage symptom, for voiding symptom, and weakest for urinary incontinence (Table 1).

Interpretation of results
This study revealed that several types of androgen blockade therapy for prostate cancer have similar impact on LUTS as AEs of drugs. Although LUTS derived from progression of prostate cancer against androgen blockade may be involved in these observations, LUTS can be worse by androgen blockade.

Concluding message
Several types of androgen blockade for prostate cancer can induce similar AEs regarding LUTS worsening.

Table. 1 ROR (95% two-sided CI)

Type of Androgen Blockade	Urinary Incontinence	Voiding Symptom	Storage Symptom	Pain-related Symptom
Antiandrogen	1.72 * (1.32, 2.12)	1.98 * (1.66, 2.29)	2.13 * (1.72, 2.55)	3.48 * (2.22, 4.75)
LHRH analogue	1.86 * (1.53, 2.19)	2.25 * (1.18, 2.51)	2.55 * (2.19, 2.91)	4.24 * (3.09, 5.38)
CAB	1.83 * (1.31, 2.35)	2.29 * (1.86, 2.73)	3.02 * (2.38, 3.66)	4.13 * (2.39, 5.86)

*: signal detected.

Disclosures
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