Impact of concomitant medications (conmeds) and co-morbidities on novel hormonal agents (NHAs) in metastatic castration resistant prostate cancer (mCRPC)

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Introduction

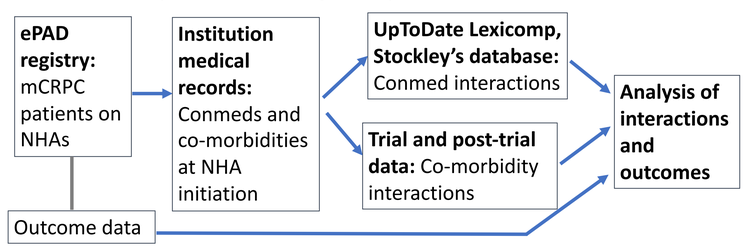
NHAs abiraterone and enzalutamide are commonly prescribed for mCRPC. Although mostly well tolerated, they differ in toxicity profiles and drug-drug interactions. In real-world mCRPC patients, competing conmeds and co-morbidities may impact NHA selection, efficacy and adverse events.

Objective

To evaluate a real-world mCRPC cohort for potential impacts of conmeds and co-morbidities on NHA use and outcomes

Methods

The prospective electronic Prostate Cancer Australian Database (ePAD) was used to identify mCRPC patients prescribed NHAs at three high-volume centres (Dec 2012 – May 2021) and their outcome data.



Conmed interactions were defined as clinically significant, with pharmacist guidance, as below:

Category C	Monitor therapy
Category D	Consider therapy modification
Category X	Avoid combination

Potentially interacting co-morbidities were identified as:

Abiraterone	Enzalutamide
Heart failure	Stroke
IHD	Seizures
Hypertension	Traumatic head injury
Diabetes	Cognitive impairment
Hyperlipidaemia	Depression or anxiety
	Falls
	Parkinson's disease

Descriptive statistics were used to report baseline characteristics, drug interactions and outcomes. Groups were compared with Chi-squared, Fisher's exact or Mann-Whitney tests. Time-to-event analyses utilised Kaplan-Meier curves and were compared through log-rank tests

Results

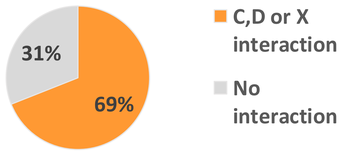
Baseline characteristics of 235 patients who received first or second line abiraterone or enzalutamide for mCRPC are shown in the table below.

Characteristics	Abiraterone, n = 116	Enzalutamide n = 135	All patients n = 235
Median age, years	74.3	71.3	72.5
ECOG, n(%)			
• 0-1	102 (88%)	126 (94%)	213 (91%)
• ≥2	12 (10%)	7 (5%)	16 (7%)
Median conmeds*, n	6	5	5
Interacting co-morbidity with abiraterone, n(%)	84 (72%)	102 (76%)	171 (73%)
Interacting co-morbidity with enzalutamide, n(%)	40 (34%)	19 (14%)	54 (23%)

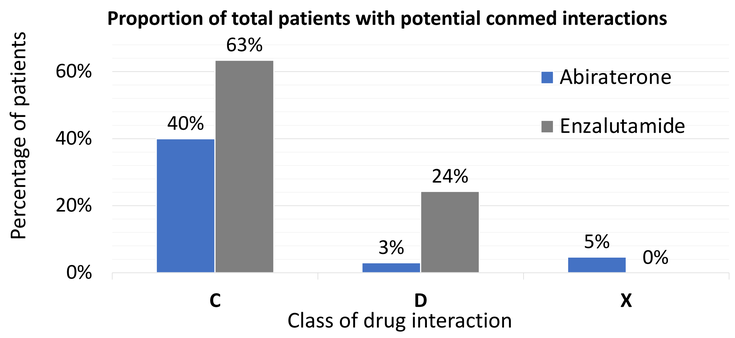
*Conmed count did not include prednisolone co-prescribed with abiraterone, but did include androgen deprivation therapy

Amongst <u>all patients prescribed NHAs</u> :

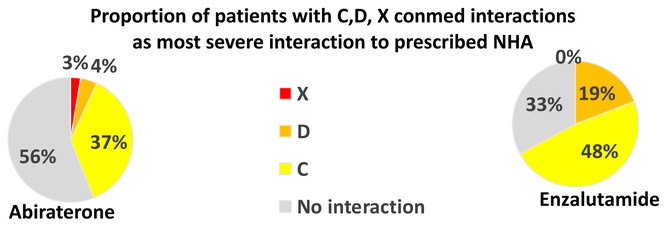
69% had potentially clinically significant conmed interactions with at least one NHA



Proportions of patients with potential category C, D and X conmed interactions are shown below



44% of <u>patients prescribed abiraterone</u> and 67% of <u>patients prescribed enzalutamide</u> had clinically significant drug interactions.



There were no significant differences between abiraterone and enzalutamide groups for PSA50 response rate, median treatment duration, or significant adverse event rate.

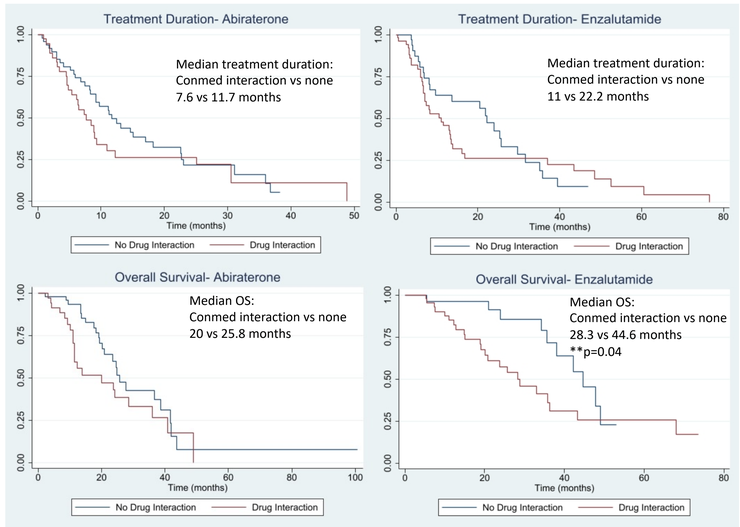
Amongst <u>first line NHA patients:</u>

Outcomes in first line	Abiraterone conmed interaction vs none	Enzalutamide conmed interaction vs none
PSA50 response rate	57% vs 44%	50% vs 74% **
Median treatment duration, months	7.6 vs 11.7	11 vs 22.2
Median OS, months	20 vs 25.8	28.3 vs 44.6 **

**p< 0.05

Patients receiving enzalutamide with clinically significant conmed interactions had a significantly lower PSA50 response rate (50% vs 74%, p=0.04) and median overall survival (OS), with a trend to shorter median treatment duration.

Patients receiving abiraterone with conmed interactions trended to shorter median OS and median treatment duration.



Conclusion

Potential conmed interactions with NHAs are common. Poorer outcomes in patients with drug-drug interactions highlight the importance of reviewing conmeds in treatment selection.

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