University Hospitals Bristol and Weston NHS Foundation Trust

Potential for Drug-Drug interactions with novel ARPIs and concomitant medications: analysis based on the Metastatic Hormone Sensitive Prostate Cancer (MHSPC) patients in the Real-World Evidence (RWE) RECOmMEnD study.

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BACKGROUND

- Prostate cancer (PC) is the most common male cancer and around a third of PC patients present with de novo metastatic hormone sensitive prostate cancer (MHSPC).
- The RECOmMEnD Study is a UK prospective real-world evaluation (RWE) of clinical outcomes in MHSPC patients treated with darolutamide in combination with docetaxel chemotherapy and androgen deprivation therapy (ADT) known as triplet therapy.
- Addition of androgen receptor pathway inhibitors (ARPIs) to ADT has been shown to increase overall survival in this patient group..
- In the UK patients have a choice of apalutamide, enzalutamide or darolutamide.
- Several factors influence the choice of ARPI prescribed but one consideration is drug-drug interactions (DDI) with concomitant medications patients are already taking.
- We therefore sought to evaluate the potential DDI of these 3 treatments on the concomitant medications taken by patients at the start of the RECOmMEnD Study.

METHODS

- 315 patients were enrolled from 21 UK centres over 20 months from November 2022.
- Concomitant medications for each patient at the start of the study were recorded.
- Disease characteristics of patients were evaluated.
- The potential DDIs and advisory for each of these concomitant medications was checked against the 3 ARTAs using Stockley's Drug Interactions Checker.

RESULTS

- 75 patients (23.8%) did not have any concomitant medications recorded.
- In total 842 concomitant medications were recorded
- Median of 3 concomitant medications per patient.
- Darolutamide showed the lowest rate of potential interactions, risk of adverse events, need for avoiding concurrent use and the advice to alter the dose of concomitant medication (Table 1).
- The DDI advisory to monitor patients on concomitant medications was also significantly lower for darolutamide (9.6%) compared with apalutamide (33.8%) or enzalutamide (35.3%).

	Concomitant medication interaction with the ARPI	Increase in adverse event risk with concurrent use	Advice given to avoid concurrent use	Advice given to alter dosing of concomitant medication
Apalutamide	38.6% (325)	0.6% (5)	2.5% (21)	32.6% (275)
Enzalutamide	37.8% (318)	0.7% (6)	1.9% (16)	22.1% (186)
Darolutamide	18.4% (155)	0.1% (1)	0.1% (1)	11.2% (94)

TABLE 1 – ARPI INTERACTIONS
842 concomitant medications were reviewed for their drug-drug interaction with apalutamide, enzalutamide or darolutamide including the advisory provided for each. Table shows percentage and actual number of concomitant medications.

CONCLUSIONS

- Darolutamide had the lowest DDI potential of the three ARPIs investigated.
- The median number of concomitant medications reported were lower than have been reported for other studies. This could reflect fitter patients with fewer co-morbidities being selected for triplet therapy or reporting limitations of RWE studies.
- However, there were still a significant number of DDI which would require management and have implications for optimal ARPI selection, patient monitoring and resource utilisation.

Drug-drug interactions are an important consideration in the choice of ARPI for treatment optimisation in MHSPC patients.

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