Treatment Patterns in Patients with Metastatic Castration-Resistant Prostate Cancer and Drug-Drug Interactions Containing Enzalutamide

Yue Cheng, MS[1,2]; Chris Delcher, PhD[1,2]; Daniela Moga, MD, PhD[1,2,3]; Bin Huang, PhD[4] ; Val Adams, PharmD[1,2]

1 Institute of Pharmaceutical Outcomes and Policy, College of Pharmacy, University of Kentucky, Lexington, KY
2 Department of Pharmacy Practice and Science, College of Pharmacy, University of Kentucky, Lexington, KY
3 Department of Epidemiology, College of Public Health, University of Kentucky, Lexington, KY
4 Kentucky Cancer Registry, Markey Cancer Center, University of Kentucky, Lexington, KY

Background

- There has been a surge in novel therapy (e.g., abiraterone (ABI), enzalutamide (ENZ)) of metastatic castration resistant prostate cancer (mCRPC) before and after docetaxel-based chemotherapy.
- ENZ, as a CYP3A4 inducer, has the potential to interact with other drugs.
- ABI, as CYP17 inhibitor, required prednisone which affect fluid and electrolytes.
- There is no preference of treatment sequences in patients with mCRPC, and real-world drug-drug interactions (DDIs) with ENZ remains unknown.

Objectives

- To evaluate the treatment pattern by lines of therapy (LOT) in patients with mCRPC.
- To describe the incidence and characteristics of co-prescribing ENZ and other medications with DDIs.

Methods

Study design and data source

- Retrospective cohort study
- SEER-Medicare database (2011-2019)

Study cohort and Design

- Patients with ≥1 mCRPC prescription between 2012-2019.
- The index date: the initiation date of mCRPC treatment
- Required ≥ 12 months of continuous enrollment in Medicare Part A, B,D, and with no mCRPC drug use and without HMO enrollment pre-index
- Patients were followed from index date until the earliest occurrence of death, disenrollment or the end of the study period.

Analyses

- All agents required a refill to be included in treatment pattern assessment
- Treatment sequences and number of patients was assessed up to three LOTs at regimen levels.
- Potential ENZ-related DDIs were determined within each LOT, defined as >7 days of concomitant use with another medication.
  - We evaluated DDIs duration in days, as well as prescriber and pharmacy.
  - Interacting drugs (risk category D or X) included warfarin, apixaban, rivaroxaban, torsemide, nifedipine, felodipine
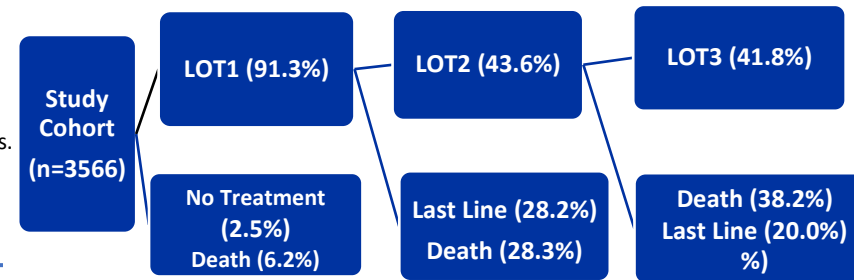
Figure 1 Patient Line of Therapy Flowchart

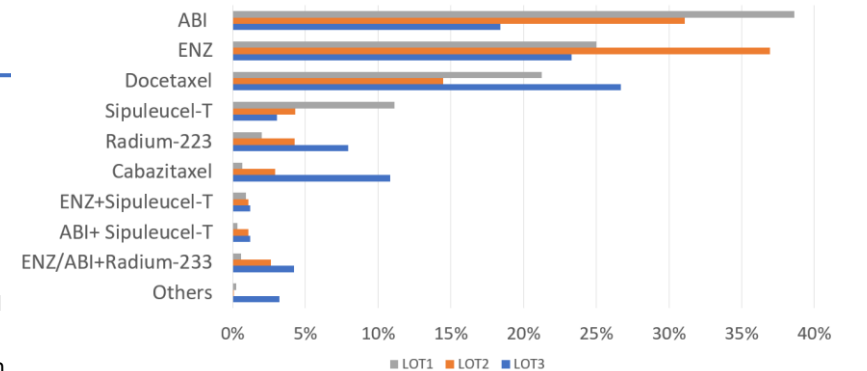**Figure 2** The percentage of patients in each LOT by regimen

Table 1 The number and percentage of ENZ users with DDIs and prescriber and pharmacy

DDI	N (%)	Median Duration	Different Prescribers	Different Pharmacies
Warfarin	142 (9.31%)	95 (8-1125)	327 (98.49%)	311 (99.70%)
Apixaban	68 (4.46%)	90 (8-768)	131 (93.57%)	139 (99.29%)
Rivaroxaban	60 (3.93%)	124 (7-748)	96 (84.21%)	112 (98.25%)
Torsemide	27 (1.77%)	91 (7-475)	71 (100%)	71 (100%)
Nifedipine	23 (1.51%)	105 (13-519)	41 (97.62%)	42 (100%)
Felodipine	10 (0.66%)	184 (61-623)	23 (100%)	23 (100%)

Note: In total, we included 1526 ENZ users

Figure 3 Sankey Diagram of Treatment Sequences
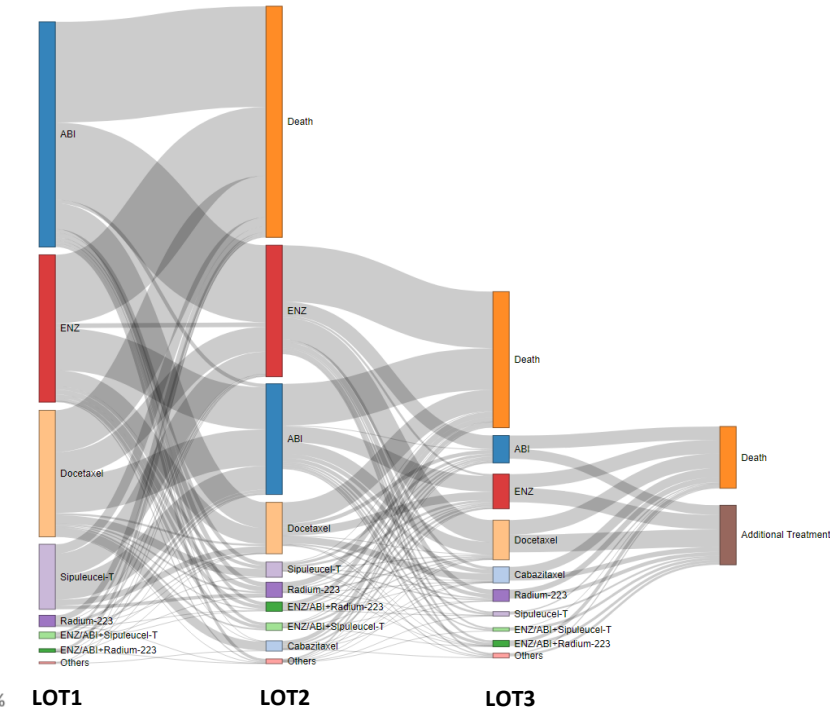
Results

- In total, 3,566 new users of mCRPC drugs were included (LOT1: 91.3%, LOT2:39.8%, LOT3: 16.6%).
- The mean age was 77 years and the median NCI comorbidity index was 0-1.
- The most commonly used agents were ABI, ENZ, and docetaxel.
- The most common DDIs were predominately anticoagulants.
- Interacting drugs were written by different prescribers 84%-100%) and dispensed by different pharmacies (98%-100%) depending on interacting agent.

Conclusion

- ABI and ENZ are the most commonly used first line treatments for mCRPC.
- To prevent DDIs, future studies are needed to enhance the digital network as well as continuing education of health providers.