Frequency, Management and Resource Use of Adverse Events (AEs) in Non-Metastatic Castrate-Resistant Prostate Cancer (nmCRPC) Patients Receiving Apalutamide or Enzalutamide: A Real-World Study.

Authors: Shan Jiang, Della Varghese, Sreevalsa Appukkuttan, Shelby Corman, Nehemiah Kebede, Kajan Gnanasakthy, Cynthia Macahilig, Reg Waldeck, Arif Hussain

Objectives: Second generation androgen receptor inhibitors (SGARIs), apalutamide (APA) and enzalutamide (ENZ) and darolutamide, are approved in the United States (US) for the treatment of nmCRPC. The objectives of this study were to describe the frequency of AEs and actions taken to manage AEs among nmCRPC patients treated with APA or ENZ and their downstream resource implications.

Methods: This is a further descriptive analysis of a retrospective chart review study conducted in 43 US nmCRPC-treating sites. In our sample, the 43 physicians identified 699 nmCRPC patients initiating treatment with APA (N=368) or ENZ (N=333) with 2 patients receiving both, between February 1, 2018 and December 31, 2018 and recorded any AEs experienced. A representative subset of patients, experiencing at least 1 AE for either APA (N=125) or ENZ (N=125), were selected randomly from the initial cohort, and their detailed chart data were extracted to understand the actions taken to manage AEs.

Results: Of the initial cohort of 701 patients, 72.0% and 78.7% of APA and ENZ users experienced ≥1 AE, respectively. The three most common AEs reported were fatigue/asthenia (APA, 30.2%; ENZ, 38.7%), hot flush (APA, 14.1%; ENZ, 13.5%), and arthralgia (APA, 14.4%; ENZ, 12.9%). A subset analysis of patients experiencing ≥1 AE (APA, 125; ENZ, 125) fits the typical nmCRPC patient profile: mostly Caucasian (APA, 72.8%; ENZ, 71.2%), with ECOG score of 0-1 (APA, 84%; ENZ, 88%), and had a median prostate specific antigen (PSA) value of 13 ng/ml and 11 ng/ml in APA and ENZ, respectively. Actions to address AEs included treatment of AE, SGARI discontinuation, dose reduction and hospitalization (Table). AEs were often not resolved (APA, 43.6%; ENZ, 39.4%), and the median duration of days to resolve AEs were 60.0 for APA and 56.0 for ENZ. The most common non-progression reason to discontinue SGARI treatment was unacceptable side effects (APA, 29%; ENZ, 50%).

Variable, n (%)	**Apalutamide (N=125)**	**Enzalutamide (N=125)**
Median duration of follow-up (years)	1.2	1.0
Patients who discontinued SGARI	35 (28.0%)	32 (25.6%)
Patients who progressed to metastasis	20 (16.0%)	16 (12.8%)
Actions taken to address AE		
Treatment for AE	46 (36.8%)	49 (39.2%)
SGARI discontinuation due to AEs	10 (8.0%)	16 (12.8%)
Dose reduction	9 (7.2%)	10 (8.0%)
Hospitalization	7 (5.6%)	5 (4.0%)

Conclusions: This real-world study highlights the clinical and resource use burden of AEs among nmCRPC patients treated with APA and ENZ. The results demonstrate the importance of safety and tolerability as key considerations in shared clinician-patient decision-making regarding SGARI therapy in nmCRPC.