Real-world overall survival (OS) with enzalutamide (ENZ) and abiraterone acetate (ABI) in patients with chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC)  

Daniel J. George, 1,2,3,8 Krishnan Ramaswamy, 1,2,3 Hongyu Yang, 1 Qing Liu, 4 Adina Zhang, 3 Alessandra Greco, 5,6,7 Jasminda Ivanova, 5,6,7 Betsy Thompson, 5,6,7 Birz Eme, 5,6,7 Agnes Hong, 6,7,8 Stephen J. Freedland1,8 1Department of Medicine, Duke Cancer Institute, Duke, Durham, NC, USA; 2Pfizer Inc., New York, NY, USA; 3Flatiron Health Inc., New York, NY, USA; 4Duke Cancer Institute, Durham, NC, USA; 5Department of Dermatology, Cedars-Sinai Medical Center, Los Angeles, CA, USA; 6Department of Medicine, Stanford University Medical Center, Stanford, CA, USA; 7Research Triangle Institute, Research Triangle Park, NC, USA; 8Flatiron Health Inc., New York, NY, USA.

Background and Objectives  
- US guidelines recommend ABI or ENZ for chemotherapy-naive mCRPC.  
- There are no head-to-head phase 3 trials comparing efficacy of ABI and ENZ as 1L treatment for mCRPC with OS as the primary endpoint.  
- Accumulating data show shorter OS for ABI versus ENZ: French National Health System and Taiwan National Health Insurance databases.  
- In the US, a detriment in OS with ABI versus ENZ has been observed in the Veteran’s Health Administration and the Flatiron electronic medical records.  
- To examine OS differences in a broadly representative US national dataset, we compared OS in chemotherapy-naïve patients with mCRPC initiating 1L ABI versus ENZ in the US Medicare population.

Results  
- 2017 patients initiated ABI and 2595 patients initiated ENZ (Figure 1): Baseline characteristics were comparable between cohorts (Table 1), with some exceptions: higher baseline long-term corticosteroid use and lower proportion of diabetes in ABI versus ENZ. Median follow-up was 10.1 months for ABI and 20.3 months for ENZ.  
- IPTW-adjusted median OS was significantly longer for ENZ versus ABI in the overall population (Figure 2) and for patients 75 years old. White patients with baseline cardiovascular disease (CVD), diabetes, both CVD and diabetes, renal disease, and across all socioeconomic strata (Figure 3).  
- Results were consistent after adjusting for variables such as age, site of metastasis, number of previous therapies, use of analgesics, and comorbidities.  
- OS was significantly shorter for ABI (10.6 months [9.6, 11.7]) compared with ENZ (13.6 months [12.4, 15.1]; HR 1.16 [95% CI: 1.06, 1.27], P < 0.001).  
- Improvement in OS was observed across subgroups, including age, site of metastasis, number of previous therapies, use of analgesics, and comorbidities (Table 2).

Methods  
- IPTW-adjusted OS comparison in the overall population of patients with chemotherapy- and NHT-naive mCRPC  
- IPTW-adjusted Cox proportional-hazards models were fitted to compare OS.  
- Subgroup OS analyses between ABI and ENZ defined by baseline characteristics and comorbidities, and based on subsequent treatment, were conducted.

Conclusion  
- In the large, representative US Medicare dataset, patients with chemotherapy-naïve mCRPC treated with ABI had significantly shorter OS than patients treated with ENZ.  
- Results validate previous real-world studies and are robust across different healthcare systems.  
- Findings may be particularly important in older patients and those with comorbidities.