O5 Safety of abiraterone and enzalutamide in prostate cancer patients treated with anticoagulants

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Goena Vives M.C.[1], Rilo I.[2], Garcia R.[1], Mañas L.[1], Beramendi J.R.[2], Quintas L.[1]

[1]Mendaro Hospital, Dept. of Cardiology, Mendaro, Spain, [2]Donostia University Hospital, Dept. of Cardiology, San Sebastian, Spain

Introduction & Objectives: Abiraterone acetate (AA) and Enzalutamide (EZ) are used for the treatment of advanced metastatic prostate cancer with similar benefits in clinical outcomes. EZ is a moderate inducer of CYP2C9, CYP2C19 and strong of CYP3A4. AA inhibits CYP2D6. These metabolic effects in anticoagulated patients(AC) can derive into sub or supratherapeutic drug levels with the subsequent risk of adverse events (BT-AEs). Objectives:evaluate the incidence of BT-AEs in patients treated with EZ or AA into the EudraVigilance (EV) database and search for differences in BT-AEs between patients with reported use of AC.

Materials & Methods: Observational analyses of the EV reference population treated with rivaroxaban, edoxaban, dabigatran, apixaban and AVK for stroke prevention in non-valvular atrial fibrillation and AA or EZ. EV database was searched for post-marketing adverse events (hemorrhagic/thrombotic) reported between January 2011-September 2018. Each report collected data on age, gender, seriousness, suspected and concomitant drugs and causality.

Results: A total of 2,115 AEs was reported on EV until database cut-off date. 71.2% of them were associated to EZ and 28.8% to AA. Figure 1 reports AEs by concomitant use of ACs and by suspected drug:

		TOTAL Aes Group Selected	
Concomitant use of ACs	Product	Total number	Proportion
Reported	Abiraterone	25	18,0%
	Enzalutamide	114	**82,0%**
Not Reported	Abiraterone	584	29,6%
	Enzalutamide	1392	**70,4%**
Total	Abiraterone	609	28,8%
	Enzalutamide	1506	**71,2%**

Differences Rep. vs. Not Rep.	Enza	Abi
Difference	**11,6%**	**11,6%**
95% CI	3,20% to 18,05%	-7,64% to 22,67%
P-value	**0,0085**	**0,2116**

These results show that there are significant differences within EZ reports AEs when ACs are concomitant. On the other hand, there are no significant differences within AA reports AEs whether ACs are reported or not as concomitant for this treatment:

		Vascular & Blood lymphatic disorders		Gastrointestinal disorders		Cardiac disorders, Renal & Urinary disorders		Respiratory, thoracic and mediastinal disorders		Nervous System disorders	
Concomitant use of ACs	Product	Total number	Proportion	Total number	Proportion	Total number	Proportion	Total number	Proportion	Total number	Proportion
Reported	Abiraterone	16	38,1%	1	7,1%	4	14,8%	2	12,5%	2	5,0%
	Enzalutamide	26	**61,9%**	13	**92,9%**	23	**85,2%**	14	**87,5%**	38	**95,0%**
Not Reported	Abiraterone	259	38,5%	48	34,5%	147	36,0%	18	16,8%	112	17,2%
	Enzalutamide	413	**61,5%**	91	**65,5%**	261	**64,0%**	89	**83,2%**	538	**82,8%**
Total	Abiraterone	275	38,5%	49	32,0%	151	34,7%	20	16,3%	114	16,5%
	Enzalutamide	439	**61,5%**	104	**68,0%**	284	**65,3%**	103	**83,7%**	576	**83,5%**
	Differences Rep. vs. Not Rep.	Enza	Abi	Enza	Abi	Enza	Abi	Enza	Abi	Enza	Abi
	Difference	0,4%	0,4%	27,4%	27,4%	21,3%	21,2%	4,3%	4,3%	12,2%	12,2%
	95% CI*	-19,16% to 17,05%	-24,07% to 20,52%	0,394% to 39,19%	-48,57% to 43,16%	1,027% to 32,26%	-26,85% to 36,48%	-21,89% to 17,28%	-57,75% to 29,75%	-0,08% to 17,20%	-52,13% to 21,60%
	P-value*	0,967	0,974	0,0469	0,5708	0,0404	0,3834	0,6864	0,8792	0,0498	0,6502

Conclusions: There seems to be an increasing number of BT-AEs reported with EZ and AA when ACs are concomitant drugs. In our analysis with EV, AA shows smaller number of AEs compared to EZ when ACs are reported as concomitant drugs. Despite these results, a randomized clinical trial would be needed to confirm these findings. In addition,analyses of real-world data may provide additional insights and establish a strategy to manage this subgroup of patients.