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Overall Adverse events of drugs for metastatic renal cell carcinoma: real world reporting patterns from eudra-vigilance database

Cosimo De Nunzio¹, Riccardo Lombardo¹, Giorgia Tema¹, Olivia Voglino¹, Fabiana Cancrini¹, Valeria Baldassarri¹, Antonio Nacchia¹, Cristina Plaza Alonso², Anton Zarraonandia Andraca², Manuel Ruibal Moldes², Andrea Tubaro¹

^{1)Department of Urology, Ospedale Sant'Andrea, Rome, Italy,}

^{2)Department of Urology, Hospital de Montecelo, Pontevra Spain}

Objectives

- ✓ Aim of our study was to analyze adverse events (AEs) associated with drugs (Axitinib, Cabozantinib, Ipilimumab, Nivolumab, Pazopanib, Pembrolizumab and Sunitinib) approved for the treatment of metastatic renal cell carcinoma reported in the eudra-vigilance database.

MATERIAL & METHODS

- ✓ Eudra-Vigilance (EV) database is the system for managing and analyzing information on suspected adverse reactions to medicines which have been authorized or being studied in clinical trials in the European Economic Area (EEA).
- ✓ AEs were analyzed for the following drugs Axitinib, Cabozantinib, Ipilimumab, Nivolumab, Pazopanib, Pembrolizumab and Sunitinib up to September 2019.
- ✓ Adverse events were evaluated for different age groups (<65 vs 65-85 vs >85 years) and by severity. Pooled Relative Risk (PRR) were used to compare data.



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Reaction Groups	Axitinib	%	Cabozantinib	%	Ipilimumab	%	Nivolumab	%	Pazopanib	%	Pembrolizumab	%	Sunitinib	%
Blood and lymphatic system disorders	155	1,6	82	2,5	399	2,2	1209	2,6	608	3,3	655	2,7	2987	4,7
Cardiac disorders	305	3,2	52	1,6	309	1,7	1109	2,4	563	3,0	568	2,3	1614	2,5
Ear and labyrinth disorders	32	0,3	6	0,2	53	0,3	120	0,3	56	0,3	40	0,2	158	0,2
Endocrine disorders	150	1,6	70	2,2	1317	7,3	2510	5,4	216	1,2	1121	4,6	1014	1,6
Eye disorders	86	0,9	10	0,3	246	1,4	555	1,2	200	1,1	334	1,4	747	1,2
Gastrointestinal disorders	1056	11,1	493	15,3	2868	15,9	3748	8,0	2384	12,8	1766	7,2	6917	10,9
General disorders	1885	19,8	442	13,7	1980	10,9	6517	13,9	4135	22,2	3581	14,7	12038	18,9
Hepatobiliary disorders	101	1,1	78	2,4	984	5,4	1802	3,9	1022	5,5	897	3,7	1079	1,7
Immune system disorders	28	0,3	3	0,1	155	0,9	391	0,8	42	0,2	455	1,9	253	0,4
Infections and infestations	359	3,8	139	4,3	649	3,6	2030	4,3	611	3,3	1196	4,9	2271	3,6
Injury and poisoning	229	2,4	164	5,1	988	5,5	3613	7,7	726	3,9	2092	8,6	1737	2,7
Investigations	672	7,1	208	6,4	803	4,4	2172	4,6	1903	10,2	1169	4,8	4722	7,4
Metabolism and nutrition disorders	456	4,8	184	5,7	597	3,3	1733	3,7	847	4,5	898	3,7	2751	4,3
Musculoskeletal disorders	300	3,2	115	3,6	501	2,8	1863	4,0	519	2,8	1013	4,1	2173	3,4
Recurrence	967	10,2	169	5,2	2436	13,5	5551	11,9	2496	13,4	2731	11,2	6032	9,5
Nervous system disorders	692	7,3	208	6,4	933	5,2	2121	4,5	1166	6,2	1137	4,7	3844	6,0
Psychiatric disorders	149	1,6	49	1,5	164	0,9	392	0,8	244	1,3	287	1,2	1167	1,8
Renal and urinary disorders	375	3,9	72	2,2	368	2,0	1068	2,3	574	3,1	642	2,6	1897	3,0
Reproductive system and breast disorders	25	0,3	12	0,4	25	0,1	79	0,2	6	0,0	63	0,3	294	0,5
Respiratory disorders	572	6,0	184	5,7	738	4,1	4407	9,4	116	0,6	1178	4,8	3058	4,8
Skin and subcutaneous tissue disorders	317	3,3	302	9,4	1111	6,1	2650	5,7	71	0,4	972	4,0	3993	6,3
Social circumstances	6	0,1	4	0,1	2	0,0	21	0,0	1	0,0	29	0,1	120	0,2
Surgical and medical procedures	7	0,1	14	0,4	177	1,0	414	0,9	2	0,0	550	2,3	61	0,1
Vascular disorders	574	6,0	143	4,4	253	1,4	625	1,3	129	0,7	1033	4,2	2769	4,3
Total	9503		3226		18085		46750		18658		24442		63749	

RESULTS

- ✓ Axitinib treatment resulted in 1620/9503 (17%) fatal events, older patients presented a higher risk of cardiac disorders (PRR=2,05-2,99, p=0,01) and of ear and labyrinth disorders (PRR=4,8-5,94,p=0,01).
- ✓ Cabozantinib treatment resulted in 233/3226 (7%) fatal events, older patients presented a higher risk of nervous system (PRR=2,15-3,29,p=0,01) and psychiatric disorders (PRR=4,44-6,24,p=0,01).
- ✓ Ipilimumab treatment resulted in 2094/18085 (12%) fatal events, older patients presented a higher risk of gastrointestinal disorders (PRR=1,17-1,47,p=0,01).
- ✓ Nivolumab treatment resulted in 6851/46750 (15%) fatal events, older patients presented a higher risk of musculoskeletal disorders (PRR=1,40-1,60 ,p=0,01).

RESULTS

- ✓ Pazopanib treatment resulted in 2911/18658 (16%) fatal events, older patients presented a higher risk of gastrointestinal disorders (PRR=3,05-4,99,p=0,01)
- ✓ Pembrolizumab treatment resulted in 3428/24442 (14%) fatal events, older patients presented a higher risk of ear disorders (PRR=3,68-4,25,p=0,01) while a lower risk of blood disorders (PRR=0,51-0,83,p=0,01).
- ✓ Sunitinib treatment resulted in 11001/63749 (17%) fatal events, older patients presented a higher risk of psychiatric disorders (PRR=2,25-3,02,p=0,01).



CONCLUSIONS

- ✓ Real life data suggest several and severe AEs in patients treated with drugs for metastatic kidney cancer. Frailly elderly patients (>85 years) presented a different AEs profile when compared to younger patients.