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Pharmacovigilance analysis of acute kidney injury associated with proteasome inhibitors in the Japanese Adverse Drug Event Report Database

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Objectives : Multiple myeloma (MM) is one of the common malignant diseases in older patients. Recently, proteasome inhibitors (PIs) have improved the prognosis of MM. On the other hand, previous studies reported that PIs induce some adverse effects (AEs), including acute kidney injury (AKI) during chemotherapy. Tumor lysis syndrome (TLS) is a typical cause of AKI due to PIs. However, some recent reports have suggested that mechanisms other than TLS may be involved in the onset of AKI. We aimed to investigate the association among AKI, TLS, and PIs in real-world MM cases through a data-mining approach.
Methods : We conducted a retrospective pharmacovigilance analysis using the Japanese Adverse Drug Event Report (JADER) database, a nationwide self-reporting database. We extracted the AE reports suspected to be related to PIs for MM in Japan (bortezomib, carfilzomib, and ixazomib) from April 2004 to September 2023. The definitions of AKI and other diseases were defined according to the preferred terminology by the Medical Dictionary for Regulatory Activities/Japanese (MedDRA/J) version 26.1. We calculated reporting odds ratio (RORs) and 95% confidence interval (CI) for each drug. RORs with a lower 95% CI limit larger than one were considered as a significant signal.
Results : There were 2318 cases considering PIs as suspected drugs (1261 in bortezomib, 698 in carfilzomib, 470 in ixazomib). The most frequent age was in 70s (39.4%). Comorbidities of hypertension and chronic kidney disease were present in 22.8% and 7.2% of cases, respectively. Among 114 AKI cases, only 14 cases had concomitant TLS. A significant association of AKI with PIs was detected in carfilzomib (ROR [95% CI]: 1.99 [1.45-2.72]), whereas not in bortezomib, ixazomib (0.92 [0.67-1.25], 1.18 [0.95-1.47], respectively).
Conclusions : We detected the signal of AKI by carfilzomib. Further investigations are warranted to clarify the mechanism of AKI by PIs.