International Comparison of Suspect Drugs for Severe Cutaneous Adverse Reactions Using Adverse Event Reporting System Databases

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Purpose
For promoting pharmacovigilance worldwide, it is important to exchange drug safety information, such as adverse event reporting system (AERS) data, constructed in many countries. Severe cutaneous adverse reaction (SCAR) is one of very serious side effects. SCAR incidences are known to vary depending on drug and ethnicity, but details in suspect drug-features among countries remain unclear. In this study, to explore international differences in SCAR-inducing drugs, we compared the suspect drugs reported among Japan, the USA and the EU countries, using the Japanese Adverse Drug Event Report database (JADER) and FDA AERS (FAERS) database, and also consider the benefit and issues in comparisons using the AERS databases.

Methods
Primary suspect drugs for SCAR (Stevens-Johnson syndrome, toxic epidermal necrolysis, or mucocutaneous ocular syndrome) reported from 2008 to 2012 were analyzed using JADER (for Japan) and FAERS (for the USA and the EU). Top 20 drugs for the reported case number and the Proportional Reporting Ratio (PRR) in each region, and case backgrounds were compared.

Results
Percent of SCAR cases per total AEs were much higher in Japan (1.1%) compared with the USA (0.06%) and the EU (0.16%). Females were commonly frequent and ratio of younger age (<20 years-old) were higher in the USA and the EU. For top 20 drugs in case numbers, antiepileptic and anti-pyretic/inflammatory drugs, including carbamazepine and acetaminophen, respectively, were common throughout the regions. For top 20 drugs in PRR, major drugs were antibiotics in the EU and the USA, and anti-pyretic/inflammatory drugs in Japan, respectively. Some drugs, such as zonisamide and clarithromycin, were higher in report ranking specifically in Japan.

Conclusion
This study revealed the unique features of suspect drugs for SCAR among three regions, which information would be useful for prioritizing drugs to be watched in each and through the regions. Because of different properties of databases, e.g., drug approved conditions and criteria for reporting, direct interpreting the results should be cautioned. Exchanging other region/ethnicity specific information, both in regulatory and scientific aspects, would be needed to promote worldwide pharmacovigilance.