ADVERSE DRUG REACTIONS, INCLUDING SJS, TEN

SERIOUS CUTANEOUS ADVERSE EVENTS ASSOCIATED WITH PD1 AND PDL1 INHIBITORS: A PHARMACOVIGILANCE ANALYSIS FROM THE RESEARCH ON ADVERSE DRUG EVENTS AND REPORTS PROGRAM (RADAR)

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Introduction: Though reports exist of serious cutaneous adverse events (sCAEs) for Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and erythema multiforme major (EMM) after exposure to some of PD-1 (nivolumab [NI], pembrolizumab [PE]) and PDL-1 (atezolizumab [AT], avelumab [AV], durvalumab [DU]) inhibitors, these associations have not been well-delineated.

Objective: The aim of this study was to determine if an association exists between sCAEs and these agents in the current FDA Adverse Event Reporting System (FAERS) database.

Material and Methods: We searched the FAERS database (for each drug from its approval date to Q12018) for MedDra terms related to SJS, TEN and EM that resulted in a serious outcome (Death, Disability, Hospitalization, Life-Threatening, Required Intervention to Prevent Permanent Impairment/Damage, or Other Serious). Proportional Reporting Ratio (PRR) for detection of a safety signal, defined as number of events >3, chi-square result (>4) and the PRR (>2) was calculated for each drug.

Results: A safety signal was detected for both PD-1 inhibitors: NI (N= 123 reports; PRR: 3.18; 95%CI: 2.67-3.81), PE (N=52; PRR: 3.33; 95%CI: 2.54-4.38), and for one PDL-1 inhibitor: AT (N=19; PRR: 4.68; 95%CI: 2.98-7.33). Notably no safety signal was detectable for DU (N= 2, too few reports) or AV (no reports).

Conclusions: PD-1 inhibitors, NI and PE, and PDL-1 inhibitor AT, were found to be significantly associated with sCAEs, supporting evolving evidence that these agents require close, ongoing dermatologist surveillance to assure adequate safety monitoring.