Cutaneous Immune-Related Adverse Events of Immune Checkpoint Inhibitors

Immune checkpoint inhibitors (ICIs) are widely used to treat multiple malignancies; however, these therapies often lead to cutaneous immune-related adverse events (cirAEs) that lead to discontinuation of therapy. Utilizing surveillance data from the World Health Organization database VigiBase, Le et al. analyzed 10,933 distinct individual cases of ICI-related cirAEs. The cirAEs that had a significant signal and at least 100 cases were vitiligo, drug eruption, lichenoid dermatitis, eczematous dermatitis, bullous pemphigoid, erythema multiforme, Stevens–Johnson syndrome, and toxic epidermal necrolysis. These cirAEs were also associated with both gastrointestinal and thyroid immune-related adverse events. Reports of cirAEs were more common among patients receiving PD-1/PD-L1 inhibitors and those receiving combination therapy. The onset of the cirAEs and the relationship of the cirAEs with certain malignancies were variable and related to the type of cirAE. This large global pharmacovigilance study highlights the types, timing, and clinical features of ICI-associated cirAEs and suggests that oncologists monitor their occurrence for early referral to dermatology to lessen the chances of therapy discontinuation. See pages 2896

A Potential Role of S100A8/A9 in the Development of High-Risk Coronary Plaque Disease in Patient with Psoriasis

Psoriasis is a disease characterized by systemic inflammation that promotes atherosclerosis and consequent cardiovascular disease. The inflammatory S100 family proteins have been implicated in psoriasis as well as in atherosclerosis and cardiovascular disease. In an observational study, Berg et al. found that S100AB/A9 were specifically associated with lipid-rich necrotic core, which is a high-risk coronary plaque feature in psoriasis. Treatment with biologic therapy, including anti-TNF, anti–IL-12/-23, and anti–IL-17 agents, reduced S100A8/A9 as well as lipid-rich necrotic core in patients with psoriasis. These observations support an important role for S100A8/A9 in psoriasis and the development of high-risk coronary plaques and suggest leverage of this factor in mitigation of psoriasis and atherosclerosis risk. See pages 2909

CD39 Expression Levels Affect Neoplastic Lymphocyte Viability and Sezary Syndrome Prognosis

Piccozza et al. used polychromatic flow cytometry to identify a bimodal distribution in CD39+ neoplastic CD4+ T cells that distinguished two groups of patients with Sezary syndrome, a rare but aggressive form of cutaneous T-cell lymphoma. The SNP A/G in rs10748643 of the CD39 gene (ENTPD1) genetiucally controls the expression of this immuno-suppressive marker, and patients with high CD39 expression carrying the A/G or G/G genotype had a better clinical outcome. Although CD39 antagonists serve as therapeutics for many cancer types, CD39 inhibition of activated Sezary cells from patients reduced their apoptosis and increased IL-2 production, cautioning that such treatment may provide a proliferative advantage to malignant cells and sustain chronic skin inflammation in patients with Sezary syndrome. See pages 3009

Psoriasis Treatment with IL-12/-23/-17 Inhibitors and Susceptibility to Candida Infections

Treatment with inhibitors of IL-17 and IL-12/-23 provides benefits to patients with psoriasis; however, the inhibited pathways are also involved in host defense against infection, including Candida infections, which are increased in patients with psoriasis treated with inhibitor therapy. Bruno et al. reported that treated patients exhibited innate and adaptive immune response defects, including complex IL-17 inactivation and downregulation of T helper (Th) 1 and Th17 cell activity as well as decreased IL-6 in patients treated with IL-12/-23 inhibitor and reduced IL-1β, IFN-γ, and IL-10 in patients treated with IL-17 inhibitor. Increased understanding of these immune defects is necessary to facilitate intervention strategies to enable the continuation of inhibitor treatment. See pages 2929

New Insights into the Genetic Landscape of Atopic Dermatitis

Despite the previous identification of many susceptibility loci for atopic dermatitis (AD), undiscovered genetic factors underlie the remaining unexplained heritability of this common inflammatory skin disease. Chen and Chen integrated transcriptome-wide association and phenome-wide association studies to perform a meta-analysis of data from >35,000 cases of AD, revealing 271 susceptibility genes, including 31 unreported genes. These studies provided further evidence for the involvement of the hemic and immune systems in AD and suggest that this disease shares links with multiple respiratory phenotypes. Together, these findings shed light on fundamental pathogenesis mechanisms of AD. See pages 2958