OPEN ACCESS
ARVO Annual Meeting Abstract | June 2024

HLA Class I Alleles are strongly associated with lamotrigine-induced SJS/TEN in a US population

Mohammadali Ashraf; Abdelrahman M. Elhusseiny; James Taekyoon Kwan; Ramy Rashad; Elizabeth Williams; Madeline Marks; Elizabeth Ergen; Benjamin Kaffenberger; Aaron Drucker; Michelle Goh; , Roni Dodiuk-Gad; Robert Micheletti; Suman Pakala; Elizabeth J Phillips; Hajirah N Saeed

+ Author Affiliations & Notes

Investigative Ophthalmology & Visual Science June 2024, Vol.65, 4234. doi:

Abstract

Purpose : Steven Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) is a severe T-cell mediated adverse drug reaction and can cause severe ocular surface disease. Lamotrigine-induced SJS/TEN, in particular, can cause significant ocular morbidity. Although there are strong class I HLA associations for SJS/TEN, the associated HLA allele(s) for lamotrigine-induced SJS/TEN in US populations have not been defined.

Methods : HLA Class I and II genotyping was performed with Illumina Miseq on DNA isolated from whole blood or saliva (Oragene-500) from patients with a history of a minimum of “probable” (ALDEN score > 4) Lamotrigine-induced SJS/TEN. Patients were assembled from the SJS Survivor and Massachusetts Eye and Ear cohorts. Diagnosis of SJS/TEN and lamotrigine as the etiologic agent was assessed by expert adjudication. Additional data collected included age at the time of onset of SJS/TEN, gender, self-reported race/ethnicity, complications of SJS/TEN, and ocular and systemic treatment. Vanderbilt University Medical Center BioVu (biobank) population was used as the genetic control with HLA class I and II imputed from Mega^{EX} typing by SNP2HLA.

Results : Twenty-six patients were identified with a history of lamotrigine-induced SJS/TEN, of which 19/26 (73%) self-identified as White and 24/26 (92%) were women. For SJS/TEN cases, HLA-B*38:01 (7/26) and HLA-C*12:03 (11/26) were strongly associated with lamotrigine-induced SJS/TEN when compared with the BioVu HLA controls (n=94,489; HLA-

B*38:01 (2173/94489); HLA-C*12:03 (6711/94489). P values corrected for multiple comparisons were significant for both associations with Pc = 0.00024 and 0.00014 for HLA-B*38:01 and HLA-C*12:03, respectively). HLA-B*38:01 and HLA-C*12:03 are also in linkage disequilibrium with each other.

Conclusions : For the first time in a US population, we define HLA-B*38:01 and HLA-C*12:03 as associated with lamotrigine-induced SJS/TEN. Future studies may inform recommendations of HLA genotyping prior to the initiation of lamotrigine to avoid this potentially fatal and blinding disease.

This abstract was presented at the 2024 ARVO Annual Meeting, held in Seattle, WA, May 5-9, 2024.