ABSTRACT BOOK ABSTRACTS



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ADVERSE DRUG REACTIONS, INCLUDING SJS, TEN

HLA-B*13:01 IS A PHARMACOGENETIC MARKER OF DAPSONE-INDUCED SCARS : NON-PHENOTYPE SPECIFIC MARKERS

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HLA-B*13:01 allele has been associated with dapsone hypersensitivity syndrome (DHS) in Han Chinese patients and in Thai patients with non-leprosy conditions. Although the parent drug may be important, there is evidence to suggest that DDS-NHOH (dapsone hydroxylamine), formed by cytochrome P450 metabolism, may also be important in pathogenesis. There are no data describing whether HLA class I/II alleles and cytochrome P450 polymorphisms (CYP2C9, CYP2C19 and CYP3A4) are a valid marker for predicting dapsone-induced SCAR in non-leprosy patients in addition to HLA-B*13:01. In a prospective cohort study, fifteen patients with dapsone-induced SCAR (4 SJS-TEN and 11 DRESS), 40 dapsone-tolerant controls and 470 general Thai population participants, were enrolled. Genotyping of HLA class I, II, CYP2C9, CYP2C19 and CYP3A4 polymorphisms was undertaken. Among all HLA alleles, HLA-A*24:07, HLA-C*03:04, HLA-DRB1*15:01 and HLA-DQB1*06:01 showed a significant association with dapsone-induced SCAR; however, only the HLA-B*13:01 allele remained significantly associated with dapsoneinduced SCAR, including of SJS-TEN and DRESS, when compared with dapsone-tolerant controls (OR = 36.00, 95% CI = 7.03 - 184.35, p = 1.4330 x 10-6 for SCAR; OR = 27.00, 95% CI = 2.24 - 324.93, p = 9.7973 x 10-3 for SJS-TEN; and OR = 40.50, 95% CI = 6.38 -257.03, $p = 1.0784 \times 10-5$ for DRESS). There was no significant association with genetic polymorphisms in the cytochrome P450 genes (CYP2C9, CYP2C19 and CYP3A4) and dapsone-induced SCAR. In conclusion, we have confirmed the association between HLA-B*13:01 and dapsone-induced SCAR, including SJS-TEN and DRESS, in Thai patients. Ttherefore, HLA-B*13:01 is an important pharmacogenetic marker for screening before initiating therapy with dapsone for prevention of dapsone-induced SCAR.

Keywords: Dapsone-induced severe cutaneous adverse reactions, HLA class I and II alleles, HLA-B*13:01, Cytochrome P450, Thai population





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