The role of HLA-B*58:01 gene typing in the prevention of allopurinol induced severe hypersensitivity reaction

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To evaluate the impact of using prospective HLA-B*58:01 screening to identify at-risk subjects for preventing life-threatening severe cutaneous adverse reactions (SCARs) induced by allopurinol, which is one of the common causes of SCARs, a prospective cohort study was carried out in 15 medical centers in different geographic regions of Taiwan from July 2009 through August 2014. 2926 subjects were included who had an indication for allopurinol treatment but had not taken allopurinol previously. DNA purified from each subject's peripheral blood was used to assess the presence of allele HLA-B*58:01. Subjects who tested positive (19.6% of the total) were advised to avoid allopurinol and were referred to an alternate medication or advised to continue with their pre-study medication; those testing negative (80.4%) were given allopurinol. Subjects were interviewed once a week for 2 months to monitor symptoms. The estimated historical incidence of allopurinol-induced SCARs was used for comparison. Only 3.3% of subjects who took allopurinol developed mild, transient rash without blisters during follow-up, none of whom were hospitalized owing to adverse drug reactions. SCARs did not develop in any of the HLA-B*58:01-negative subjects receiving allopurinol. In contrast, the historical nationwide incidence of allopurinol induced SCARs was 0.30% with 95% confidence interval of 0.28% to 0.31% (P = 0.0026, the two-side one-sample binomial test; 95% confidence interval 0% to 0.17%). We conclude that prospective screening of the HLA-B*58:01 allele coupled with an alternative medication for carriers significantly decreased the incidence of allopurinol-induced SCARs.