

# Should patients of Thai, Han Chinese and Hong Kong Chinese origin be tested for HLA-B\*1502 allele prior to phenytoin treatment?

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## Background

Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN) reactions (Fig. 1) are potentially fatal adverse drug reactions.

- SJS/TEN reactions are ten times higher in the Thai, Han Chinese and Hong Kong Chinese (T/HC/HKC) due to the presence of the human leukocyte antigen HLA-B\*1502.
- HLA-B\*1502 presents in 6.1%/9%/7.2% of the T/HC/HKC population respectively.
- Carbamazepine (CBZ) induced SJS/TEN is greater in patients with HLA-B\*1502 allele.
- Medicines and Healthcare products Regulatory Agency (MHRA) and the Food and Drug Administration (FDA) advise testing for HLA-B\*1502 prior to initiation of CBZ in the T/HC/HKC population.
- MHRA and FDA only advise avoiding Phenytoin (PHT) if the patient is known to have HLA-B\*1502 and do not advise routine testing for the allele.
- The increasing evidence regarding the link between HLA-B\*1502 and PHT-induced SJS/TEN may alter the management of patients of T/HC/HKC origin.

Figure 1. Typical pattern of SJS: Widespread purpuric macules with blisters



Table 1 HLA-B\*1502 allele frequencies in various populations

Continent	Population/Ethnicity	HLA-B*1502	Sample size
Asia	Thailand	0.085	142
	China, Southern Han	0.073	264
	China, Northern Han	0.019	105
Europe	Wales, White	0.000	1798
	Northern Ireland	0.000	1000

## Objective

Assess the association of HLA-B\*1502 and PHT-induced SJS/TEN in patients of T/HC/HKC origin.

## Study Design

- Literature search on PubMed and ScienceDirect databases until October 2014.
- Search words “phenytoin”, “HLA-B\*1502”, “Steven-Johnson Syndrome” and “Toxic Epidermal Necrolysis”
- Other articles used were those cited in papers identified via the literature search
- Analysis was restricted to systematic reviews and meta-analyses to establish the odds ratio (OR).

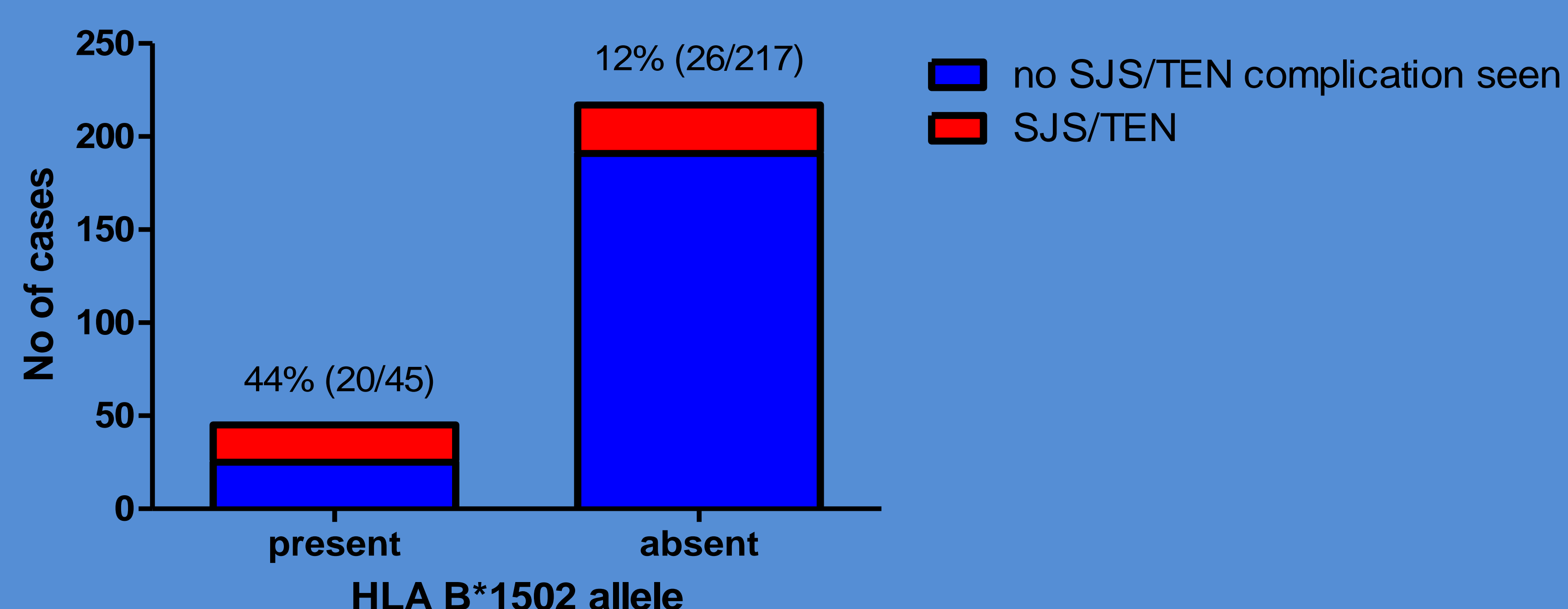
## Results and discussion

In total, 45 cases and 217 controls assessed. There was an increased risk of PHT-induced SJS/TEN in patients with HLA-B\*1502 allele compared to those that did not possess the allele.

A table to show the statistical significance reflecting the risk of developing SJS/TEN for patients with HLA-B\*1502 compared to those who do not have the allele when receiving phenytoin

Statistically significant	Odds ratio	95% confidence intervals	P value
	5.87	2.87 to 12.04	<0.0001

A graph to show the number of cases in patients with allele HLA B\*1502 developing SJS compared to those that do not possess the allele when taking phenytoin



## Conclusion

There is strong evidence associating PHT-induced SJS/TEN and individuals with HLA-B\*1502 of T/HC/HKC origin. The incidence of SJS/TEN could be reduced by routine testing for HLA-B\*1502 allele in patients of T/HC/HKC origin prior to initiation of phenytoin, and thus one can avoid the use of phenytoin treatment in this subset of patients.

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