

Effects of cigarette smoking on clopidogrel

Smoking induces cytochrome P450 1A2 ([CYP1A2](#)), a hepatic enzyme involved in the metabolism of [clopidogrel](#). Clopidogrel shows better inhibition of [platelet](#) aggregation in [smokers](#) than nonsmokers ¹⁾ and smokers are less likely to be hyporesponders than nonsmokers ²⁾.

Cho et al. investigated the association between smoking status and post-clopidogrel platelet reactivity in patients with acute myocardial infarction. Differences in the clinical situation and timing of the platelet test could explain the differences with the Bliden study ³⁾.

[Cigarette smoking](#) seems to positively modify the beneficial effect of [clopidogrel](#) on angiographic and [clinical outcomes](#). A study of Desai et al., demonstrates that common clinical factors that influence the [metabolism](#) of [clopidogrel](#) might impact its clinical [effectiveness](#) ⁴⁾.

However, whether it influences the association between [CYP2C19](#) genetic variants and clopidogrel efficacy is not clear.

2961 patients from the [CHANCE trial](#) were involved in a substudy and successfully genotyped for both two [single nucleotide polymorphisms](#) of [CYP2C19](#) (*2 and *3). [Cox regression](#) model was used to evaluate the interactions between CYP2C19 *2 and *3 carrier status and clopidogrel efficacy stratified by smoking status.

There were marginal significant interactions between CYP2C19 *2 and *3 [alleles](#) carrier status and antiplatelet treatment regimen for the risk of recurrent stroke and composite events ($p = 0.054$, $p = 0.051$, respectively) among smokers, but not in non-smokers. Among smokers, clopidogrel plus aspirin decreased the recurrence rate of stroke compared with aspirin alone in noncarriers (3.8% vs 11.8%, hazard ratio [HR], 0.32; 95% confidence interval [CI], 0.15-0.65, $p = 0.002$), but not in carriers. Similar results were also found for the recurrence rate of composite events in smokers. No significant difference was found for hemorrhage events in all groups.

Among patients with minor [stroke](#) or [TIA](#), marginal significant interactions between CYP2C19 *2 and *3 alleles carrier status and clopidogrel efficacy were found in smokers, but not in non-smokers. Among smokers, clopidogrel plus aspirin might decrease the recurrence rate of stroke in noncarriers of *2 and *3 alleles of CYP2C19 compared with aspirin alone. However, more caution should be taken to interpret this findings for several limitations in the study ⁵⁾.

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