CYP2C19

Cytochrome P450 2C19 is an enzyme protein. It is a member of the CYP2C subfamily of the cytochrome P450 mixed-function oxidase system. This subfamily includes enzymes that catalyze the metabolism of xenobiotics.

It is a liver enzyme that acts on at least 10% of drugs in current clinical use, most notably the antiplatelet treatment clopidogrel (Plavix) also drugs that treat pain associated with ulcers, such as omeprazole, antiseizure drugs such as mephenytoin, the antimalarial proguanil, and the anxiolytic diazepam.

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 [1].

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 [2].

1)
Desai NR, Mega JL, Jiang S, Cannon CP, Sabatine MS. Interaction between cigarette smoking and clinical benefit of clopidogrel. J Am Coll Cardiol. 2009 Apr 14;53(15):1273-8. doi: 10.1016/j.jacc.2008.12.044. PubMed PMID: 19358940; PubMed Central PMCID: PMC2675920.
2)
Wang T, Pan Y, Lin J, Anand R, Wang D, Johnston SC, Meng X, Li H, Zhao X, Liu L, Wang Y, Wang Y; CHANCE investigators. Influence of smoking on CYP2C19 genetic variants and clopidogrel efficacy in patients with minor stroke or TIA. Eur J Neurol. 2019 Apr 11. doi: 10.1111/ene.13962. [Epub ahead of print] PubMed PMID: 30974489.

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