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Pharmacokinetic and pharmacodynamic evaluation of Vicagrel, a novel acetate analog of clopidogrel among healthy Chinese volunteers

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Statement of the Problem: Vicagrel is a novel analog of Clopidogrel, which was expected to be hydrolyzed into its active metabolites via esterase instead of CYP2C19. In addition, both, Vicagrel and Clopidogrel have same active metabolites and dose of Vicagrel can be reduced 6~7 times as compared with Clopidogrel. Vicagrel was expected to reduce the Clopidogrel resistance and improve safety by decreasing unexpected bleeding. This study was designed to evaluate the pharmacokinetics, pharmacodynamics and tolerability of different dose of Vicagrel as compared to Clopidogrel in healthy Chinese volunteers.

Methodology & Theoretical Orientation: Study-1 was a dose escalating (5-15 mg) study, which included three treatment groups: 9 subjects were given Vicagrel, 3 subjects each were administered Clopidogrel or placebo. Study-2 was conducted to assess drug-drug interaction between Vicagrel and Aspirin among 15 healthy subjects. The plasma concentration and platelet aggregation were all assessed.

Findings: The plasma concentration of the active metabolite of Vicagrel reached its peak within 0.33~0.50 hours and the Cmax and AUC increased proportionally to the dose of Vicagrel from 5 mg to 15 mg. The pharmacokinetics of active metabolite of Clopidogrel was similar to those of 5 mg Vicagrel. After a single loading dose of Vicagrel (LD-30 mg) and once-daily maintenance dose (MD-7.5 mg) for 8 days, the maximum inhibition of platelet aggregation was similar to that seen with combined use of Vicagrel and Aspirin (100 mg/day). Among Vicagrel treated subjects, CYP2C19-predicted phenotype group was not associated with platelet aggregation.

Conclusion & Significance: As compared with Clopidogrel, Vicagrel had greater (~10 folds) exposure to the active metabolite. Pharmacodynamic responses were consistent across all treatment groups. The AUC and Cmax of the active metabolite of Clopidogrel, but not those of Vicagrel, were CYP2C19 genotype dependent. Single and multi-dosing of Vicagrel were generally well tolerated.

Biography

Xiaojiao Li has received her Master's degree in Drug Analysis and Pharmacokinetics at Jilin University. She has been working at Phase-I Clinical Trial Laboratory, The First Hospital of Jilin University, China as a Pharmacist. She has also worked as a Study Coordinator, responsible for 7 CFDA BE and pharmacokinetic studies of chemical drugs and 2 FDA BE studies. Presently, she is working in the QA and responsible for the quality of clinical trials. She has published 9 SCI articles in past 5 years.

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