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Clinical outcome in patients with cardiovascular pathologies treated with clopigogrel: Impact of genotype profile, clopidogrel metabolites PK and comedication on the clinical results

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Clopidogrel presents a complex metabolism; in last years', special attention was dedicated to identify genotypes resistant to treatment and FDA introduced a boxed warning in product leaflet for specific patient groups. Meanwhile it was observed that statins (some), proton pump inhibitors and other drugs interfere significantly with clopidogrel metabolism. In this study, patients (n=213) hospitalized for major cardiovascular problems (stable angina, ST elevation myocardial infarction, non-ST elevation myocardial infarctions) were given clopidogrel and followed clinically ≥2 years; patients received also other drugs (i.e., statins, antidiabetic, aspirin etc.) for concomitant pathologies and/or other invasive therapy (i.e., stenting) according to their lesion severity. All subjects were CYP2C19 genotyped (considered critical by FDA) and plasmatic levels of clopidogrel and 3 relevant metabolites (including the active-one) were determined at one time point to assess PK characteristics. Three groups of data were then obtained (clinical, genotype and PK) and correlations between them were statistically analyzed. Extremely interesting results have been obtained: 1) Genotype data actually poorly correlated with clinical data; 2) Clopidogrel PK seems unrelated to genotype while metabolites PK, especially of inactive-ones, correlate very well; 3) Concomitant therapies with several drugs have a highly relevant influence on clopidogrel metabolites PK (less with clopidogrel parent); 4) PK data of metabolites correlated very well with subjects survival. These data show the importance to carefully choose concomitant therapies when using clopidogrel, while genotype seems not to be as relevant as thought; the evaluation of clopidogrel metabolites PK is highly promising in clopidogrel therapy optimization.

Biography

Luigi Silvestro graduated in Medicine in Turin (Italy) in 1984 and specialized in Pharmacology in 1988. From 1989 he is applying HPLC-MS in quantitation of bioanalytical samples as well as identification of drug metabolites. In 1996, he co-founded 3S-Pharmacological Consultation & Research GmbH, a consultation company and CRO, in Germany and is still actively involved in the development of innovative analytical methods. From 1998 the company has expanded the activity in East Europe (Romania, Moldavia) creating an analytical laboratory in Romania (Bucharest). In his scientific activity he has contributed to more than 50 articles in international scientific journals.

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