Clinical relevance of the assessment of deferasirox trough levels in thalassemia patients

D. Massano[1], S. De Francia[2], F. Longo[1], A. Sandri[1], F.M. Piccione[2], E. Pirro[2], S. Allegra[3], A. D'Avolio[3] and A. Piga[1]

[1]Dept. of Paediatrics, Centre for Microcitemie, University of Turin, S. Luigi Gonzaga Hospital, Orbassano (TO), Italy
[2]Clinical Pharmacology, Dept. of Clinical and Biological Sciences, University of Turin, S. Luigi Gonzaga Hospital, Orbassano (TO), Italy
[3]Unit of Infectious Diseases, Dept. of Medical Sciences, University of Turin, Amedeo di Savoia Hospital, Turin (TO), Italy

Clinical response to deferasirox (Exjade®) in the treatment of transfusional iron overload shows an high inter-patient variability in the iron burden changes. Some recent studies have suggested that this characteristic could be explained by a broad variability of deferasirox plasma concentrations.
Objective of our study was to investigate a potential clinical role of the therapeutic drug monitoring of deferasirox in order to predict the drug efficacy and the development of side effects.
We designed a monocentric, prospective cohort study of 65 thalassemia patients treated with deferasirox. Patients enrolled trough levels were measured by HPLC-UV validated method (De Francia, 2012) during the follow-up, defined as time between two consecutive liver iron determination. Side effects were monitored by liver and kidney function markers analysis. Main outcome has been the association between deferasirox trough levels and deferasirox efficacy.
Patients with a negative trend of liver iron concentration or with lower serum ferritin had a significantly higher trough levels of deferasirox. We identified a potential cut-off to discern good to non-responders to deferasirox treatment at the concentration of 18 ?g/ml. This cut-off was the only that could predict the clinical response to deferasirox in the multivariate logistic regression analysis (OR 4.66).
Moreover the trough levels of deferasirox had a positive relationship to the serum creatinine and an inverse relationship to glomerular filtration rate. No relationship to liver function markers were observed.
In conclusion assessment of therapeutic drug monitoring of deferasirox trough levels could help clinicians in predicting patients response to treatment and to optimize deferasirox therapy on the metabolic characteristics of each patient. Additional longitudinal studies are required.

De Francia (2012). *J Chromatogr B Analyt Technol Biomed Life Sci.* 893-894, 127-133.