Potential cost-effectiveness of therapeutic drug monitoring of antiretroviral drugs in the routine clinical management of HIV-infected patients.

V. Perrone[1], D. Cattaneo[1], S. Radice[1], D. Sangiorgi[2], E. Pallone[3], L. Degli Esposti[2], E. Clementi[1,4]
[1]Unit of Clinical Pharmacology, Department of Biomedical and Clinical Sciences, Luigi Sacco University Hospital, University of Milan, 20157 Milan, Italy; [2]CliCon Srl, Health, Economics and Outcomes Research, 48100 Ravenna, Italy; [3]U.O. Quality - Clinical Risk and Accreditation, Luigi Sacco University Hospital, 20157 Milan, Italy; [4]Scientific Institute, IRCCS Eugenio Medea, 23842 Bosisio Parini, Lecco, Italy.

Highly Active Anti-Retroviral Therapy (HAART) has reduced the morbidity and mortality of Human Immunodeficiency Virus (HIV) - infected patients. Still a significant percentage of patients is only partially responsive to HAART.
Recent studies have documented that high interindividual variability in the pharmacokinetics of antiretroviral drugs plays an important role in this. Inadequate exposure to antiretroviral drugs may increase the risk of poor virologic response, whereas higher drug concentrations have been associated with increased incidence of adverse events. The reduced efficacy of HAART is a major economic burden for the regional and national health services. Therapeutic Drug Monitoring (TDM) is a useful diagnostic tool that can help the clinicians to optimise drug dosage such that drug concentrations associated with the highest therapeutic efficacy are obtained with reduced risk of adverse effects..
A retrospective cohort study was carried out at the "L. Sacco" Hospital in Milan, Italy. The aim of the study was to compare HIV-infected patients treated with antiretroviral drugs subjected or not to TDM in relation to clinical outcomes, including hospitalisations (related to reduced therapeutic response and/or occurrence of serious adverse drug reactions), and cost of illness. Plasma concentrations were determined by validated HPLC methods. Administrative databases (including pharmaceutical prescriptions and hospital admissions) were matched with the laboratory test databases (including TDM values, viral load and CD4+ T lymphocyte counts). In compliance with privacy laws, the patients' identification code was encrypted and the individuals/bodies involved in processing of the data for the purposes of the analysis were blind to the patients identification.
HIV-infected patients (aged ≥ 18 years) with at least one prescription of antiretroviral drugs and/or with at least one TDM evaluation were enrolled. The inclusion period was from January 2010 to December 2011 and the follow up period was of 12 months. Antiretroviral therapy included in the analysis took into consideration all drugs prescribed during the observation period. The therapeutic regimen was analysed in relation to the backbone and the third drug. The chronological analysis of prescriptions identified any replacements or therapeutic combinations. Treatment adherence was calculated according to literature methods[1] and cost-per-unit for resource uses were collected from DRGs, National Tariffs and Drugs Formulary.
The cohort consisted of 5341 patients (3861 males and 1486 females), with an average age of 43.9 ± 12.5 years. Seventy-two percent of them had been treated with antiretroviral drugs and TDM was applied in 143 patients. The proportion of adherent patients (defined as those having at least 80% of observation time covered by drugs dispensation) showed a strong relationship between the patients with concentration-controlled (95%) versus 81% for the patients with conventional antiretroviral therapy. 28% in TDM group vs 20.3% of patients without TDM switched to a new treatment regimen during the follow up. The mean length-of-stay for HIV-related hospitalisations was 0.90 vs 1.64 days per patients with and without TDM respectively. The average cost of hospitalisation was significantly higher in the group without TDM (€ 802 vs € 683).
We found that the inclusion of TDM as part of the clinic's routine for the optimisation of drug dosing in HIV-infected patients is associated with higher adherence to therapy, less hospitalisations and a significant reduction in the cost for the health systems. In a context of limited health care resources, pharmacoeconomic considerations are crucial to help policy markers in delivering the most appropriate decision on resource allocation. In the case of antiretroviral drugs we demonstrate that such decision is not in contrast with optimal treatment for patients.

[1] Degli Esposti L et al. (2011) *ISPOR 14th*. A233-A510