P230 -Dolutegravir tolerability in clinical practice: results from the SCOLTA cohort

Conference Paper · November 2016

23 authors, including:

Giordano Madeddu
Università degli Studi di Sassari

Elena Ricci
Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico

Roberto Gulminetti
Policlinico San Matteo Pavia Fondazione IRCCS

Paola Bagella
Università degli Studi di Sassari

HIV Drug Therapy 2016 GLASGOW

P230

HIV DRUG THERAPY 2016
October 23-26, 2016, Glasgow, UK

CISAI

DOLUTEGRAVIR tolerability in clinical practice : results from the SURVEILLANCE COHORT LONG-TERM TOXICITY ANTIRETROVIRALS/ANTIVIRALS (SCOLTA) Cohort.

G. Madeddu[1], E. Ricci[2], R. Gulminetti[3], P. Bagella[4], N. Squillace[5], G. De Socio[6], B. Menzaghi[7], G. Orofino[8], C. Molteni[9], S. Rusconi[10], B.M. Celesia[11], C. Bellacosa[12], A. Di Biagio[13], G. Pellicanò[14], C. Martinelli[15], L. Carenzi[2], L. Valsecchi [2], L. Calza [16], K. Falasca[17], F. Vichi[18], G. Penco[19], P. Bonfanti [9]

1.University of Sassari, Unit of Infectious Diseases, Department of Clinical and Experimental Medicine Sassari Italy; 2.ASST Fatebenefratelli Sacco Department of Infectious Diseases Milan Italy; 3.San Matteo Polyclinic Foundation - IRCCS Unit of Infectious Diseases Pavia Italy; 4.University of Sassari Unit of Infectious Diseases, Department of Clinica Sassari Italy; 5.San Gerardo Hospital - University of Milano-Bicocca Infectious Diseases Unit Monza Italy; 6.Santa Maria Hospital Infectious Diseases Unit Perugia Italy; 7.ASST della Valle Olona Unit of Infectious Diseases Busto Arsizio Italy; 8.Amedeo di Savoia Hospital Department of Infectious Diseases Turin Italy; 9.A. Manzoni Hospital Unit of Infectious Diseases Lecco Italy; 10.University of Milan, DIBIC Luigi Sacco Infectious Diseases Unit Milan Italy; 11.Garibaldi Hospital Unit of Infectious Diseases Catania Italy; 12.University of Bari Infectious Diseases Clinic Bari Italy; 13.IRCCS San Martino Hospital - IST Unit of Infectious Diseases Genoa Italy; 14.University of Messina Infectious Diseases Unit Messina Italy; 15.Careggi Hospital Unit of Infectious and Tropical Diseases Florence Italy; 16.Univerisity of Bologna, S. Orsola Malpighi Hospital Department of Infectious Diseases Bologna Italy; 17.University of Chieti Infectious Diseases Unit Chieti Italy; 18.Santa Maria Annunziata Hospital Infectious Diseases Unit Florence Italy; 19.Galliera Hospital Infectious Diseases Unit Genoa Italy;

Background

- Dolutegravir (DTG) is the only second-generation integrase inhibitor (INI) available in clinical practice. It has advantages in comparison to first generation INIs including unboosted daily dosing, limited cross resistance, and a high barrier to resistance.
- In clinical trials DTG proved efficacious and safe in naive and experienced patients. However, a recent study in a real life setting reported an unexpectedly high rate of discontinuation mainly due to central nervous system (CNS) events.

Methods

- Patients initiating DTG were enrolled in the SCOLTA project, a prospective, observational, multicenter study created to assess the incidence of adverse events in patients receiving new antiretroviral drugs.
- The statistical significance of changes from baseline was evaluated by paired t-test, after testing the normality of distributions.

Purpose of the study

- To evaluate the tolerability of DTG based HAART in clinical practice.
- We therefore aimed to describe the modification of eGFR, lipid and hepatic profile in a cohort of HIV-infected patients and causes of DTG discontination.

Results 1

- A total of 358 HIV-infected patients were included, 266 (74.3%) males and 113 (31.6%) were heterosexuals. CDC stage was A in 156 (43.6%) patients. Mean age at enrolment was 46.9±11.4 years, mean CD4 cell count 520±383 cell/µL and mean HIV-RNA 2.0±1.9 log10 cp/ml. Eighty-three (23.2%) patients were HCV Ab+ and 60 (16.7%) were naive. Baseline characteristics of enrolled patients are shown in Table 1.

Parameters	Cohort (n=358)
Age (years), mean ±standard deviation	46.9.9 ±11.4
Male gender	266 (74.3%)
Caucasians	345 (96.4%)
Naives	60 (16.7%)
Heterosexuals	113 (31.6%)
CDC stage A	156 (43.6.%)
Mean CD4 (cell/µl), mean ±standard deviation	520±383
Mean HIV RNA (log_{10}cp/ml), mean ±standard deviation	2.0±1.9
HCV Antibodies positive	83 (23.2%)
Total cholesterol (mg/dl), mean ±standard deviation	189.2±46.1
HDL cholesterol (mg/dl), mean ±standard deviation	44.7±14.9
Tryglicerides (mg/dl), median (interquartile range)	129 (90-204)
eGFR (ml/min/1.73 m^2), mean ±standard deviation	93.9 ±24.8

Results 2

- After a median follow up of 7 (IQR 6-11) months, 20 (5.6%) therapy interruptions were reported. These were caused by virological failure in 4 (1.1%), death in 3 (0.8%), therapy simplification in 2 (0.5%), adverse events in 8 (2.2%), lost to follow up in 1 and other reasons in 2 cases (Figure 1).
- Among adverse events-related interruptions 2 were ≥ grade 3 reactions, 1 acute renal failure and 1 rash, and 6 grade 1-2, 1 creatinine increase, 1 myalgia+rhabdomyolysis, 1 transaminase increase, 2 CNS events (1 somnolence and 1 headache) and 1 gastrointestinal (vomiting), as shown in Figure 1.

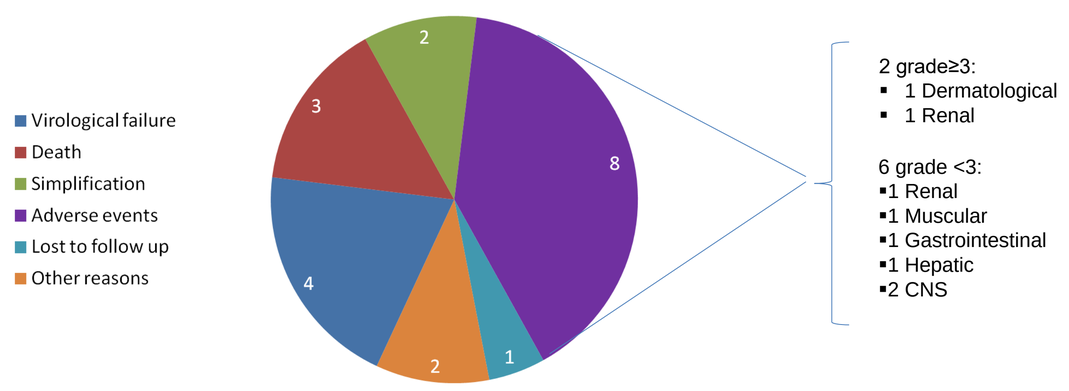

Figure 1. Causes of dolutegravir treatment discontinuation.

Results 3

- Among patients with available follow up data at week 24 and 48 we found a significant reduction in eGFR at both follow up times (-11.7 ml/min/1.73m2, p<0.0001 and -9.1 ml/min/1.73m2 p=0.001, respectively), as shown in Figure 2.
- Regarding lipid profile we observed a non significant reduction in total cholesterol at week 24 and 48 and a slight increase in HDL cholesterol. Triglycerides level showed a significant reduction at week 24 (-22.0 mg/dl, p=0.015) and a further decrease at week 48 (-9.4 mg/dl, p=n.s.), as depicted in Figure 3. Finally, both AST and ALT levels decreased during follow up.

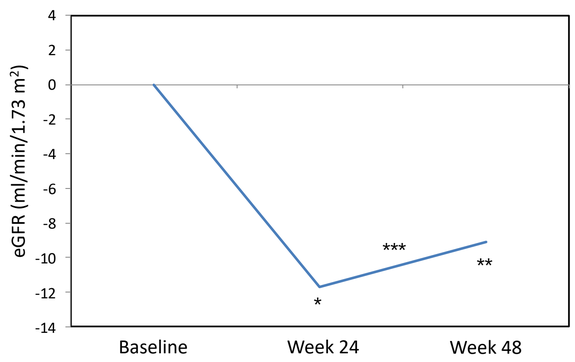

Figure 2. Mean change from baseline in estimated glomerular filtration rate (eGFR).
*p < 0.0001 WeeK 24 vs Baseline;
**p = 0.001; Week 48 vs Baseline;
***p= 0.30; Week 48 vs Week 24.

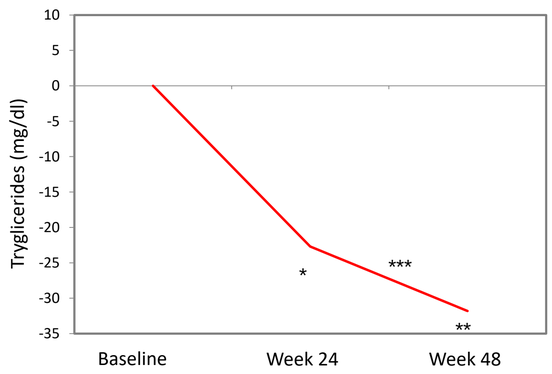

Figure 3. Mean change from baseline in tryglicerides.
*p = 0.015 WeeK 24 vs Baseline;
**p = 0.15; Week 48 vs Baseline;
***p= 0.58; Week 48 vs Week 24.

Acknowledgements

CISAI Working Group
Bari: Paolo Maggi, Chiara Bellacosa, Carmen Rita Santoro; **Bologna**: Leonardo Calza, Eleonora Magistrelli; **Busto Arsizio**: Tiziana Quirino, Barbara Menzaghi, Maddalena Farinazzo; **Cagliari**: Marzia Garau, Goffredo Angioni, Chiara Bolliri, Marta Motzo; **Catania**: Benedetto Maurizio Celesia, Maria Gussio, Mauro Maresca; **Cesena**: Carmela Grosso; **Chieti**: Jacopo Vecchiet, Katia Falasca, Claudio Ucciferri; **Firenze (S.M. Annunziata)**: Francesca Vichi; **Firenze (Careggi)**: Canio Martinelli, Elena Salomoni, Paola Corsi; **Genova (Galliera)**: Giovanni Penco, Giovanni Cenderello, Alberto Venturini; **Genova (S.Martino)**: Antonio Di Biagio, Lucia Taramasso, Laura Ambra Nicolini; **Lecco:** Paolo Bonfanti, Chiara Molteni; **Messina**: Giuseppe Nunnari, Giovanni Pellicanò; **Milano (Sacco, I Divisione)**: Laura Carenzi, Simone Passerini, Carlo Magni; **Milano (Sacco, II Divisione)**: Laura Valsecchi, Laura Cordier; **Milano (Sacco, CMI)**: Stefano Rusconi, Valeria Colombo; **Monza**: Nicola Squillace, Valentina Ferroni, Valeria Pastore; **Padova**: Marzia Franzetti; **Pavia**: Roberto Gulminetti, Alberto Gatti Comini; **Perugia**: Giuseppe De Socio, Aria Patacca, Giorgia Angeli; **Pescara**: Giustino Parruti, Donatella Cibelli; **Sanremo**: Chiara Dentone; **Sassari**: Maria Stella Mura, Giordano Madeddu, Paola Bagella, Vito Fiore, Francesca Peruzzu; **Torino**: Giancarlo Orofino, Marta Guastavigna.

Conclusions

- Dolutegravir was well tolerated during follow up as confirmed by the low rate of both total DTG-based regimen discontinuations (5.6%) and adverse-events related interruptions (2.2%).
- eGRF showed an initial reduction but a stabilization during follow up as already shown in clinical trials, possibly attributable to the inhibition of the OCT-2 creatinine transporter in the proximal tubular cells.
- Dolutegravir was also associated with an improvement of the lipid profile with significant reduction of triglycerides

Correspondence to: giordano@uniss.it