Liver enzymes levels, metabolic and renal profile modifications after switching from TDF to TAF- based regimens Among ART experienced PLWH in the ICONA cohort

P155

M. Poliseno1, S. Lo Caputo1, A. Tavelli2, R. Gagliardini3, L. Gazzola2, A. Saracino4, T. A. Santantonio1, N. Squillace5, M. Puoti6, S. Cicalini3, A. Antinori3 , A. d'Arminio Monforte2, A. Cozzi-Lepri7

1. Unit of Infectious Diseases, University of Foggia, Foggia, Italy
2. Clinic of Infectious Diseases, San Paolo Hospital, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Italy.
3. National Institute for Infectious Diseases "L. Spallanzani" IRCCS, Via Portuense 292, 00149 Rome, Italy;
4. Operative Unit of Infectious Diseases, Hospital-University Polyclinic of Bari, Bari, Italy.
5. Infectious Diseases Unit ASST-Monza, San Gerardo Hospital-University of Milano-Bicocca, Monza, Italy.
6. nfectious Diseases Unit, Niguarda Hospital, Milan, Italy.
7. Institute for Global Health UCL, University College London, London, UK.

HIV Drug Therapy GLASGOW 2022 | HYBRID

BACKGROUND

- Alanine aminotransferase (ALT) elevation during treatment with Tenofovir Disoproxil Fumarate (TDF) and their reduction after switching toTenofovir Alafenamide (TAF) have been described among ART-experienced PLWH.
- However, the concomitant change of metabolic and renal markers and the possible role of the anchor drug in this condition remain unclear.

AIMS

To describe the incidence and explore the size of the modification of liver enzymes among ART-experienced PLWH switched from a TD to a TAF-based regimen; to evaluate the modification of participants' renal function and metabolic profile concomitant to the changes in liver enzymes; to outline a possible correlation between changes in liver enzymes levels and those in renal function and metabolic profile.

STUDY DESIGN AND METHODS

- All undetectable, ART-experienced, >18 years PLWH in the ICONA Foundation cohort who switched from a TDF- to a TAF-based regimen and had ≥2 ALT assessments while on TDF and TAF, were enrolled. Values measured before and after the switch were compared using a paired t-test. Pearson rho was used to evaluate baseline correlations among hepatic, metabolic, and renal profiles.
- Mixed models with random intercept and slope with a change in slope at 1 year after switch were used to evaluate the trajectories of the markers. A quadratic model with interactions was used to assess the effect of the 3rd drug used in the TAF regimen on ALT changes.

RESULTS

Patients' characteristics

- 2,911 PLWH, 81% males, median (IQR) age 45 (37-53) years, were switched to a TAF-based regimen after having received TDF for a median of 31 (19-47) months. At baseline, weak correlations were found between ALT and HDL Cholesterol (ρ=-.07, p<0.0001), Triglycerides (ρ=.13, p<.001), and Glucose (ρ=.08, p<.001).
- Over a median of 42 (34-47) months follow-up, a moderate decrease in ALT values (mean [±SD] 35.66 [±49.74] *vs* 34.28 [±49.74] U/L) was observed during the first year on TAF compared to when on TDF, followed by a slight increase (34.28 [±49.74] *vs* 35.66 [±99.15] U/L, p<.01). The opposite trend was reported for metabolic and renal profiles, although none of the changes was clinically significant (**Table 1.**)

Table 1- Slopes from fitting a step-linear mixed model with change at 1 year after the switch.

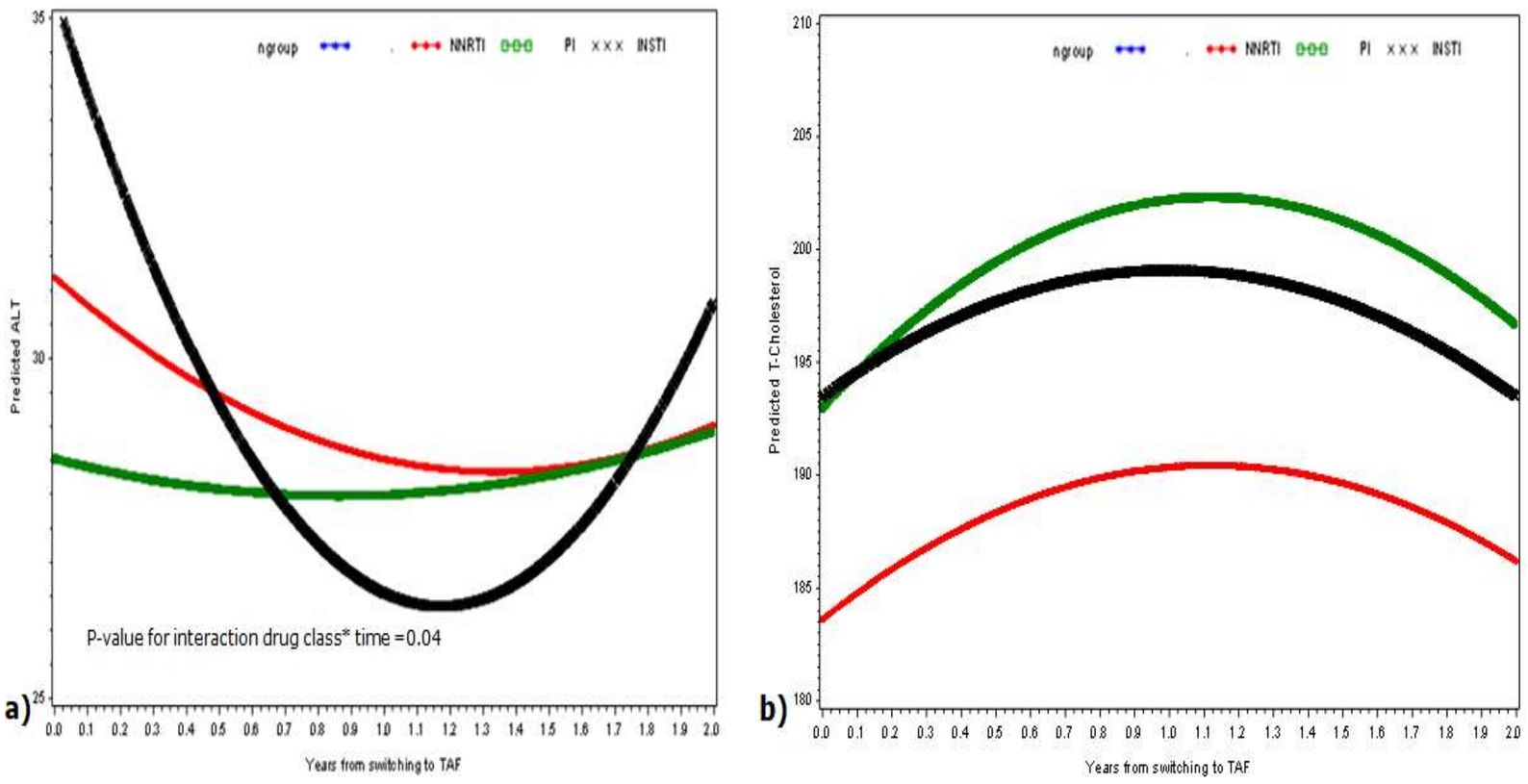
	Slopes/year by window periods					
Laboratory parameter	Pre-switch		0-1 year after switch		>1 year after switch	
	Mean	p-value*	Mean	p-value*	Mean	p-value*
Metabolic profile						
LDL Chol	3.5 (2.7, 4.2)	<.001	7.8 (6.1, 9.5)	<.001	-16.2 (-18.9, -13.4)	<.001
T-Chol	4.2 (3.6, 4.9)	<.001	10.2 (8.7, 11.8)	<.001	-21.1 (-23.6, -18.5)	<.001
Triglicerydes	1.4 (-0.6, 3.3)	0.163	10.5 (5.7, 15.3)	<.001	-14.3 (-22.1, -6.6)	<.001
T-Chol/HDL ratio	-0.0 (-0.1, 0.0)	0.080	0.1 (0.0, 0.2)	0.020	-0.2 (-0.3, -0.1)	0.006
Glucose	-0.3 (-0.6, 0.1)	0.176	2.5 (1.6, 3.4)	<.001	-2.5 (-3.9, -1.0)	<.001
Hepatic profile						
ALT	3.1 (-0.0, 6.1)	0.051	-24.4 (-32.5, -16.3)	<.001	30.3 (17.3, 43.4)	<.001
AST	1.5 (-0.5, 3.4)	0.146	-12.7 (-17.9, -7.5)	<.001	17.2 (8.8, 25.7)	<.001
GGT	-1.3 (-2.7, 0.1)	0.070	-4.6 (-8.0, -1.2)	0.008	5.9 (0.4, 11.4)	0.035
ALP	-2.6 (-3.7, -1.4)	<.001	-13.6 (-16.3, -10.9)	<.001	22.9 (18.4, 27.4)	<.001
Renal profile						
Creatinine	-0.0 (-0.1, 0.0)	0.101	0.1 (-0.0, 0.1)	0.172	-0.1 (-0.2, 0.0)	0.185
eGFR	-2.6 (-2.8, -2.4)	<.001	2.3 (1.7, 2.8)	<.001	-1.5 (-2.4, -0.6)	<.001

*Wald test

LDL Col: Low-density Lipoprotein Cholesterol; *T-Chol:* Total Cholesterol; *ALT:* Alanine aminotransferase; *AST:* Aspartate transaminase; *GGT:* Gamma Glutamil Transpeptidase; *ALP*: Alcaline Phosphatase; *egfr:* esteemed glomelural filtration rate; *TDF:* Tenofovir Disoproxil Fumarate; *TAF:* Tenofovir Alafenamide

- U-shaped trajectories of ALT (interaction p-value=0.04) and Cholesterol from switch to 2 years according to 3rd drug are shown in **Figure 1 a)** and **b),** respectively.

Figure 1–Predictions of ALT (**Fig.1 a)**) and Total Cholesterol (**Fig. 1 b)**) changes after switch to TAF from fitting a quadratic mixed model, stratified by class of anchor drug used in the TAF-based regimen.



CONCLUSIONS

After 42 months of follow-up, no clinically significant changes were observed in hepatic and metabolic markers after the switch from TDF to TAF in our cohort. The anchor drug used appeared to affect the shape of ALT changes. Further studies are warranted to define possible differences in liver markers after changing TDF to TAF in PLWH co-infected with HBV.

Acknowledgments

ICONA Foundation Study Group

BOARD OF DIRECTORS: *A d'Arminio Monforte (President), A Antinori (Vice-President), S Antinori, A Castagna, F Castelli, R Cauda, G Di Perri, E Girardi, R Iardino, A Lazzarin, GC Marchetti, C Mussini, L Sarmati, F von Schloesser, P Viale.* ***SCIENTIFIC SECRETARY:*** *A d'Arminio Monforte, A Antinori, A Castagna, F Ceccherini-Silberstein, A Cingolani, A Cozzi-Lepri, E Girardi, A Gori, S Lo Caputo, G Marchetti, F Maggiolo, C Mussini, M Puoti, CF Perno.* ***STEERING COMMITTEE:*** *C Agrati, A Antinori, F Bai, A Bandera, S Bonora, A Calcagno, D Canetti, A Castagna, F Ceccherini-Silberstein, A Cervo, S Cicalini, A Cingolani, P Cinque, A Cozzi-Lepri, A d'Arminio Monforte, A Di Biagio, R Gagliardini, A Giacomelli, E Girardi, N Gianotti, A Gori, G Guaraldi, S Lanini, G Lapadula, M Lichtner, A Lai, S Lo Caputo, G Madeddu, F Maggiolo, V Malagnino, G Marchetti, C Mussini, S Nozza, CF Perno, S Piconi, C Pinnetti, M Puoti, E Quiros Roldan, R Rossotti, S Rusconi, MM Santoro, A Saracino, L Sarmati, V Spagnuolo, N Squillace, V Svicher, L Taramasso, A Vergori.* ***STATISTICAL AND MONITORING TEAM:*** *F Bovis, A Cozzi-Lepri, I Fanti, M Ponzano, A Rodano', A Tavelli, F Vinci.* ***COMMUNITY ADVISORY BOARD****: A Bove, M Cernuschi, L Cosmaro, M Errico, A Perziano, V Calvino.* ***BIOLOGICAL BANK INMI AND SAN PAOLO****: S Carrara, S Graziano, G Prota, S Truffa, D Vincenti, Y D'Errico.* ***PARTICIPATING PHYSICIANS AND CENTERS****: Italy A Giacometti, A Costantini, V Barocci (Ancona); A Saracino, C Santoro, E Milano (Bari); F Maggiolo, C Suardi (Bergamo); P Viale, V Donati, G Verucchi (Bologna); E Quiros Roldan, C Minardi, (Brescia); B Menzaghi, C Abeli (Busto Arsizio); L Chessa, F Pes (Cagliari); P Maggi, L Alessio (Caserta); B Cacopardo, B Celesia (Catania); J Vecchiet, K Falasca (Chieti); A Pan, S Dal Zoppo (Cremona); L Sighinolfi, D Segala (Ferrara); F Vichi, MA Di Pietro (Firenze); T Santantonio, S Ferrara (Foggia); M Bassetti, E Pontali, A Alessandrini, N Bobbio, G Mazzarello (Genova); M Lichtner, L Fondaco (Latina); S Piconi, C Molteni (Lecco); A Chiodera, P Milini (Macerata); G Nunnari, G Pellicanò (Messina); A d'Arminio Monforte, S Antinori, A Lazzarin, G Rizzardini, M Puoti, A Gori, A Castagna, A Bandera, V Bono, MV Cossu, A Giacomelli, R Lolatto, MC Moioli, L Pezzati, C Tincati (Milano); C Mussini, C Puzzolante (Modena); P Bonfanti, G Lapadula (Monza); V Sangiovanni, I Gentile, V Esposito, G Di Flumeri, G Di Filippo, V Rizzo (Napoli); AM Cattelan, S Marinello (Padova); A Cascio, C Colomba (Palermo); D Francisci, E Schiaroli (Perugia); G Parruti, F Sozio (Pescara); P Blanc, A Vivarelli (Pistoia); C Lazzaretti, R Corsini (Reggio Emilia); M Andreoni, A Antinori, R Cauda, C Mastroianni, A Cingolani, V Mazzotta, S Lamonica, M Capozzi, A Mondi, M Rivano Capparuccia, G Iaiani, C Stingone, L Gianserra, J Paulicelli, MM Plazzi, G d'Ettore, M Fusto (Roma); M Cecchetto, F Viviani (Rovigo); G Madeddu, A De Vito (Sassari); M Fabbiani, F Montagnani (Siena); A Franco, R Fontana Del Vecchio (Siracusa); BM Pasticci, C Di Giuli (Terni); GC Orofino, G Calleri, G Di Perri, S Bonora, G Accardo (Torino); C Tascini, A Londero (Udine); V Manfrin, G Battagin (Vicenza); G Starnini, A Ialungo (Viterbo).*

Funding

ICONA Foundation is supported by unrestricted grants from, Gilead Sciences, Janssen-Cilag, MSD, Thera Technologies and ViiV Healthcare

Contact Information

Poliseno Mariacristina, MD
University of Foggia, V.le Pinto 1, 71122 Foggia, Italy - polisenomc@gmail.com