

The prevalence and predictive value of dipstick urine protein (DUP) in HIV-positive persons in Europe

A Mocroft¹, L Ryom², G Lapadula³, P Reiss⁴, A Blaxhult⁵, HJ Furrer⁶, G Kutsyna⁷, J Gatell⁸, J Begovac⁹, P Domingo¹⁰, O Kirk², JD Lundgren² for EuroSIDA in EuroCoord

¹University College London, London UK; ²CHIP, Department of Infectious Diseases and Rheumatology, Section 2100, Rigshospitalet – University of Copenhagen; ³"San Gerardo" Hospital, Monza, Italy; ⁴Academic Medical Center, Div. of Infectious Diseases and Dept. of Global Health, University of Amsterdam, The Netherlands; ⁵Venhaelsan-Sodersjukhuset, Stockholm, Sweden; ⁶Inselspital Bern, Bern, Switzerland; ⁷Luhansk State Medical University; Luhansk, Ukraine; ⁸Hospital Clinic i Provincial, Barcelona, Spain; ⁹University Hospital of Infectious Diseases, Zagreb, Croatia; ¹⁰Hospital Sant Pau, Barcelona, Spain

INTRODUCTION

Proteinuria is an important marker for the development and progression of renal disease, cardiovascular disease and death¹⁻³, but there is limited information about the prevalence and factors associated with confirmed proteinuria in European HIV+ persons with an estimated glomerular filtration rate (eGFR) >60mL/min/1.73m².

PATIENTS AND METHODS

Baseline was defined as the first of 2 consecutive dipstick urine proteinuria (DUP) measurements during prospective follow-up >1/6/2011 (when routine collection of DUP began). Proteinuria (PTU) was defined as 2 consecutive DUP ≥1+ (>30 mg/dL) >3 months apart; persons with eGFR≤60⁴ at either DPU measurement were excluded. Logistic regression investigated factors associated with PTU.

RESULTS

- 1640 persons were included (**Table 1**). 69 persons had PTU (4.2%, 95% CI 3.2–4.7%)
- Persons with diabetes had increased odds of PTU, as did those with a prior non-AIDS⁵ or AIDS event and those with prior exposure to indinavir
- Females, those with a normal eGFR (>90) and those with prior abacavir use had lower odds of PTU (**Figure 1**)
- There was no significant association between past or current use of potentially nephrotoxic ARVs tenofovir, lopinavir, atazanvir (boosted or unboosted) or any other boosted PI and PTU (p>0.2)
- Limited follow-up after baseline but persons with PTU were more likely to develop CKD (**Table 2**)

CONCLUSIONS

1 in 25 HIV+ persons with an eGFR>60mL/min/1.73m² had confirmed proteinuria at baseline. Factors associated with PTU were similar to those associated with CKD. The lack of association with ARVs at higher eGFR levels deserves further investigation (**Table 3**).

Our findings suggest PTU is an early marker for impaired renal function and that routine dipstick urine monitoring may improve identification and clinical management of those at risk of renal impairment

References

- Hemmelgarn BR et al. JAMA 2010;303:423-9.
- Bello AK et al. Clin J Am Soc Nephrol 2011;6:1418-26.
- Peralta CA et al. JAMA 2011; 305:1545-52.
- Levey AS et al. Ann Intern Med 2009 May 5;150(9):604-12.
- Mocroft A et al. J Acquir Immune Defic Syndr 2010;55:262-70.

The EuroSIDA Study Group

Argentina: (M Lasso), M Kundiño, Hospital JM Ramos Mejia, Buenos Aires; **Austria:** (N Vetter), Pulmologisches Zentrum der Stadt Wien, Vienna; R Zangerle, Medical University Innsbruck, Innsbruck; **Belarus:** (I Karпов), A Vassilenko, Belarus State Medical University, Minsk; VM Mitsura, Gomel State Medical University, Gomel; D Paduto, Regional AIDS Centre, Svetlogorsk; **Belgium:** (N Clumeck), S De Wit, M Delforge, Saint-Pierre Hospital, Brussels; E Florence, Institute of Tropical Medicine, Antwerp; L Vandekerckhove, University Ziekenhuis Gent, Gent; **Bosnia-Herzegovina:** (V Hadziosmanovic), Klinicki Centar Univerziteta Sarajevo, Sarajevo; **Bulgaria:** (K Kostov), Infectious Diseases Hospital, Sofia; **Croatia:** (J Begovac), University Hospital of Infectious Diseases, Zagreb; **Czech Republic:** (L Machala), D Jilich, Faculty Hospital Bulovka, Prague; D Sedlacek, Charles University Hospital, Plzen; **Denmark:** (J Nielsen), G Kronborg, T Benfield, M Larsen, Hvidovre Hospital, Copenhagen; J Gerstoft, T Katzenstein, A-B E Hansen, P Skinhøj, Rigshospitalet, Copenhagen; C Pedersen, Odense University Hospital, Odense; L Ostergaard, Skejby Hospital, Aarhus, U B Dragsted, Roskilde Hospital, Roskilde; L N Nielsen, Hillerød Hospital, Hillerød; **Estonia:** (K Zilmer), West-Tallinn Central Hospital, Tallinn; Jelena Smidt, Nakkusosakond Siseklinik, Kohtla-Järve; **Finland:** (M Ristola), Helsinki University Central Hospital, Helsinki; **France:** (C Katlama), Hôpital de la Pitié-Salpêtrière, Paris; J-P Viard, Hôtel-Dieu, Paris; P-M Girard, Hospital Saint-Antoine, Paris; P Vanhems, University Claude Bernard, Lyon; C Pradier, Hôpital de l'Archet, Nice; F Dabis, D Neau, Unité INSERM, Bordeaux; C Duvalier, Hôpital Necker-Enfants Malades, Paris; **Germany:** (J Rockstroh), Universitäts Klinik Bonn; R Schmidt, Medizinische Hochschule Hannover; J van Lunzen, O Degen, University Medical Center Hamburg-Eppendorf, Infectious Diseases Unit, Hamburg; HJ Stellbrink, IPM Study Center, Hamburg; C Stefan, JW Goethe University Hospital, Frankfurt; J Bogner, Medizinische Poliklinik, Munich; G. Fäkenheuer, Universität Köln, Cologne; **Georgia:** (N Chikharishvili), Infectious Diseases, AIDS & Clinical Immunology Research Center, Tbilisi; **Greece:** (J Kosmidis), P Gargalianos, G Xylomenos, J Perdios, Athens General Hospital; H Sambatakou, Ippokraton General Hospital, Athens; **Hungary:** (D Banhegyi), Szent László Hospital, Budapest; **Iceland:** (M Gottfredsson), Landspítali University Hospital, Reykjavik; **Ireland:** (F Mulcahy), St. James's Hospital, Dublin; **Israel:** (I Yust), D Turner, M Burke, Ichilov Hospital, Tel Aviv; E Shahar, G Hassoun, Rambam Medical Center, Haifa; H Elinav, M Haouzi, Hadassah University Hospital, Jerusalem; ZM Sthoeger, AIDS Center (Neve Or), Jerusalem; **Italy:** (A D'Amminio Monforte), Istituto Di Clinica Malattie Infettive e Tropicale, Milan; R Esposito, I Mazzei, Ospedale Generale Regionale, Bolzano; R Pristera, Ospedale Generale Regionale, Bolzano; A Gabbuti, Ospedale S Maria Annunziata, Firenze; V Vullo, M Lichtner, University of Roma la Sapienza, Rome; M Zaccarelli, A Antonini, R Acinapura, G D'Onofri, Istituto Nazionale Malattie Infettive Lazzaro Spallanzani, Rome; A Lazzarin, A Castagna, N Gianotti, Ospedale San Raffaele, Milan; M Galli, A Ridolfo, Osp. L. Sacco, Milan; Latvia (B Rozentalis), Infectology Centre of Latvia, Riga; **Lithuania:** V Uzdaviniene, Lithuanian AIDS Centre, Vilnius; **Luxembourg:** (T Staub), R Hemmer, Centre Hospitalier, Luxembourg; **Netherlands:** (P Reiss), Academisch Medisch Centrum bij de Universiteit van Amsterdam, Amsterdam; **Norway:** (V Ormaasen), A Maeland, J Bruun, Ullevål Hospital, Oslo; **Poland:** (B Knyasz), J Gasiorowski, M Inglot, Medical University, Wrocław; A Horban, E Bakowska, Centrum Diagnostyki i Terapii AIDS, Chorzów; T Smiatecz, Medical University, Gdansk; E Jablonowska, E Malolepsza, K Flisiak, Medical University, Białystok; M Parczewski, M Pytnik, K Maciejewska, Medical University, Szczecin; M Benkowski, E Mularska, Osrodek Diagnostyki i Terapii AIDS, Chorzów; T Smiatecz, Medical University, Gdansk; E Jablonowska, E Malolepsza, K Wojcik, Wojewodzki Szpital Specjalistyczny, Łódź; I Mozer-Lisewska, Poznan University of Medical Sciences, Poznan; **Portugal:** (M Doroana), L Caldeira, Hospital Santa Maria, Lisbon; K Mansinho, Hospital de Egas Moniz, Lisbon; F Maltz, Hospital Curry Cabral, Lisbon; **Romania:** (R Radoi), C Oprea, Spitalul de Boli Infectioase si Tropicale; Dr. Victor Babes, Bucuresti; **Russia:** (A Rakhmanova), Medical Academy Botkin Hospital, St Petersburg; A Rakhmanova, St Petersburg AIDS Centre, St Petersburg; T Trofimova, Novgorod Centre for AIDS, Novgorod; I Khronova, Centre for HIV/AIDS & and Infectious Diseases, Kaliningrad; E Kuzovkova, Nizhny Novgorod Scientific and Research Institute, Nizhny Novgorod; **Serbia:** (D Jevtic), The Institute for Infectious and Tropical Diseases, Belgrade; **Slovakia:** A Shunhar, D Staneková, Dérer Hospital, Bratislava; **Slovenia:** (J Tomazic), University Clinical Centre Ljubljana, Ljubljana; **Spain:** (J González-Lahoz) S Moreno, J. M. Rodriguez, Hospital Ramon y Cajal, Madrid; B Clotet, A Jou, R Paredes, C Tural, J Puig, Hospital Germans Trias i Pujol, Badalona; JM Gatell, JM Miró, Hospital Clinic Universitari de Barcelona, Barcelona; P Domingo, M Gutierrez, G Mateo, MA Sambate, Hospital Sant Pau, Barcelona; JM Laporte, Hospital Universitario de Alava, Vitoria-Gasteiz; **Sweden:** (A Blaxhult), Venhaelsan-Sodersjukhuset, Stockholm; L Flanholm, Malmö University Hospital, Malmö, A Thälme, A Sonnerberg, Karolinska University Hospital, Stockholm; **Switzerland:** (B Ledergerber), R Weber, University Hospital, Zürich; M Cavassini, Centre Hospitalier Universitaire Vaudois, Lausanne; A Calmy, Hospital Cantonal Universitaire de Geneve, Geneve; H Furrer, Inselspital Bern, Bern; M Battegay, L Elzi, University Hospital Basel; P Schmid, Kantonsspital, St. Gallen; **Ukraine:** (E Kravchenko), N Chentsova, Kiev Centre for AIDS, Kiev; V Frolov, G Kutsyna, I Baskakov, Luhansk State Medical University, Luhansk; S Serovskiy, Odessa Region AIDS Center, Odessa; A Kuznetsova, Khar'kov State Medical University, Khar'kov; G Kyselova, Crimean Republican AIDS centre, Simferopol; **United Kingdom:** (B Gazzard), St. Stephen's Clinic, Chelsea and Westminster Hospital, London; AM Johnson, E Simons, S Edwards, Mortimer Market Centre, London; A Phillips, MA Johnson, A Mocroft, Royal Free and University College Medical School, London (Royal Free Campus); C Orkin, Royal London Hospital, London; J Weber, G Scullard, Imperial College School of Medicine at St. Mary's, London; M Fisher, Royal Sussex County Hospital, Brighton; C Leen, Western General Hospital, Edinburgh.

The following centers have previously contributed data to EuroSIDA: Bernhard Nocht Institut für Tropenmedizin, Hamburg, Germany; 1st I.K.A Hospital of Athens, Athens, Greece; Ospedale Riuniti, Divisione Malattie Infettive, Bergamo, Italy; Ospedale Cologno, III Divisione Malattie Infettive, Napoli, Italy; Hospital Carlos III, Departamento de Enfermedades Infecciosas, Madrid, Spain; EuroSIDA Steering Committee: J Gatell, B Gazzard, A Horban, I Karпов, B Ledergerber, M Lasso, A d'Amminio Monforte, C Pedersen, A Rakhmanova, M Ristola, A Phillips, P Reiss, J Lundgren, J Rockstroh, S De Wit, Chair: J Rockstroh, Vice-chair: S De Wit, Study Co-leads: A Mocroft, O Kirk, EuroSIDA Representatives to EuroCoord: O Kirk, A Mocroft, J Granup, P Reiss, A Cozzi-Lepri, R Thiebaut, J Rockstroh, D Burger, R Paredes, L Peters, EuroSIDA staff, Coordinating Centre Staff: D Podlekareva, L Peters, JE Nielsen, C Matthews, AH Fischer, A Bojesen, D Raben, D Kristensen, K Granborg Laul, JF Larsen. **Statistical Staff:** A Mocroft, A Phillips, A Cozzi-Lepri, D Grint, L Shepherd, A Schultze. **Funding:** Primary support for EuroSIDA is provided by the European Commission BIOMED 1 (CT94-1637), BIOMED 2 (CT97-2713), the 5th Framework (QLK2-2000-00773), the 6th Framework (LSHP-CT-2006-018632), and the 7th Framework (FP7/2007-2013, EuroCoord n° 260694) programmes. Current support also includes unrestricted grants by Janssen R&D, Merck and Co. Inc., Pfizer Inc., GlaxoSmithKline LLC. The participation of centres from Switzerland was supported by The Swiss National Science Foundation (Grant 108787).

Table 1

Characteristics of HIV+ persons with ≥2 DUP in EuroSIDA					
		No PTU		PTU	
		N	%	N	%
All		1571	78.6	69	4.2
Gender	Male	1296	79.0	62	90.0
HIV risk	MSM	809	49.3	33	47.8
Ethnicity	White	1454	92.6	63	91.3
On cART	Yes	1477	94.0	66	95.7
eGFR < 60	Yes	117	7.5	8	11.6
		Median	IQR	Median	IQR
Age	Years	45	37 – 52	49	40 – 57
CD4	/mm ³	570	409 – 760	566	380 – 785
eGFR	mL/min/1.73m ²	100	87 – 111	89	78 – 104
Baseline	Month/year	2/12	11/11 – 6/12	2/12	11/11 – 6/12

DUP; dipstick urine proteinuria. PTU; proteinuria; confirmed (>3 months apart) DUP ≥1+

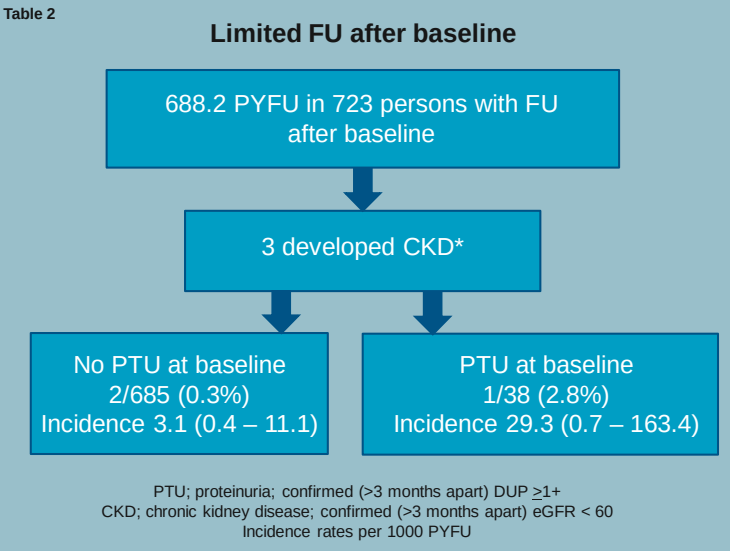
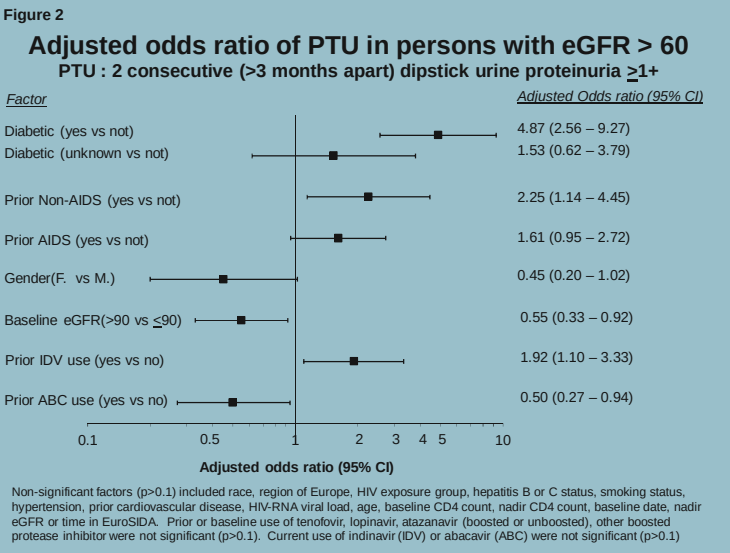


Table 3

Relationship between ARVs and PTU
No significant association between past or current use of TDF, LPV/r, ATV or ATV/r, any other boosted PI and PTU (p>0.2)
WHY?
Using confirmed DUP measurements
Analyses restricted to those with eGFR>60
Cross sectional design of this study
Limited FU after baseline
Other early markers needed to capture deteriorating renal function associated with ARVs may be needed at higher eGFRs

Download poster at: www.chip.dk



Rigshospitalet

