

## Factors associated with poor clinical outcome among HIV-infected patients with tuberculosis (TB) in Eastern Europe. The HIV/TB collaborative study

DN Podlekareva<sup>1</sup>, A Mocroft<sup>2</sup>, FA Post<sup>3</sup>, V Riekstina<sup>4</sup>, JM Miro<sup>5</sup>, H Furrer<sup>6</sup>, M Bruyand<sup>7</sup>, AM Pantelev<sup>8</sup>, E Girardi<sup>9</sup>, JJ Toibaro<sup>10</sup>, J Caylá<sup>11</sup>, R Miller<sup>12</sup>, N Obel<sup>13</sup>, AE Skrahin<sup>14</sup>, E Malashenkov<sup>15</sup>, JD Lundgren<sup>1,13</sup>, O Kirk<sup>1</sup> and the HIV/TB study group

<sup>1</sup>Copenhagen HIV Programme, University of Copenhagen, Faculty of Health Science, Denmark; <sup>2</sup>Royal Free and University College Medical School, London, UK; <sup>3</sup>King's College London School of Medicine, UK; <sup>4</sup>State Agency of TB and Lung Diseases, Riga, Latvia; <sup>5</sup>Hospital Clinic - IDIBAPS, University of Barcelona, Spain; <sup>6</sup>University Hospital of Bern, Switzerland; <sup>7</sup>INSERM, U 897, "epidemiology and biostatistics", Bordeaux, France; <sup>8</sup>TB Hospital #2, St. Petersburg, Russia; <sup>9</sup>Instituto Nazionale Malattie Infettive L Spallanzani, Rome, Italy; <sup>10</sup>Hospital JM Ramos Mejia, Buenos Aires, Argentina; <sup>11</sup>Servicio de Epidemiología. Agencia de Salud Pública de Barcelona. CIBER Epidemiología y Salud Pública (CIBERESP), Spain; <sup>12</sup>Mortimer Market Centre, London, UK; <sup>13</sup>Department of Infectious Diseases, Rigshospitalet, Copenhagen, Denmark; <sup>14</sup>Research Institute of Pulmonology and Pulmonary Tuberculosis, Minsk, Belarus; <sup>15</sup>Botkin Hospital of Infectious Diseases, St. Petersburg, Russia

### OBJECTIVES

- To assess possible regional diversity in the clinical characteristics, management and outcome of HIV/TB patients in Europe and Argentina
- Analyse risk factors associated with a fatal outcome after TB diagnosis in the cART era with special attention on Eastern Europe

### METHODS

1075 consecutive HIV-patients starting TB treatment between 1/2004 and 12/2006 in 47 clinics across Europe and Argentina were included. Patients were stratified according to region of residence:

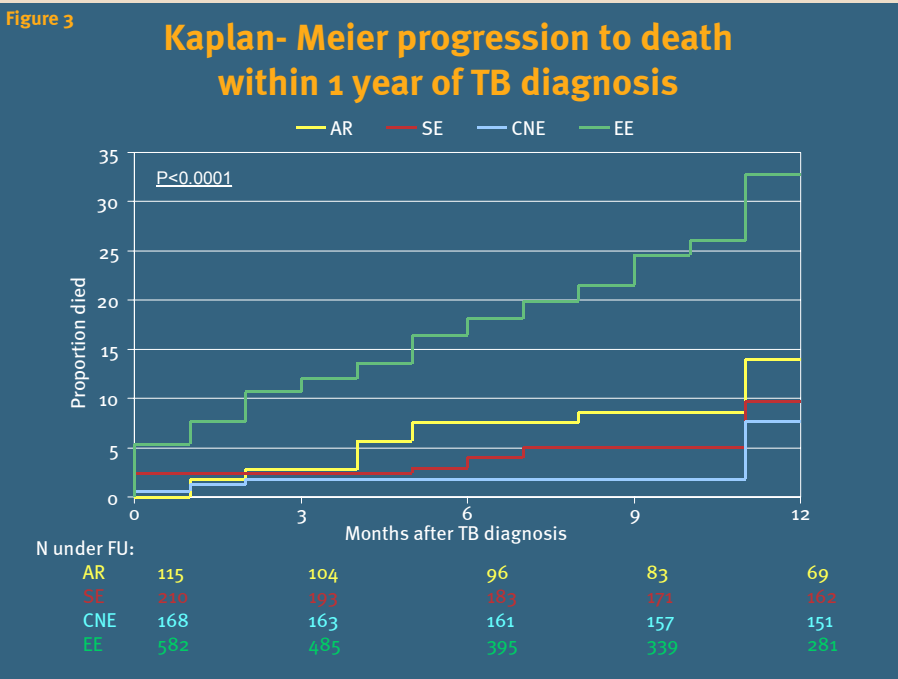
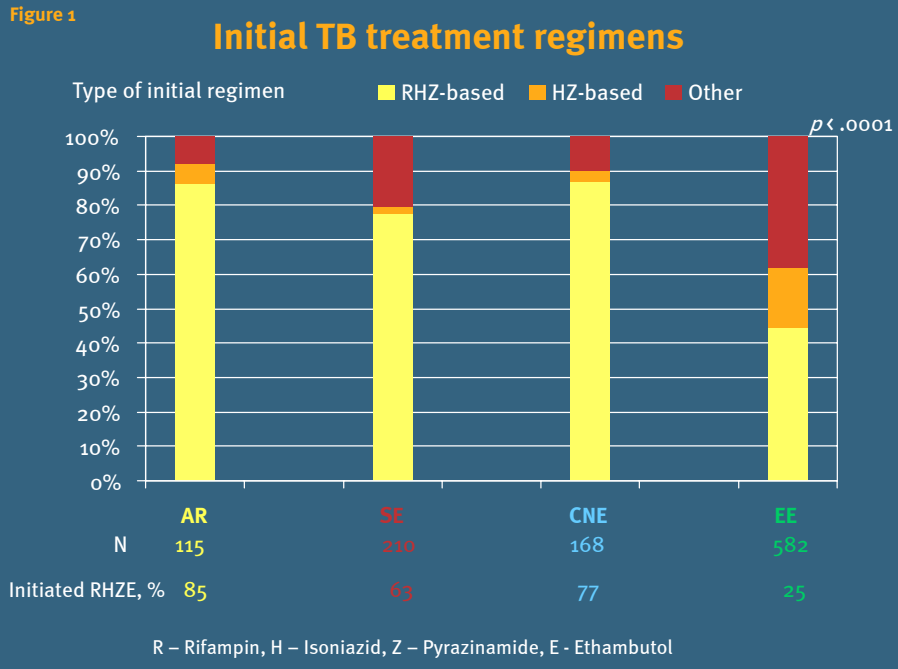
- Argentina (AR), N=115
- Southern Europe (SE), N=210
- Central/Northern Europe (CNE), N=168
- Eastern Europe (EE), N=582

Kaplan-Meier estimation and Cox proportional hazards regression models were used to estimate the probability of death

### RESULTS

Pronounced regional differences were observed in patients characteristics

- Patients from EE:
  - younger, white, and from the same country as where treated for TB (95%). Up to 80% had a history of injection drug use (IDU) and 46% coinfectd with HCV (vs. 9-25% in other regions, p<0.0001)
- Patients from CNE:
  - migrants from non-European countries (60%), female (53%) and with heterosexual HIV acquisition (65%)
- Patients from SE:
  - more often had TB diagnosis in the past: 18% vs. 7%, 9% and 6% in AR, CNE and EE resp., p<0.0001
- Patients from AR:
  - more pronounced immunodeficiency: median (IQR) CD4 cell count at Baseline: 92 (41-228), compared to 146 (55-291), 145 (54-284), 212 (89-463), in SE, CNE and EE resp., p<0.0001



**Study groups:** Argentina, Buenos Aires: M. H. Losso (PI); Project Manager: J. J. Toibaro; Hospital Interzonal General de Agudos DR. D. PROISSIEN: E. Warley, N. Tamayo, M. Cristina Ortiz; Hospital General. de Agudos Donación F. Santojanni: P. Scapellato, E. Bottaro; Hospital Provincial Petrona V. de Cordero. San Fernando: F. Murano; Hospital San Juan de Dios (La Plata): M. Miachans, J. Contarelli, L. Massera; Hospital Interzonal HIGA Oscar Alende (Mar del Plata): J. Corral, M. Huaique, C. Miglioranza; Hospital de Infecciosas Francisco Muñiz: M. Corti, H. Metta; Hospital General. de Agudos Dr. T. Álvarez: A. Casinó, R. Cuiñi; Hospital Posadas: H. Laplume; Hospital Rawson (Cordoba): D. David, C. Marson; C.A.I.C.I.: S. Lupo, L. Trape; Hospital Piñero: O. García Messina, O. Gear; Hospital General de Agudos J.M. Ramos Mejía: J. J. Toibaro, J. M. Bruguera **Belarus**, Minsk: University Hospital of Infectious Diseases: I. Karpov (PI), A. Vasilenko; Research Institute of Pulmonology and Pulmonary Tuberculosis: E. Skrahina, A. Skrahin; Gomel: University Hospital of Infectious Diseases: S. Zhavoronok, V. Mitsura, D. Ruzanov, University Hospital of Tuberculosis: V. Bondarenko; Svetlogorsk: Gomel Region AIDS centre: O. Suetnov, D. Paduto **Denmark**: Danish HIV Cohort: N. Obel (PI); Rigshospitalet: J. Gerstoft; Hvidovre University Hospital: G. Kronborg; Odense University Hospital: C. Pedersen; Aarhus University Hospitals, Skibby: C.S. Larsen; Århus Hospital: G. Pedersen; Herning Hospital: A.L. Laursen; Helsingør Hospital: L. Nielsen; Kolding Hospital: J. Jensen **France**: Aquitaine Cohort: F. Dabis (PI); Epidemiology: G. Chêne, F. Dabis, S. Lawson-Ayayi, M. Bruyand, R. Thibaut; M. Winkler. Infectious diseases-internal medicine: N. Bernard, M. Dupon, D. Lacombe, D. Malvy, P. Mercier, P. Morlat, D. Neau, J.L. Pellegrin, J.M. Ragnaud, Immunology: J.F. Moreau, P. Blanco Virology: H. Fleury, M.E. Lefebvre, B. Masquelier, I. Pellegrin Pharmacovigilance: Ghada Miremont Clinical Pharmacology: Dominique Breilh Monitoring, Data Management and Statistical Analysis: M.J. Blaiseau, M. Decoin, S. Delvaux, D. Dutot, S. Gellard, C. Hanapier, J. Houinou, S. Labarrière, V. Lavignolle-Aurillac, G. Palmer, D. Touchard, B. Uwamaliye-Nyuyumba Clinical Centers (participating physicians): Bordeaux University Hospital: P. Morlat (I. Bernard, M. Bonarek, F. Bonnet, K. Lacombe, P. Gellie, D. Lacombe, F. Paccalin, M.C. Pertusa), M. Dupon (H. Dutronc, F. Dauchy, S. Lafarie), M. Longy-Boursier (P. Mercier, D. Malvy, T. Pistonne, M.-C. Receveur, P. Thibaut), J.M. Ragnaud (C. Cazorla, D. Chambon, C. De La Taille, T. Galpérine, D. Neau, A. Ochoa), J.L. Pellegrin (J.F. Viallard, O. Caubet, C. Nouts), P. Couzigou (L. Castera), Dax Hospital: P. Loste (L. Caunégre) Bayonne Hospital: F. Bonnal (S. Farbos, M.C. Gernain), Libourne Hospital: J. Ceccaldi (S. Tchamgoué), Mont de Marsan Hospital: S. De Witte **Italy**: Clinica di Malattie Infettive, Modena: C. Musadini (PI), F. Prati, S. Castelletti; ICONA cohort: E. Girardi (PI) **Latvia**, Riga: State Agency of TB and Lung Diseases: V. Riekstina (PI); Infectology Centre of Latvia: P. Aldins **Romania**, Bucharest: Spitalul de Boli Infectioase si Tropicale: D. Duiculescu (PI) **Russia**, St. Petersburg: Botkin Hospital of Infectious Diseases A. Rakhmanova (PI), E. Malashenkov, A. Kozlov, St. Petersburg City TB Hospital №2, A. Pantelev; Nizhny Novgorod city AIDS Centre: S. Buzunova **Spain**: Barcelona: Hospital Clinic - IDIBAPS, University of Barcelona: J. M. Miro (PI), J. F. García-González, A. Moreno-Camacho, J. A. Martínez, J. González, F. García-Alejaide, E. de Laza, J. M. Gatell, Hospital del Mar: P. Sanchez, J.L. Lopez-Colomes, Mutua de Terrassa: X. Martínez-Lacasa, Hospital Universitari Vall d'Hebron: V. Falcó, I. Oñativia, R. Vidal, Hospital Universitari de Sant Pau: M. A. Sambateu, Agencia de Salud Pública de Barcelona: J. Caylá, A. Moreno-Martínez, A. Orcau **Switzerland**: Swiss HIV Cohort: Zurich: R. Weber (PI); Basel: M. Battegay; Geneva: B. Hirschel; Lausanne: M. Cavassini; Lugano: E. Bernasconi; St. Gall: P. Schmid; Bern: H. Furrer; Data Center Lausanne: M. Rickenbach **United Kingdom**: London: King's Hospital: F. Post, L. Campbell; Mortimer Market Centre: R. Miller **Ukraine**: Kiev City AIDS Centre: N. Chentsova (PI) **EuroSIDA**: J. D. Lundgren **Coordinating centre (CHIP)**: D. Podlekareva, O. Kirk, A. Mocroft, J. Kjer, M. Ellefson **Steering Committee**: N. Chentsova, H. Furrer, E. Girardi, M. Bruyand, M. H. Losso, J. Lundgren, A. Pantelev, R. Miller, JM Miro, N. Obel, F. Post, V. Riekstina, A. Skrahin, J. J. Toibaro

### Differences in diagnostic procedures, resistance patterns, TB treatment and cART Patients in EE:

- 69% had microbiologically or pathologically confirmed TB, vs. 72%, 79% and 86% in AR, SE and CNE respectively
- 50% with performed resistance test were infected with *M. tuberculosis* resistant to at least one TB drug, vs. 7%, 13% and 7% respectively (p<0.0001)
- 28% with resistance to at least Rifamycin, vs. 3%, 2% and 3% respectively (p<0.0001)
- Were less likely to:
  - initiate TB treatment with four standard first line TB drugs (Figure 1)
  - receive cART during first year after TB diagnosis (Figure 2)

### Outcome of TB disease and factors associated with death:

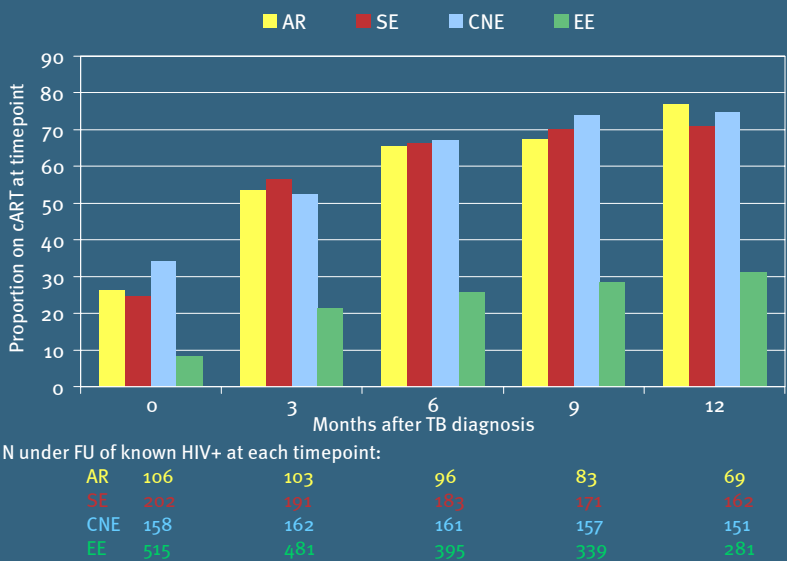
- Outcome according to WHO classification reported for 965 patients
- Less patients from EE experienced Treatment success (cure/treatment completed): 48% vs. 64%, 66%, and 85% respectively
- Death rates and factors associated with higher mortality rates are presented on Figures 3 and 4

### CONCLUSIONS

- Pronounced differences observed clinical characteristics, management and survival prognosis after TB diagnosis in HIV/TB patients across Europe and Argentina
- Higher mortality rate in EE compared with other regions can partially be explained by differences in:
  - patterns of anti-TB treatment
  - presence of TB drug-resistance
  - access to cART and baseline CD4 cell count
- There is an urgent need to further understand why these differences exist and how outcome of HIV/TB in Eastern Europe can be improved

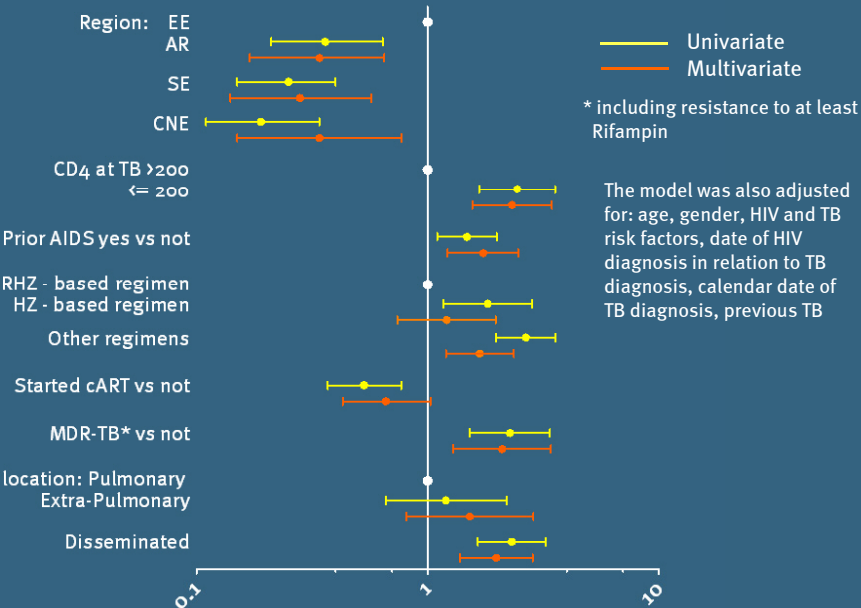
### Figure 2

### Use of cART during the 1<sup>st</sup> year after TB diagnosis



### Figure 4

### Relative Hazards of death



Download poster at: [www.cphiv.dk](http://www.cphiv.dk)