HYPONATREMIA IS A MARKER OF SEVERITY OF HIV DISEASE IN COMBINED ANTIRETROVIRAL THERAPY-NAIVE PATIENTS: A SINGLE CENTRE RETROSPECTIVE COHORT STUDY

BRACONNIER Philippe[a, b], DELFORGE Marc[a], GARJAU Maria[c], WISSING Karl Martin[b, c], DE WIT Stéphane[a]

[a]Department of Infectious Diseases, AIDS Reference Center, Saint-Pierre University Hospital, Université Libre de Bruxelles, Brussels, Belgium. [b]Department of Nephrology, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel, Brussels, Belgium. [c]Department of Nephrology, Centre Hospitalier Universitaire Brugmann, Brussels, Belgium.

OBJECTIVES

- Hyponatremia is the most common electrolyte abnormality in the general patient population:
  - Prevalence: 4-7% in an ambulatory setting and 15-30% in hospital care
- Hyponatremia is associated with an increased risk of death in hospitalized and in ambulatory patients

Study objectives:
- Investigate the prevalence of hyponatremia in HIV-infected patients in the recent cART-era
- Provide a detailed description of health conditions associated with hyponatremia
- Study hypothesis: hyponatremia is an independent risk factor for death of HIV-positive patients

METHODS

- Single-center retrospective cohort study
- AIDS Reference Center, St Pierre University Hospital in Brussels, Belgium

> Inclusion of all cART-naïve HIV patients followed at the AIDS Reference Center St Pierre between 1 January 1998 and 31 December 2013
> n = 1196

> Na < 135 mmol/l
> n = 177

> Na ≥ 135 mmol/l
> n = 1019

- Collection of demographic, clinical and laboratory data
- Long term follow-up (15 years)
- The outcomes of interest were the occurrence of death and number of hospitalizations

RESULTS

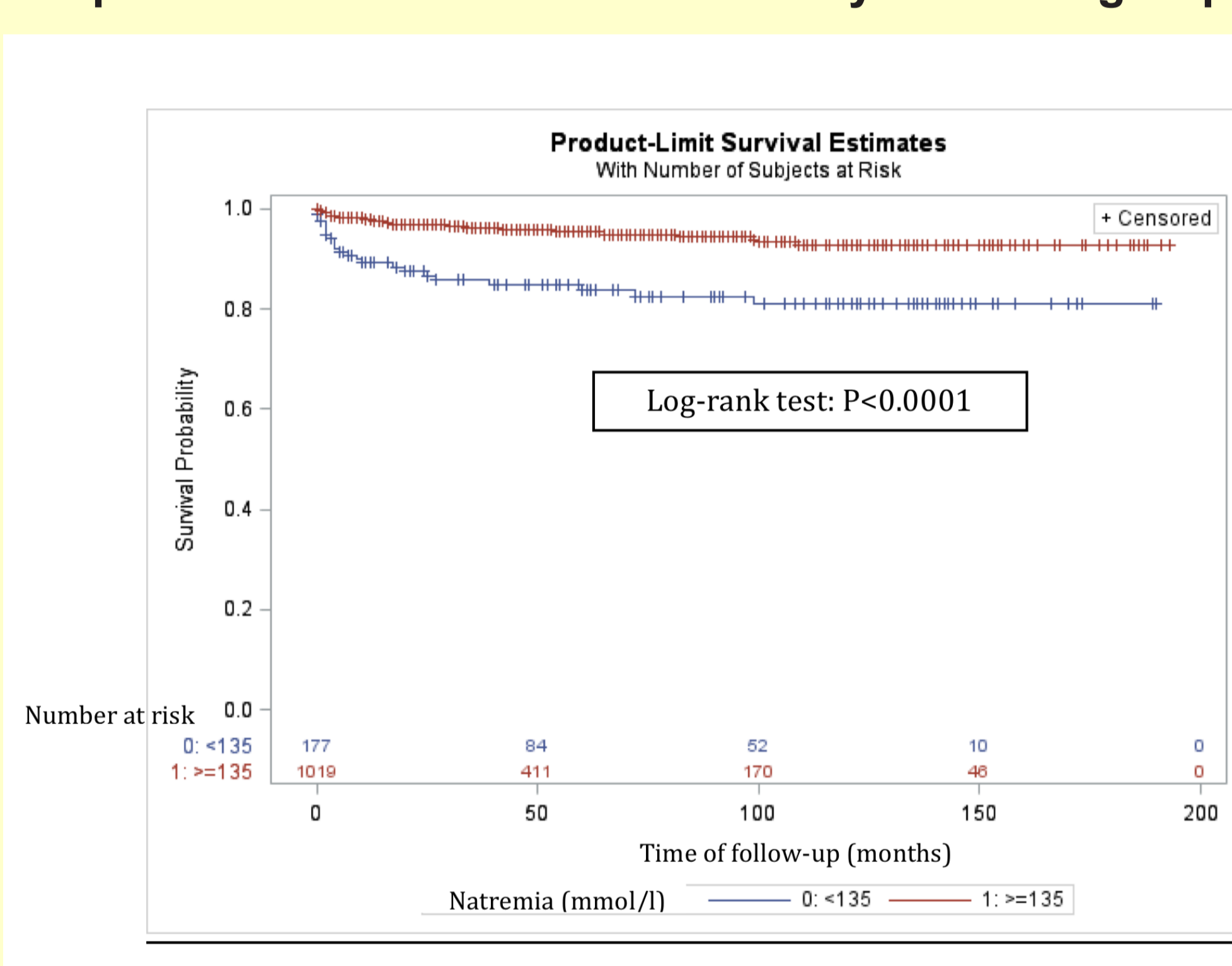### Main characteristics of hyponatremic and normonatremic patients

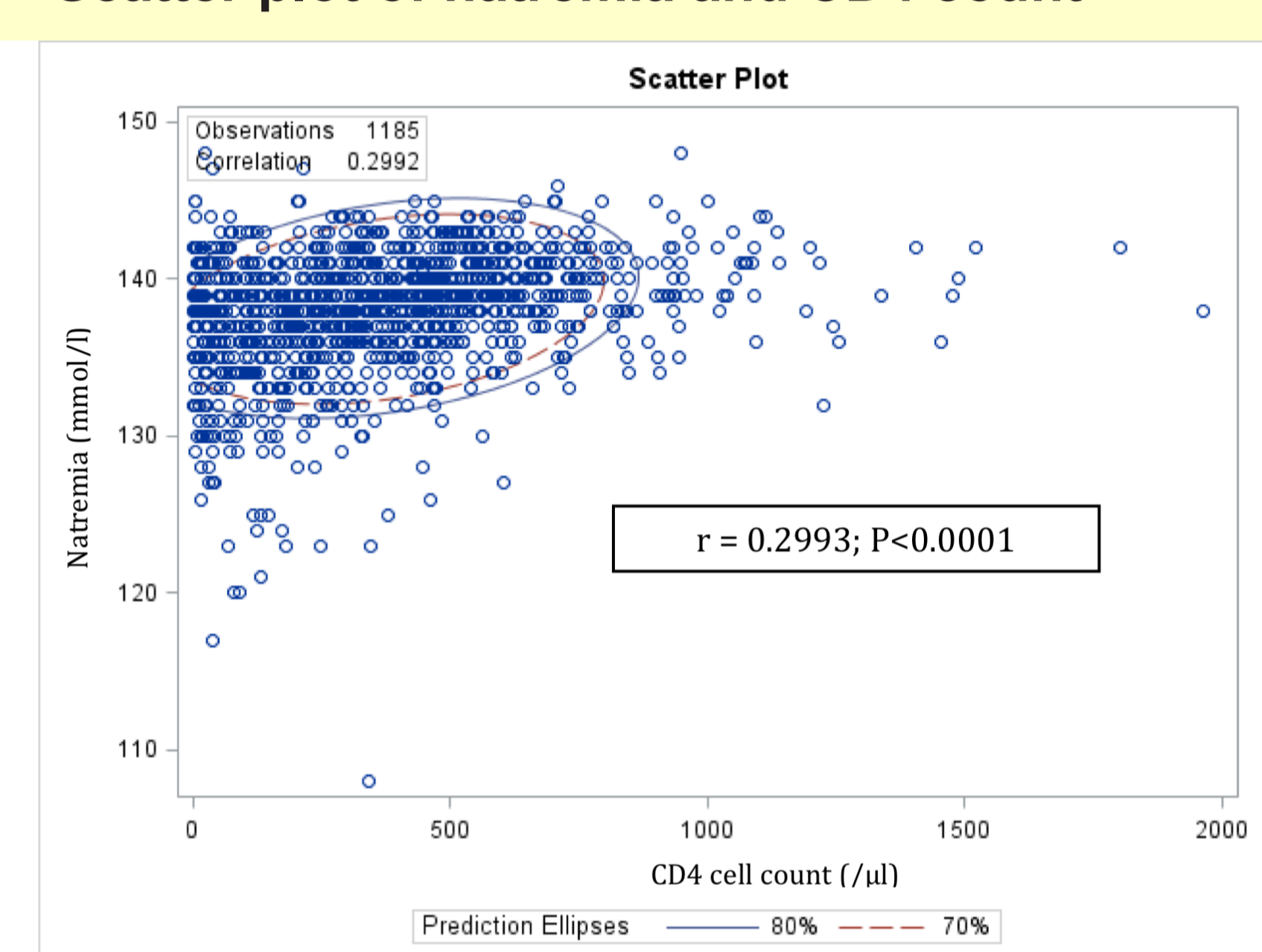| Characteristics	Total (N=1196)	Na < 135 mmol/l (N=177)	Na ≥ 135 mmol/l (N=1019)	P-value
Age (years)[1]	36.8±10.7	37.4±10.0	36.7±10.9	0.238
Female gender (n)	445 (37.2%)	90 (50.8%)	355 (34.8%)	<0.0001
African ethnicity (n)	612 (51.2%)	125 (70.6%)	487 (47.8%)	<0.0001
Homo-bisexual orientation (n)	395 (33.0%)	26 (14.7%)	369 (36.2%)	<0.0001
Natremia (mmol/l)[2]	139.0 (136.0-141.0)	132.0 (130.0-134.0)	139.0 (137.0-141.0)	<0.0001
Hospitalization at first contact (n)	332 (27.7%)	128 (72.3%)	204 (20.0%)	<0.0001
Acquired immunodeficiency syndrome (AIDS) (n)	215 (18.0%)	89 (50.3%)	126 (12.4%)	<0.0001
CD4 cell count (/μl)[1]	371.8±275.3	207.5±197.7	400.4±277.0	<0.0001
CD4 cell count < 350/μl (n)	611 (51.1%)	143 (80.8%)	468 (45.9%)	<0.0001
CD4 nadir (/μl)[1]	362.8±267.6	200.8±184.1	391.2±269.9	<0.0001
CD4 nadir < 200/μl (n)	360 (30.1%)	106 (59.9%)	254 (24.9%)	<0.0001
HIV viral load (copies/ml)[2]	71600 (13500-100000)	100000 (55000-313500)	58750 (11800-100000)	<0.0001
HIV viral load > 100 000 copies/ml (n)	465 (38.9%)	104 (58.7%)	361 (35.4%)	<0.0001
Hepatitis B (n)	69 (5.8%)	14 (7.9%)	55 (5.4%)	0.223
Hepatitis C (n)	69 (5.8%)	12 (6.8%)	57 (5.6%)	0.478
Fib 4 score > 3.25 (n)	77 (6.4%)	28 (15.8%)	49 (4.8%)	<0.0001
Anemia (n)	597 (50%)	138 (78%)	459 (45%)	<0.0001
Hyperlipidemia (n)	418 (34.9%)	58 (32.8%)	360 (35.3%)	0.550
Mean triglyceridemia[1]	111.1±68.5	132.4±79.9	108.0±66.0	<0.0001
Diabetes mellitus (n)	52 (4.3%)	14 (7.9%)	38 (3.7%)	0.0254
Antihypertensive drugs (n)	39 (3.3%)	4 (2.2%)	35 (3.4%)	0.645

[1]mean±standard deviation

[2]median (interquartile range)

[3]excluding patients hospitalized at first contact

Kaplan-Meier estimates of survival by natremia group

Scatter plot of natremia and CD4 count

Outcomes in hyponatremic and normonatremic patients

Characteristics	Total (N=1196)	Na < 135 mmol/l (N=177)	Na ≥ 135mmol/l (N=1019)	P-value
Follow-up (months)[1]	36.0 (9.0-80.0)	41.0 (4.0-115.0)	35.0 (10.0-77.0)	0.554
Loss to follow-up (n)	414 (34.6%)	71 (40.1%)	343 (33.7%)	0.104
Deaths (n)	63 (5.3%)	24 (13.5%)	39 (3.8%)	<0.0001
Death rate/1000 patient-years (95% CI)	12.5 (9.6-16.0)	28.3 (18.1-42.2)	9.33 (6.6-12.7)	<0.0001
Hospitalization rate/1000 patient-years (95% CI)	440 (422-458)	785 (725-845)	370 (252-388)	<0.0001
Mean number of hospitalizations per patient (n)[2]	2.2±4.9	4.3±9.5	1.8±3.3	<0.0001
Median time to death (months)[1]	12.0 (3.0-34.0)	6.0 (2.0-22.5)	14.0 (4.0-39.0)	0.169
Median time to first hospitalization (months)[1,3]	12.0 (2.0-28.0)	2.0 (0.0-12.0)	13.0 (2.0-29.0)	0.0012

[1]median (interquartile range)

[2]mean±standard deviation

[3]excluding patients hospitalized at first contact

Risk factors for mortality of patients in univariate/multivariate Cox's proportional hazard models

Risk factors	Univariate Model Hazard ratio (95% Confidence interval)	P-value	Multivariate Model Hazard ratio (95% Confidence interval)	P-value
Age < 35 years	0.51 (0.29-0.87)	0.014	0.91 (0.48-1.73)	0.782
Female gender	1.68 (1.01-2.80)	0.045	1.65 (0.86-3.16)	0.132
African ethnicity	1.29 (0.77-2.15)	0.366		
Homo-bisexuel orientation	0.28 (0.13-0.59)	0.0003	0.90 (0.34-2.34)	0.827
Na < 135mmol/l	3.94 (2.30-6.74)	<0.0001	1.03 (0.54-1.97)	0.935
AIDS	8.83 (5.18-15.06)	<0.0001	5.24 (2.59-10.62)	<0.0001
CD4 cell count < 350/μl	11.71 (4.66-29.43)	<0.0001	6.58 (1.89-23.06)	0.003
HIV viral load > 100 000 copies/ml	3.36 (1.87-6.03)	<0.0001	1.15 (0.56-2.37)	0.702
Hepatitis B	0.23 (0.032-1.71)	0.172		
Hepatitis C	2.54 (1.15-5.60)	0.0259	2.70 (1.172-6.23)	0.02
Fib4 score > 3.25	3.84 (1.95-7.55)	<0.0001	1.69 (0.77-3.74)	0.192
Anemia	4.30 (2.95-6.27)	<0.0001	1.15 (0.75-2.84)	0.263
Hyperlipidemia	0.93 (0.54-1.59)	0.892		
Diabetes mellitus	4.22 (1.96-9.11)	0.0011	2.07 (0.88-4.85)	0.096
Inclusion period 1998-2004	2.54 (1.52-4.25)	0.0004	1.32 (0.72 – 2.42)	0.372

CONCLUSIONS

- Baseline hyponatremia is common in cART naïve HIV-infected patients (14.8%)
- Baseline hyponatremia is associated with an increased risk of mortality in HIV patients in univariate analysis
- Hyponatremia is not an independent risk factor for mortality
- Hyponatremia is a marker of severity of HIV-related disease
- Serum sodium concentration correlates positively with CD4 cell count
- HIV-patients with a low serum sodium at baseline might benefit from a close follow-up to improve outcomes