Results from the Module ‘’Anemia” and Evaluation of the Iron Store in PD Patients with the MR Imaging

Issad.B, Cohen.Y, Griuncelli.M, Beaudreuil.S, Ghali.N, Verger.Ch, Rostoker.G,

Service de Néphrologie CHU Pitié Salpêtrière Paris,1
Service de Radiologie CHP Claude Galien 2
CHP Claude Galien à Quincy,3
CHU Kremlin-Bicêtre 4, CH Marc jacquet à Melun 5 et RDPLF –Pontoise 6

Recent Awareness by Nephrologists of a very Wide Use of Injectable Iron Derivatives over the Last Decade in Hemodialysis for Economic Reasons

(Épargne d'ASE: USA Bundling/Europe et France: réintégration des ASE dans le forfait de dialyse)

Conférence des KDIGO en Mars 2014 à San Francisco:
«Controversies conference on iron management in chronic kidney disease »

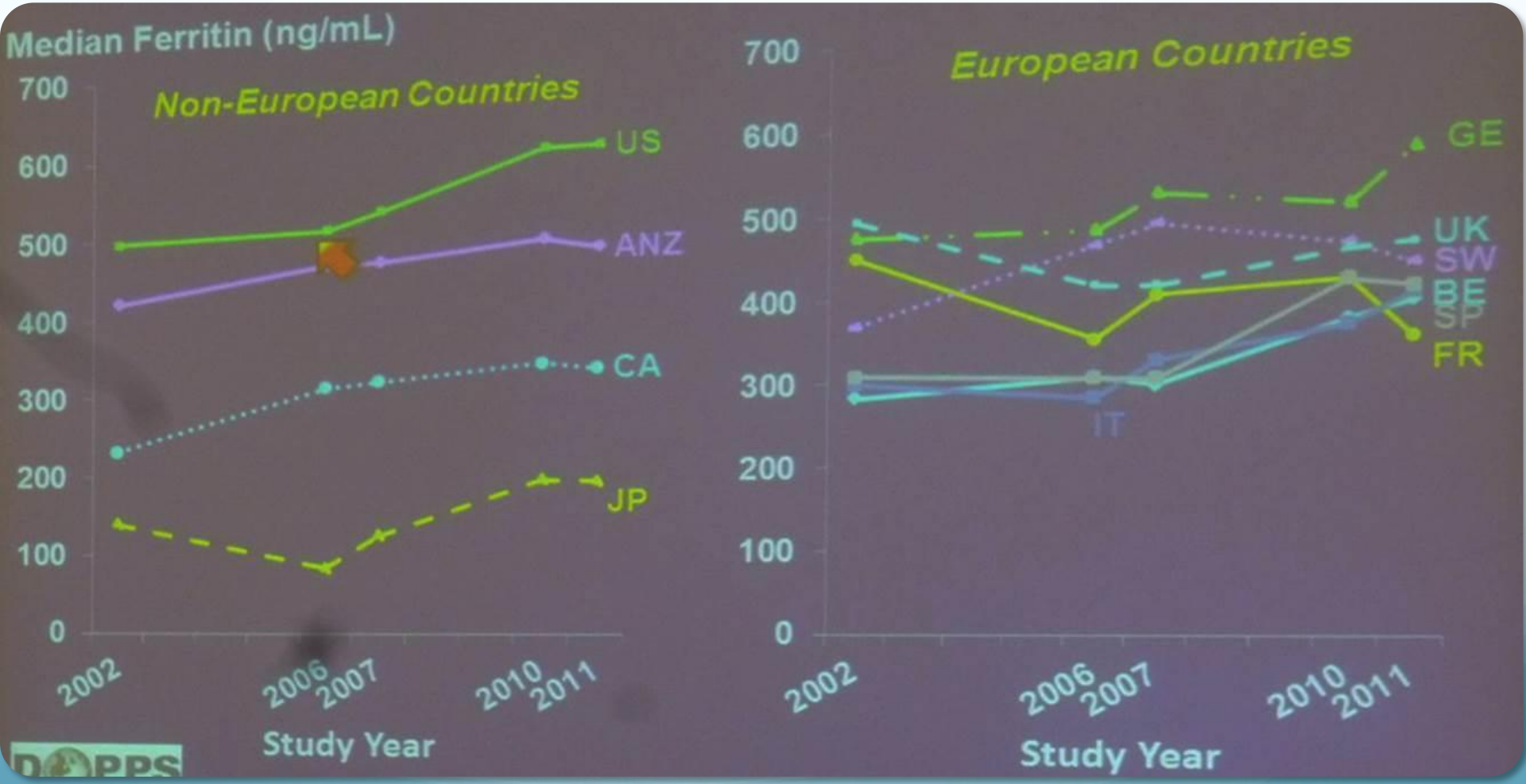
Statement of the American Society of Nephrology: online december 2014 JASN:
«Considerations and challenges in defining optimal iron utilization in hemodialysis»

DOPPS-Session ASN Novembre 2012- San Diego - Ramirez S.P.

Anemia care is changing dramatically: potential implications of higher iron dosing

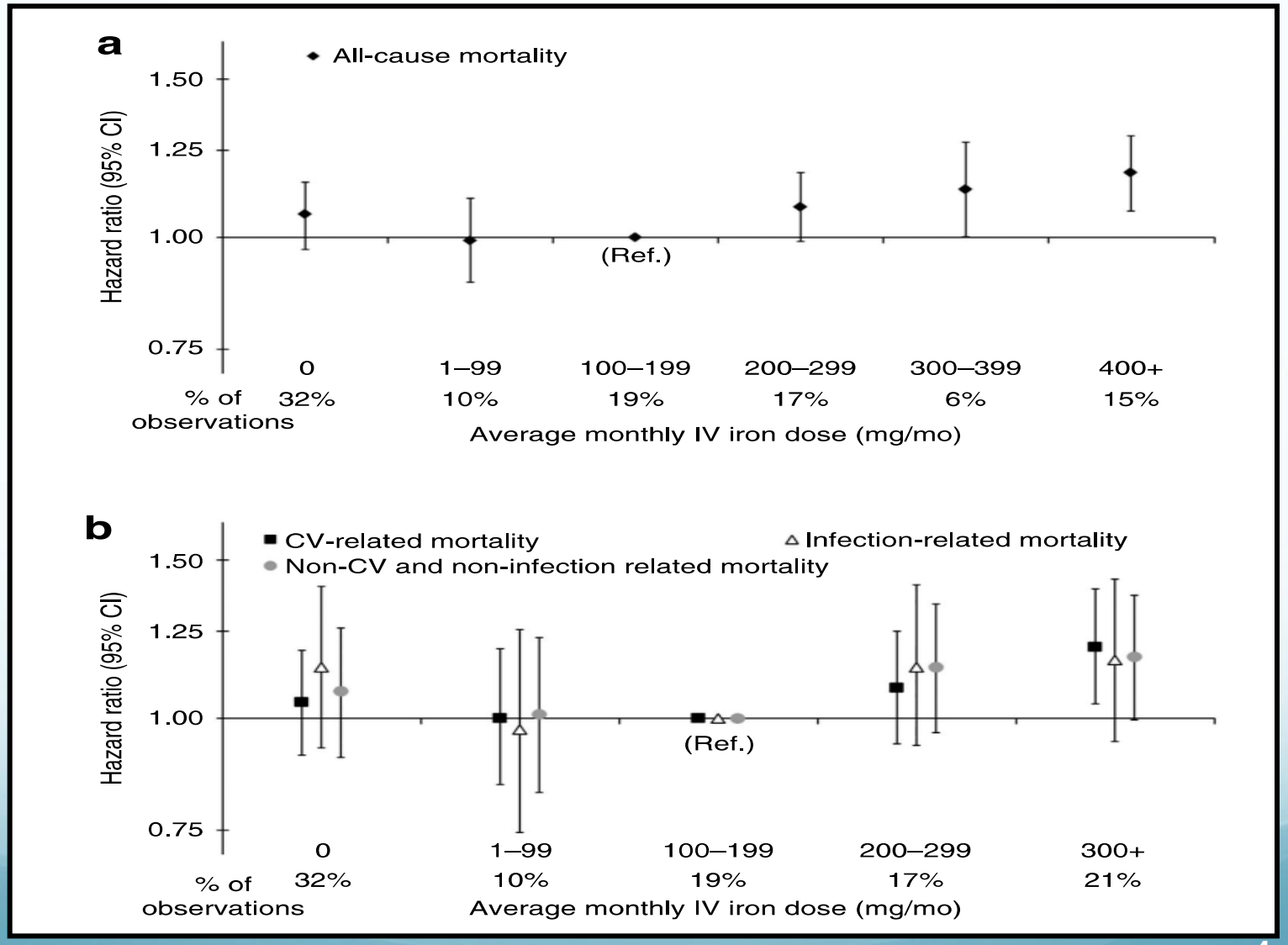
Median Ferritin Trends by Country

DOPPS 2-4 Sample Patients (2002-2011)



Relationship Between Strong Intravenous Iron and Mortality in Hemodialysis

G. Bailie et al: Data from DOPPS validate an association between high intravenous iron doses and mortality. Kidney Int., 30 july 2014 online



Etude du Stock Martial hépatique en DP:

A contrasted iron world : hemodialysis versus peritoneal dialysis

	Peritoneal dialysis	Hemodialysis
Iron losses	- Digestives loss: Idem chronic renal disease 3.15 ml/day so 1130 ml/year - Secondary loss due to biological samples: 428 ml/year - Total blood loss: 1.5 l/year (750 mg of iron)	**Iron loss in the hemodialysis patient** Loss related to the hemodialysis technique (dialyzers + circuits): 165 ml of blood (82.50 mg of iron/year) Digestive loss (micro-bleeding): 2257 ml of blood/year (1129 mg of iron/year) Biological samples for biological follow-up of uremic state: 428 ml of blood/year (214 mg of iron/year) Care of dialysis catheters: 2680 ml of blood/year (1340 mg of iron/year) Patients with fistula: 2680 ml of blood/year (1340 mg of iron/year) Patients with permanent catheter: 5320 ml of blood/year (2765 mg of iron/year)
Ferritin target	> 100 µg/L (KDIGO 2012, ERBP 2103)	- 250 µg/L to 500 µg/L (KDIGO 2012) - 100 µg/L to 300 µg/L (ERBP 2013)
Use of IV iron products	Scarce 2nd or 3rd line of therapy(oral iron intolerance) or severe iron deficiency	Almost constant 1st line of therapy

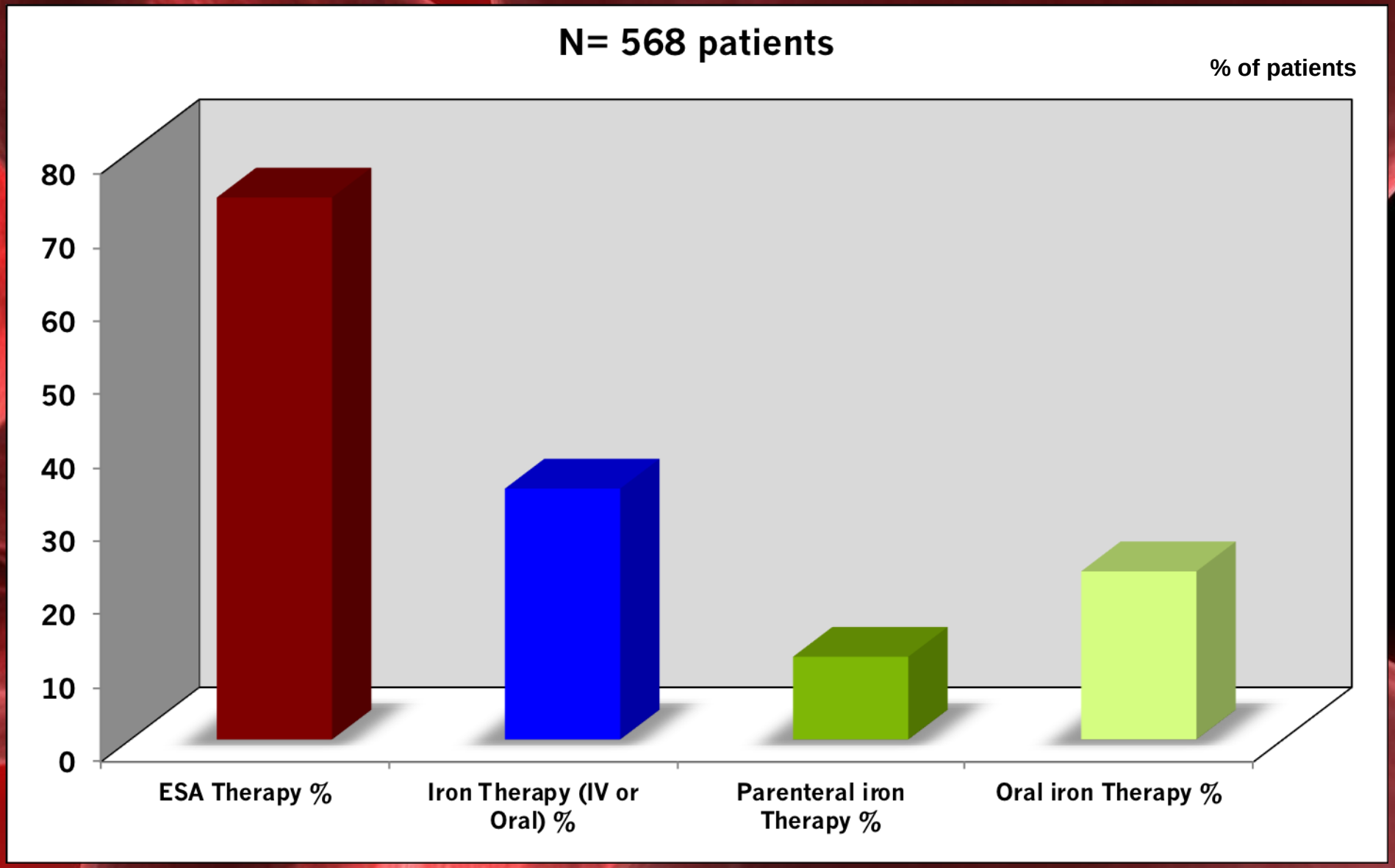
D'après Rottembourg J., Rostoker G. Nephrol Ther 2015 Dec; 11(7): 531-42

Demographic and characteristics of anemia management of 568 patients treated by peritoneal dialysis in France on RDPLF register (2010-2017)

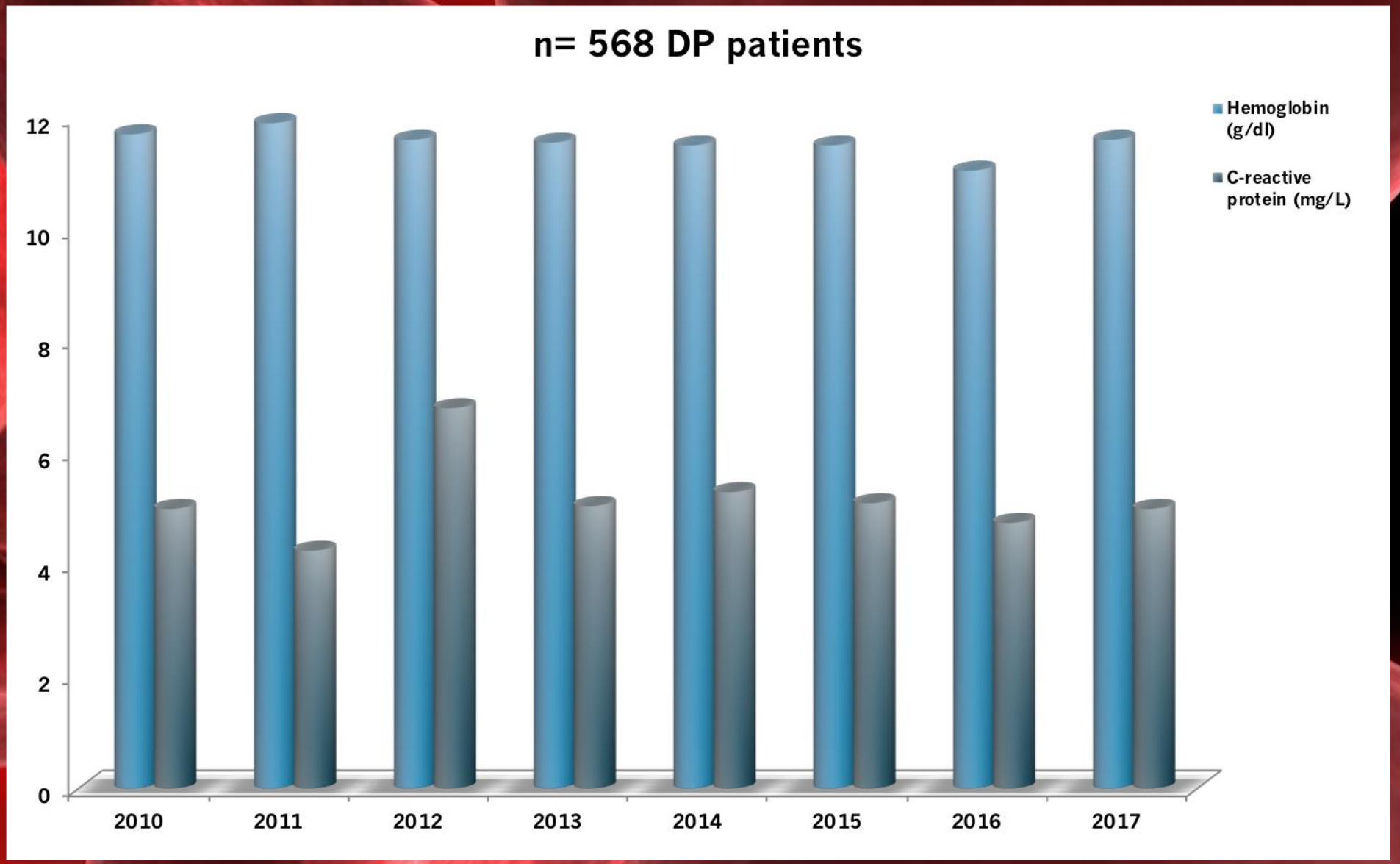
Variables	Peritoneal dialysis patients (N= 568)
Age (years)	71.2 (18.2 - 93.3)
Sex, female (%)	42.43% (241/568)
Duration of dialysis (months)	13.57 (11.99 - 23.36)
ESA therapy (%)	73.77 % (419/568)
Iron therapy (IV or oral) (%)	34.15% (194/568)
Parenteral iron therapy (%)	11.27% (64/568)
Oral iron therapy (%)	22.89% (130/568)
Diabetes (%)	40.49% (230/568)

Values shown are median (range), % of patients or number (n) of patients.

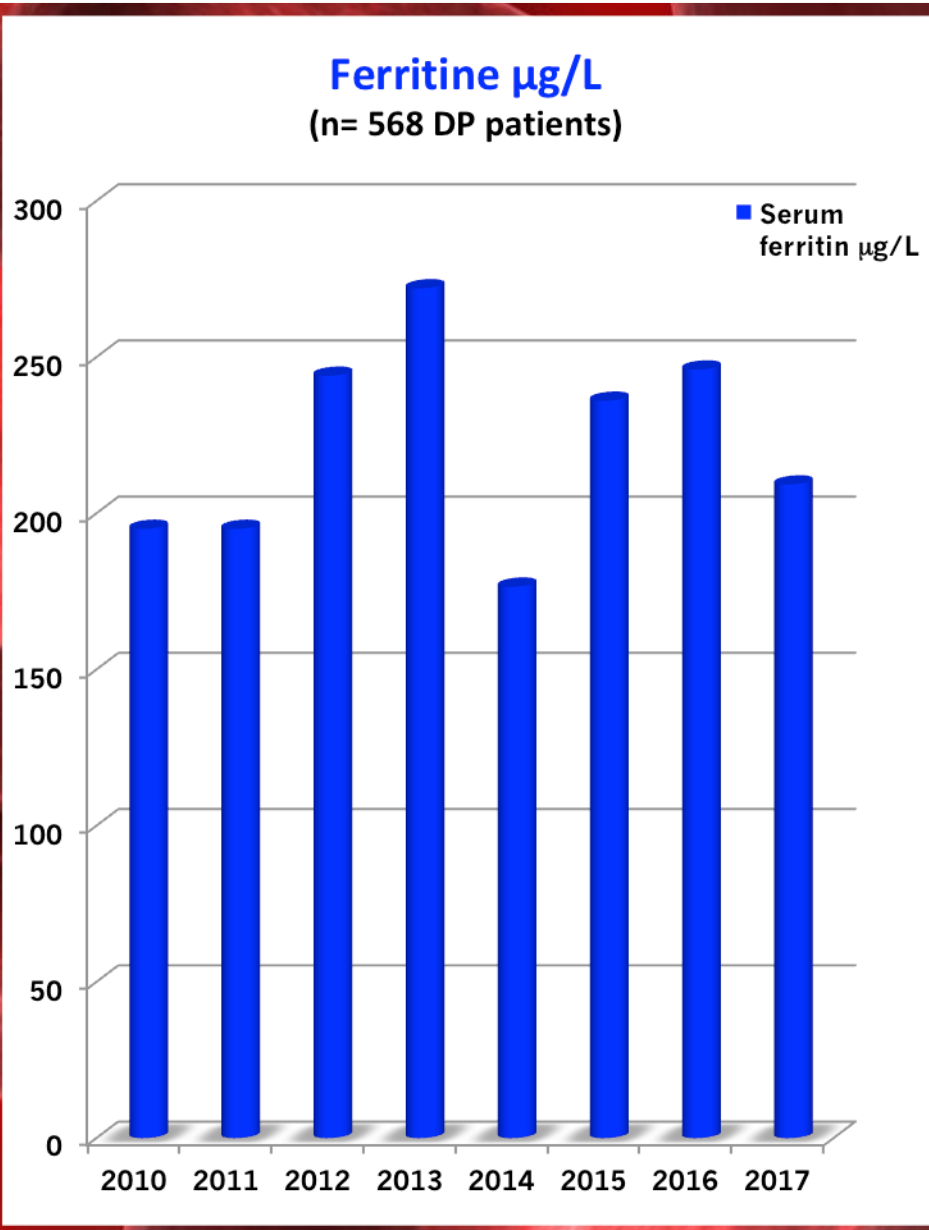
Characteristics of anemia management of 568 patients treated by peritoneal dialysis in France on the RDPLF register (2010-2017)

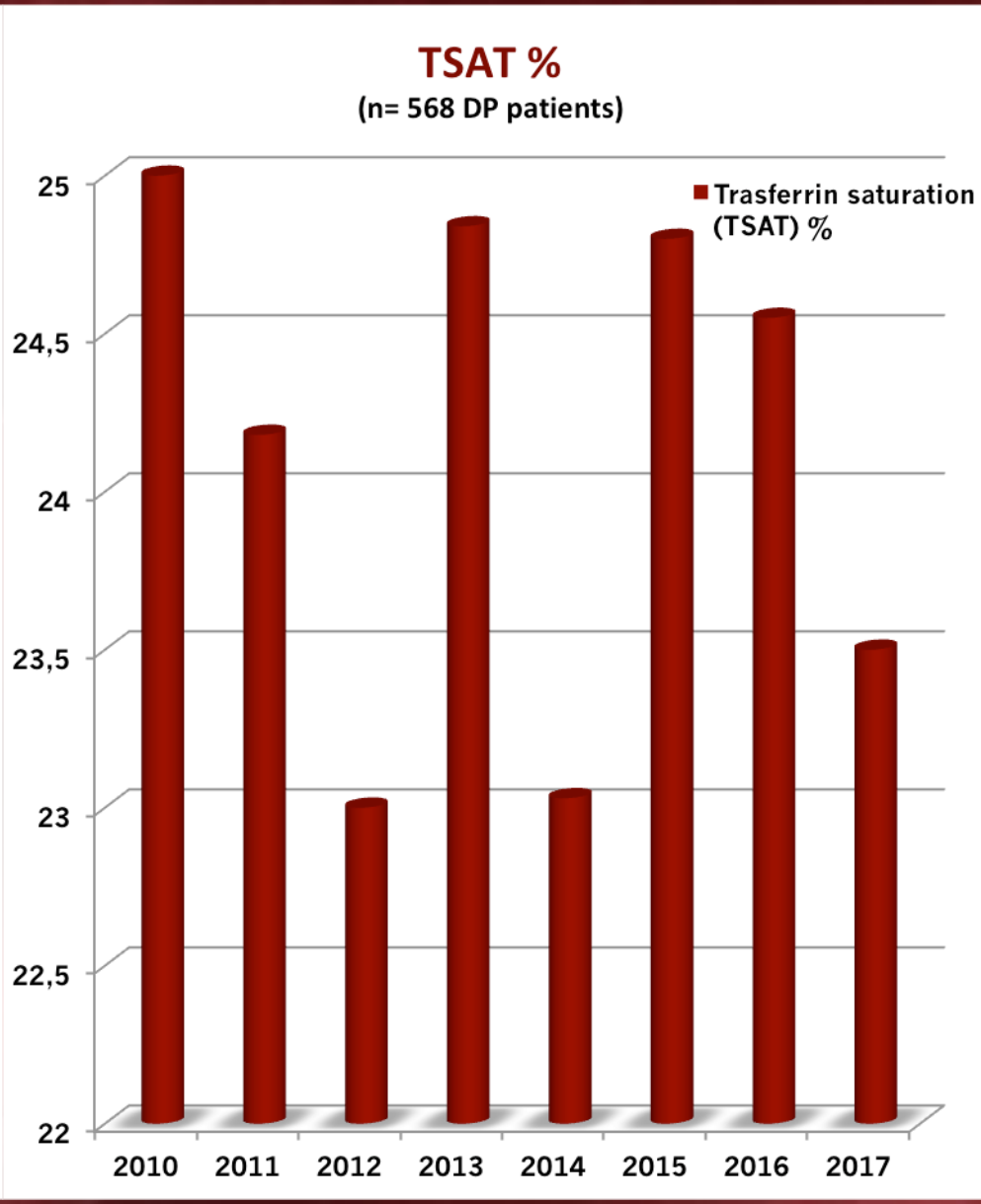


Hemoglobin and C-reactive protein levels of 568 patients treated by peritoneal dialysis in France on RDPLF register (2010-2017)



Biochemical markers of iron metabolism of 568 patients treated by peritoneal dialysis from RDPLF register (2010-2017)





Which hepatic iron load in peritoneal dialysis patients ?

Peritoneal dialysis is also the correct model for studying iron hepatic metabolism and liver iron concentration in ESRD, almost independently of the use of IV iron

Prospective study of liver iron concentration (LIC) in peritoneal dialysis patients studied by quantitative MRI (1)

- **Objective: To compare the frequency and degree of iron overload in PD patients (aim n= 50 patients to include) as compared to hemodialysis patients (Quincy cohort n° 1 of 119 patients published in Am. J. Med in 2012 and Quincy cohort n° 2 of 80 patients published in Plos One in 2014).**

- **Hypothesis to be tested: iron supplementation practices strongly differ between HD and PD with lower usage of IV iron with probable lower frequency of iron liver overload.**

- **Multicenter Study in Great Paris area: CHU Pitié Salpêtrière, CH Marc Jacquet at Melun, CHU Kremlin-Bicêtre, CHP Claude Galien at Quincy**

- **Inclusion Criteria: PD patients for at least 3 months**

- **Exclusion Criteria : those of the study published in HD Patients in Am. J. Med in 2012 in HD: claustrophobia, pacemaker, metallic heart valves, malnutrition, significant bleeding, recent transfusions, cancer not controlled by therapy, major co-morbidities**

Prospective study of liver iron concentration (LIC) in peritoneal dialysis patients studied by quantitative MRI (3)

- **PRELIMINARY RESULTS OF 32 PATIENTS**
- **BEGINNING OF INCLUSIONS: JUNE 2014**
- **CURRENTLY 32 DP PATIENTS STUDIED BY QUANTITATIVE MRI WITH RECOVERY DATA**
- **END OF INCLUSIONS AT DECEMBER 30, 2018**

(with the goal of studying 50 DP patients)

Prospective study of liver iron concentration (LIC) in peritoneal dialysis patients studied by quantitative MRI (2)

- **MRI technique performed centrally:**

-Division of radiology CHP Claude Galien, Quincy sous Sénart

-Blindly (absence of informations on the treatments received and biological results of patients)

-Signal intensity ratio according Rennes University

-With a delay of 7 days between the realization of the MRI and the lastest infusion of IV iron or withdrawal of iron oral supplementation for at least 7 days

-Routine biological data of martial metabolism and CRP

- **Demographic data and analysis of treatment received for anemia (transfusions, ASE, IV iron, oral iron)**
- **Statistical analyses: comparison of DP patients versus HD patients by non-parametric tests (Kruskaul-Wallis and Mann and Whitney tests for quantitative parameters and X2 for qualitative parameters).**

Hepatic Iron Load at Magnetic Resonance Imaging Is Normal in Most Patients Receiving Peritoneal Dialysis

Table 1. Demographic and clinical characteristics of 32 patients treated by peritoneal dialysis and studied by MRI to determine liver iron content

Variable	Peritoneal dialysis patients (N = 32)
Age (yr)	64.5 (34–92)
Sex, female (%)	46.9
Duration of dialysis (mo)	12.5 (2–52)
ESA therapy (%)	71.9
Darbepoetin dose (μg/mo)	59.1 (0–150)
Iron therapy (i.v. or oral) (%)	37.5
Parenteral iron therapy (%)	12.5
Parenteral iron therapy (mg/PD mo)	0 (0–112.5)
Oral iron therapy (%)	25
Oral iron therapy ingested (mg/PD mo)	0 (0–2560)
Charlson Comorbidity Index	5 (2–15)
Diabetes (%)	34.4
Normal LIC at MRI (≤ 50 μmol/g), n	26
Abnormal LIC at MRI (> 50 μmol/g), n	6
Mild hepatic iron overload at MRI (51–100 μmol/g), n	5
Moderate hepatic iron overload (101–200 μmol/g), n	0
Severe hepatic iron overload (> 200 μmol/g), n	1

LIC, liver iron concentration; MRI, magnetic resonance imaging.
Values shown are median (range), percentage (%) of patients, or number (n) of patients.

Table 2. Biochemical markers of iron metabolism in 32 patients treated by peritoneal dialysis and studied by MRI to determine liver iron content

Variable	Patients treated by peritoneal dialysis (N = 32)
Hemoglobin (g/dl)	11.5 (8.7–16.2)
Serum ferritin (μg/l)	144 (11–885)
Serum iron (μmol/l)	13.2 (5.5–24.3)
Serum transferrin (g/l)	2.3 (1.5–3.6)
Transferrin saturation (TSAT) (%)	23.2 (1.1–50.0)
Serum transferrin soluble receptors (sTfR) (mg/l)	3.3 (2.3–7.9)
C-reactive protein (mg/l)	6.7 (1.3–67.6)

MRI, magnetic resonance imaging.
Values shown are median (range).

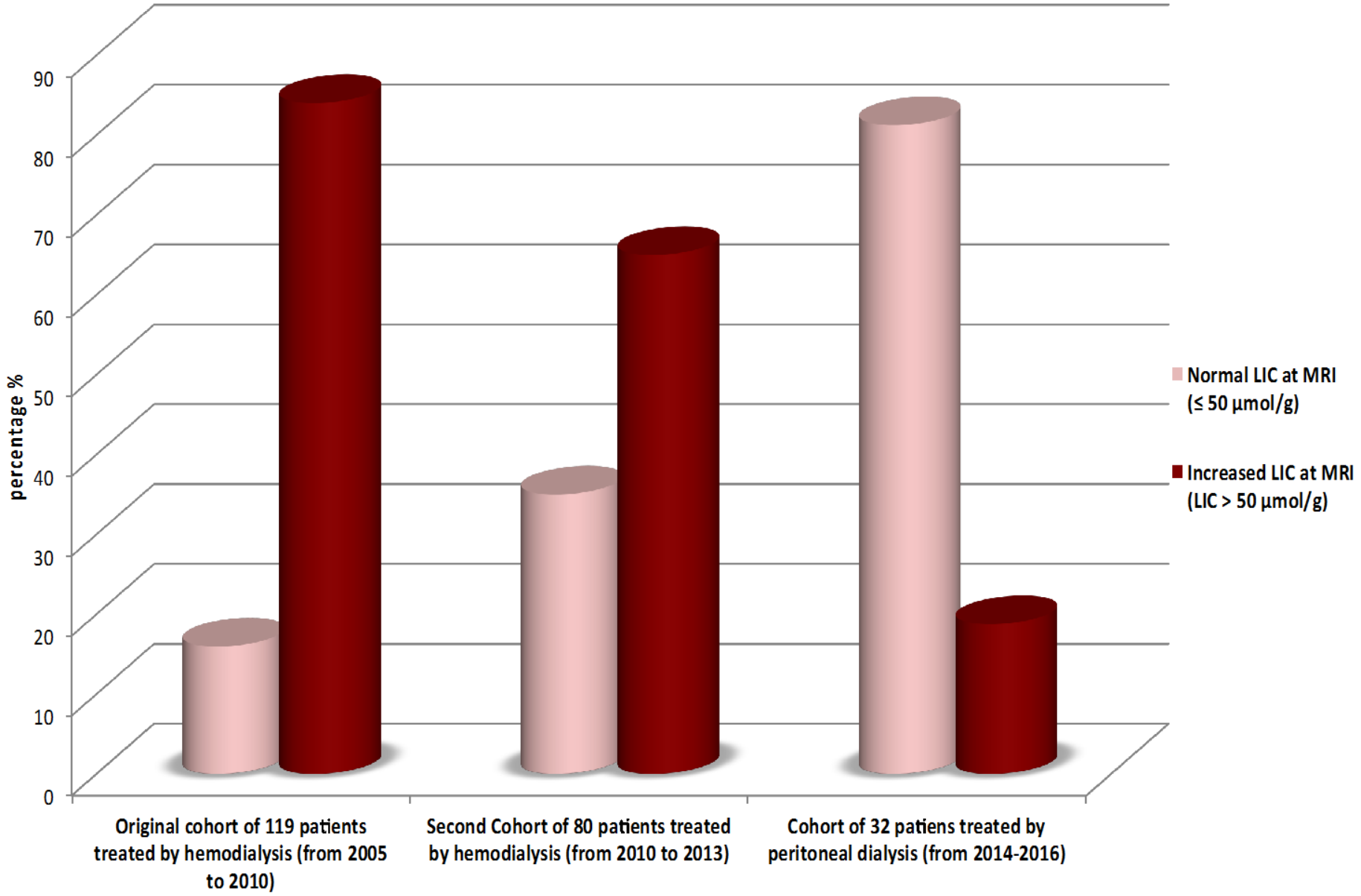
Absence of link between martial overload in PD

and

-Gène HFE (mutation majeure C282Y de l'hémochromatose génétique)

-Score AUDIT (addiction and alcohol consumption)

Figure 2: Histogram of repartition of liver iron content at MRI characterized as normal or abnormal according the modality of dialysis



CONCLUSIONS

- End of study with 50 PD patients planned for December 2018
- In PD , because of the lower use of IV iron with smaller doses, hepatic iron overload is rare, unlike hemodialysis, where it is very common
- The paucity of liver iron overload in PD shows that end-stage disease « per se » is not the culprit of dialysis-associated hemosiderosis