Ante 2025

XXXII Corso Nazionale di Aggiornamento Tecnici Emodialisi

Dialisi e Tecnologia

" Nuove Opportunità per Vecchi Avversari"

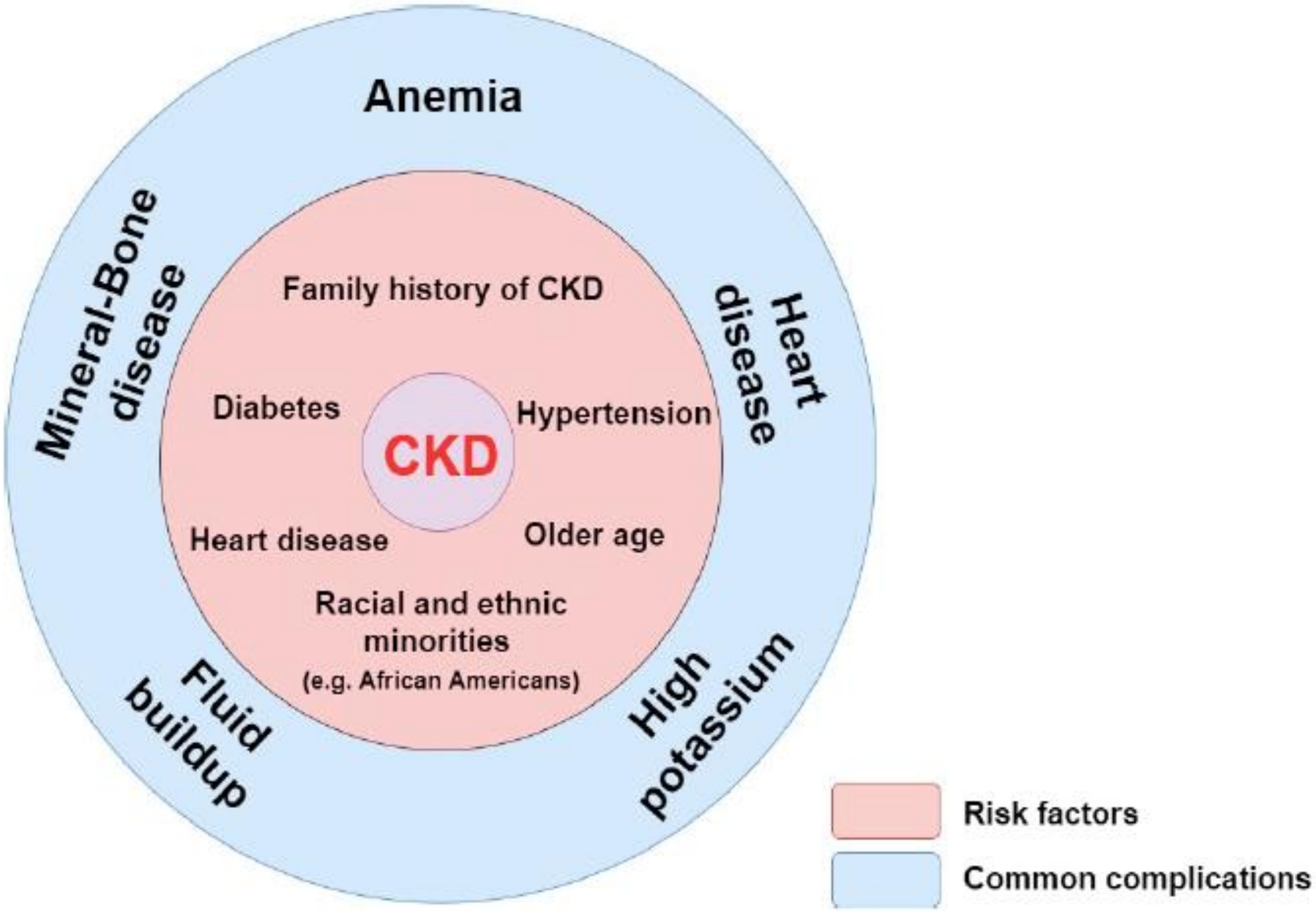
28 - 29 - 30 aprile Hotel Corallo Riccione

10.30-11.00

Anemia resistente nel Dializzato

P. Fabbrini

COMPLICANZE DELLA CKD



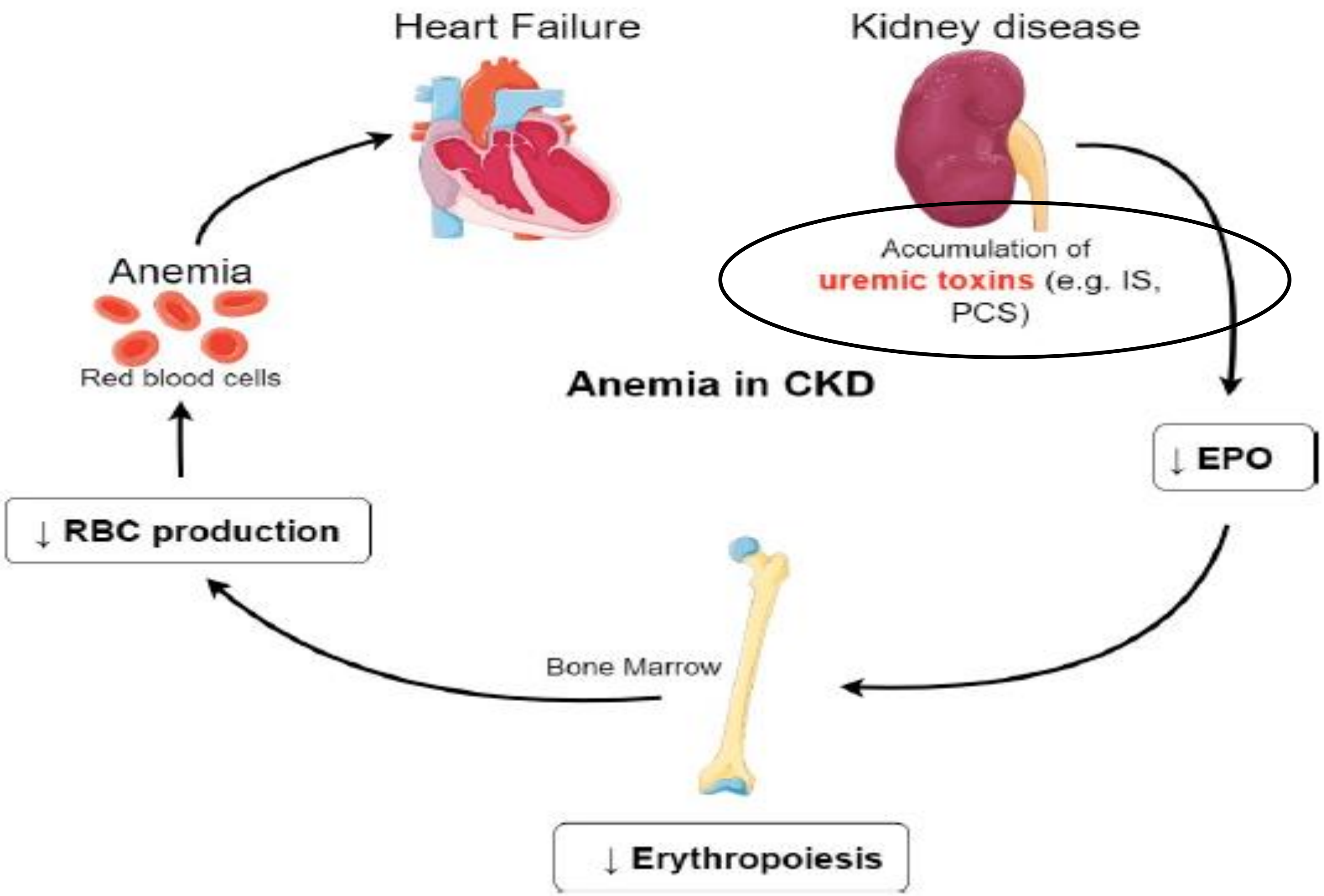
cells

Review

Uremic Toxins Affect Erythropoiesis during the Course of Chronic Kidney Disease: A Review

Eya Hamza [1], Laurent Metzinger [1,*] and Valérie Metzinger-Le Meuth [1,2]

FISIOPATOLOGIA



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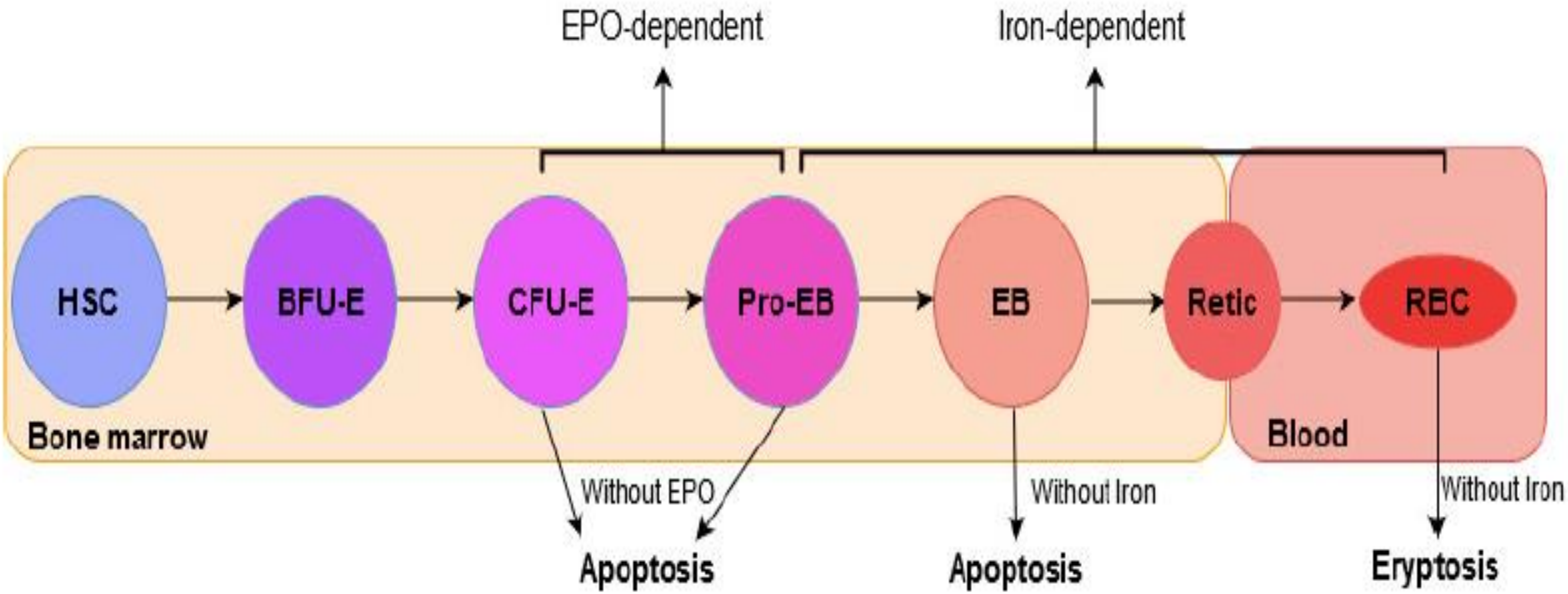


AJN
American Journal
of Nephrology

In-Depth Topic Review

Am J Nephrol 2021;52:450–466
DOI: 10.1159/000516901

Received: March 1, 2021
Accepted: April 26, 2021
Published online: July 19, 2021

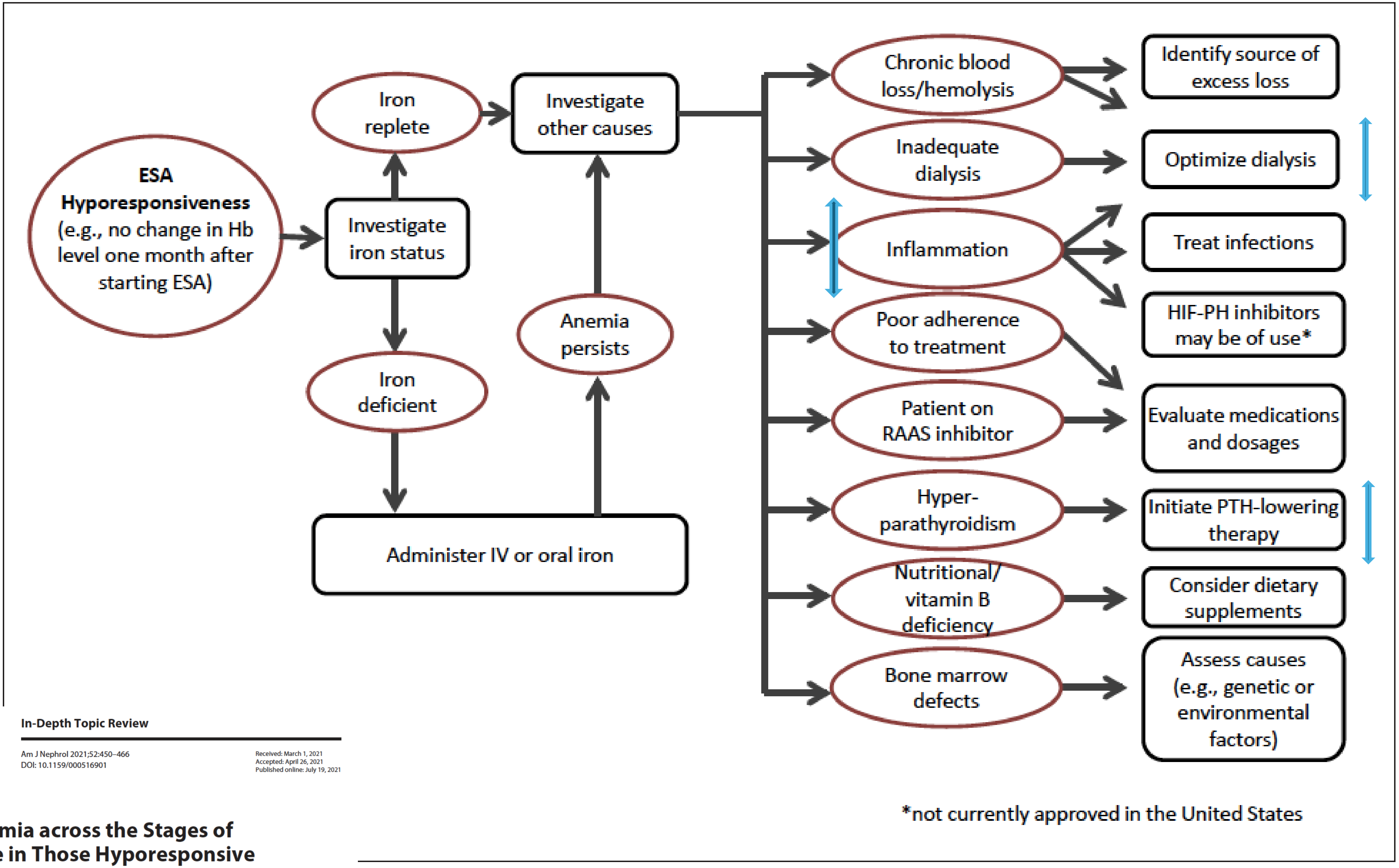
Managing Anemia across the Stages of Kidney Disease in Those Hyporesponsive to Erythropoiesis-Stimulating Agents

DEFINIZIONE

Table 1. Definitions of ESA hyporesponse

Source	Definition of ESA hyporesponse
NKF-KDOQI [21]	450 units/kg per week i.v. EPO or 300 units/kg per week s.c. EPO
KDIGO [11]	No increase in Hb concentration from baseline after the first month of ESA treatment on appropriate weight-based dosing
NICE best practices/The Renal Association [18]	Failure to reach the target Hb level despite s.c. epoetin dose >300 IU/kg/week (450 IU/kg/week i.v. epoetin) or darbepoetin dose >1.5 µg/kg/week
ERI [16]/EHRI [22]	Weight-adjusted weekly ESA dose divided by the Hb value >12.7–20.0 IU weekly/kg/Hb, g/dL

NKF-KDOQI, National Kidney Foundation-Kidney Disease Outcomes Quality Initiative; KDIGO, Kidney Disease Improving Global Outcomes; EHRI, ESA hyporesponsiveness index; EPO, erythropoietin; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; ERI, ESA response index.



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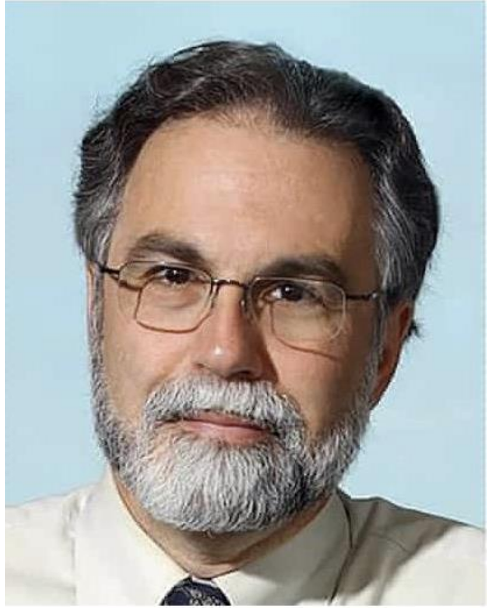


OXYGEN SENSING BY HIF HYDROXYLASES

Christopher J. Schofield* and Peter J. Ratcliffe‡

NATURE REVIEWS | MOLECULAR CELL BIOLOGY VOLUME 5 | MAY 2004 | 343

2019

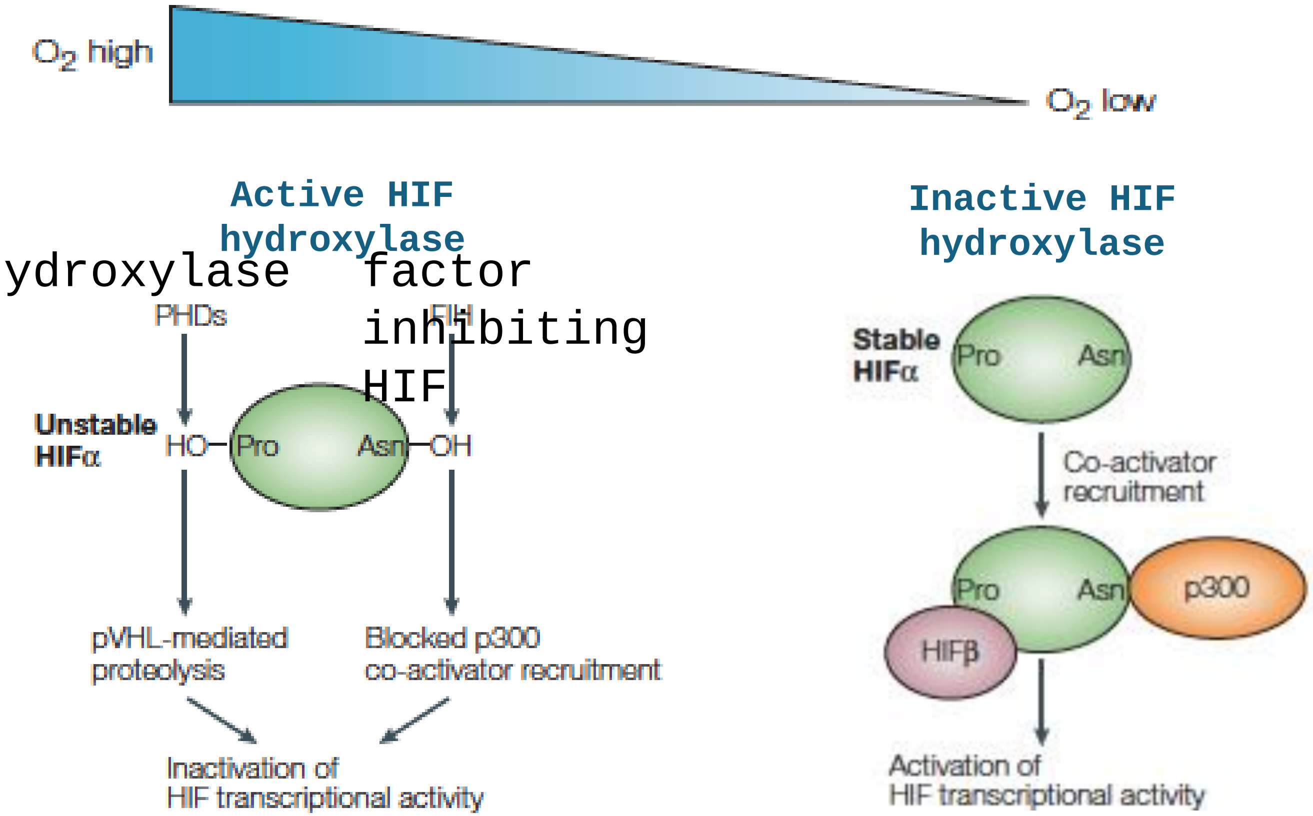
OXYGEN SENSING BY HIF HYDROXYLASES

Active HIF hydroxylase

Inactive HIF hydroxylase

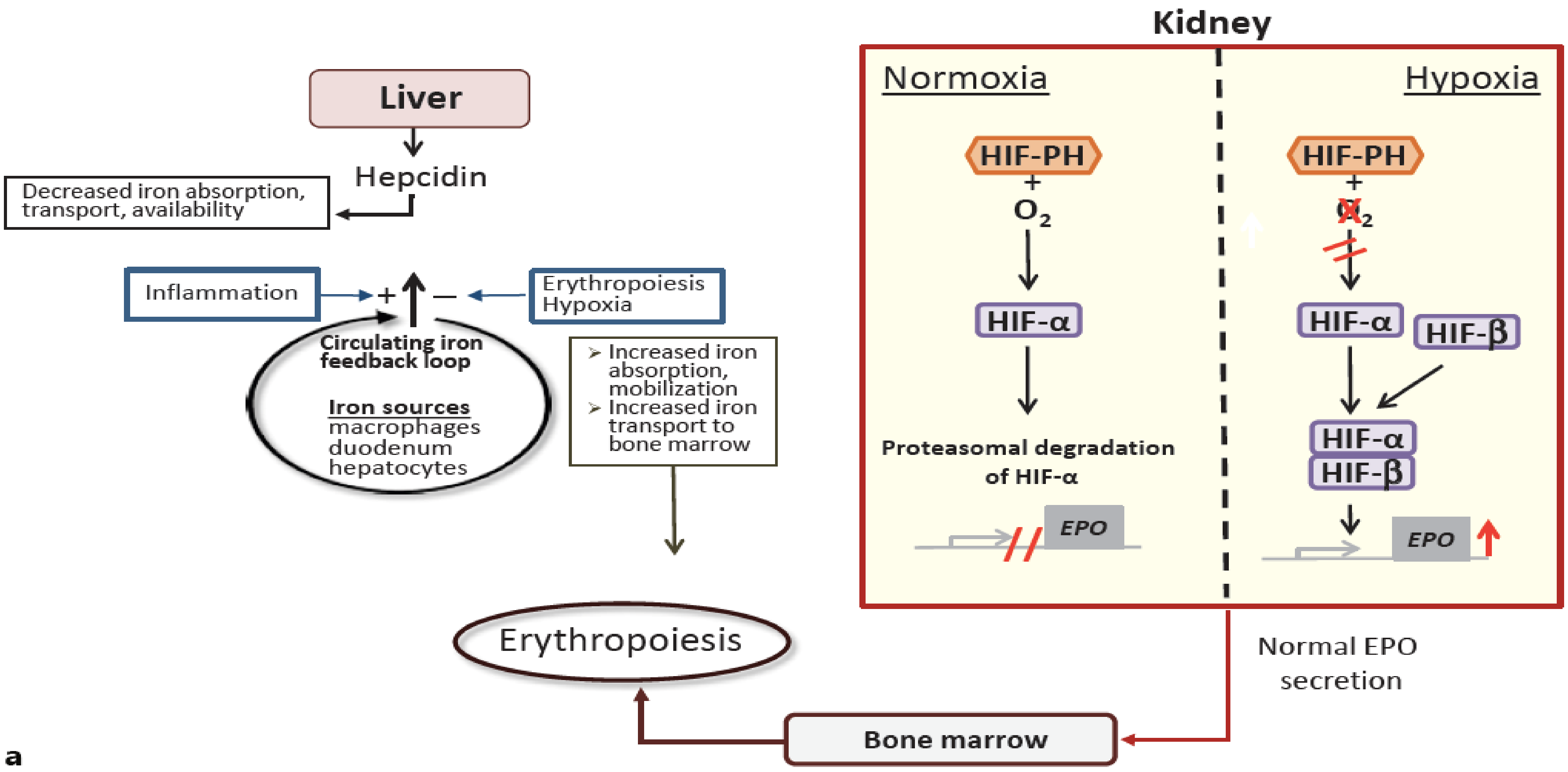
prolyl hydroxylase domains

factor inhibiting HIF

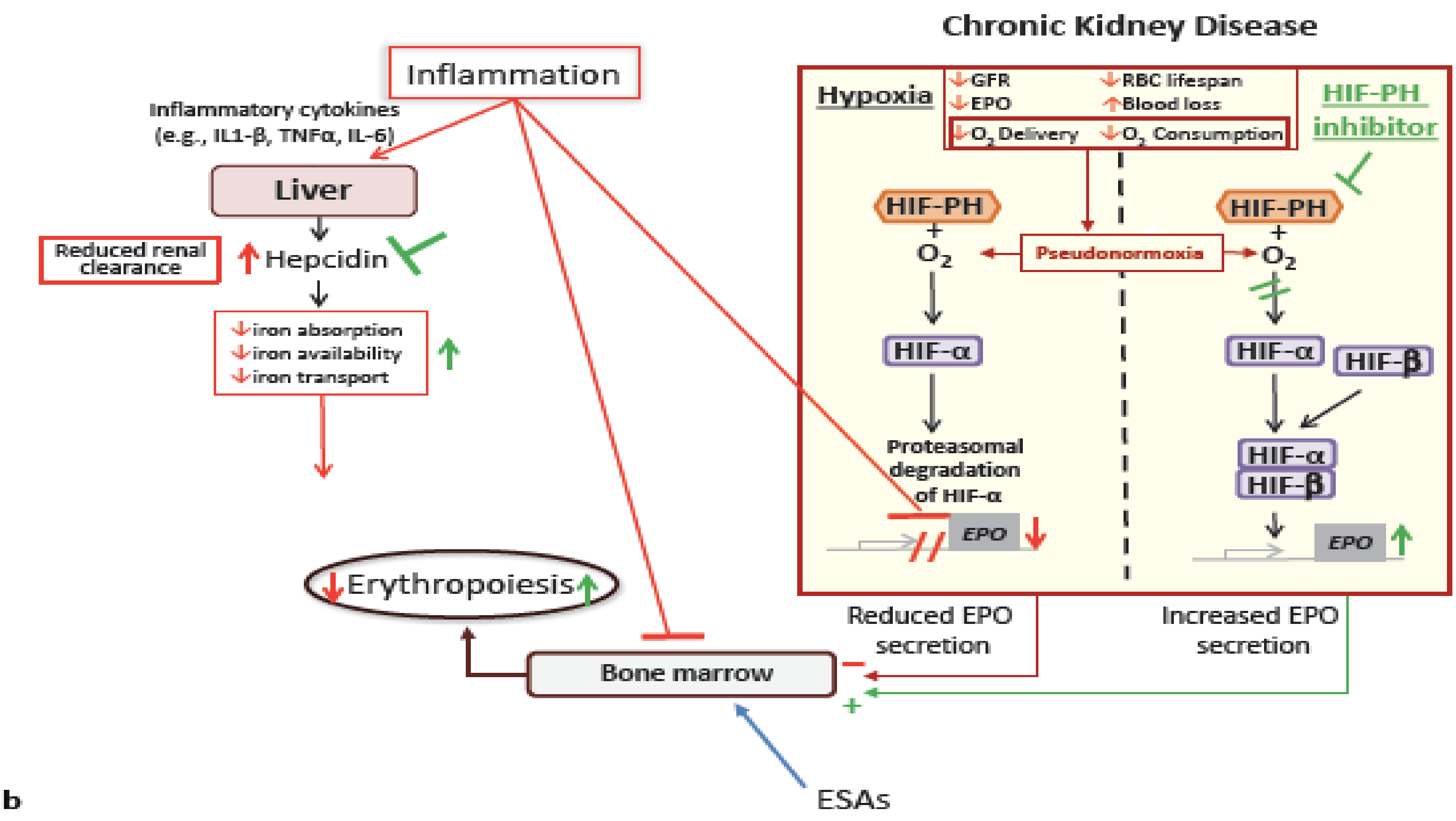


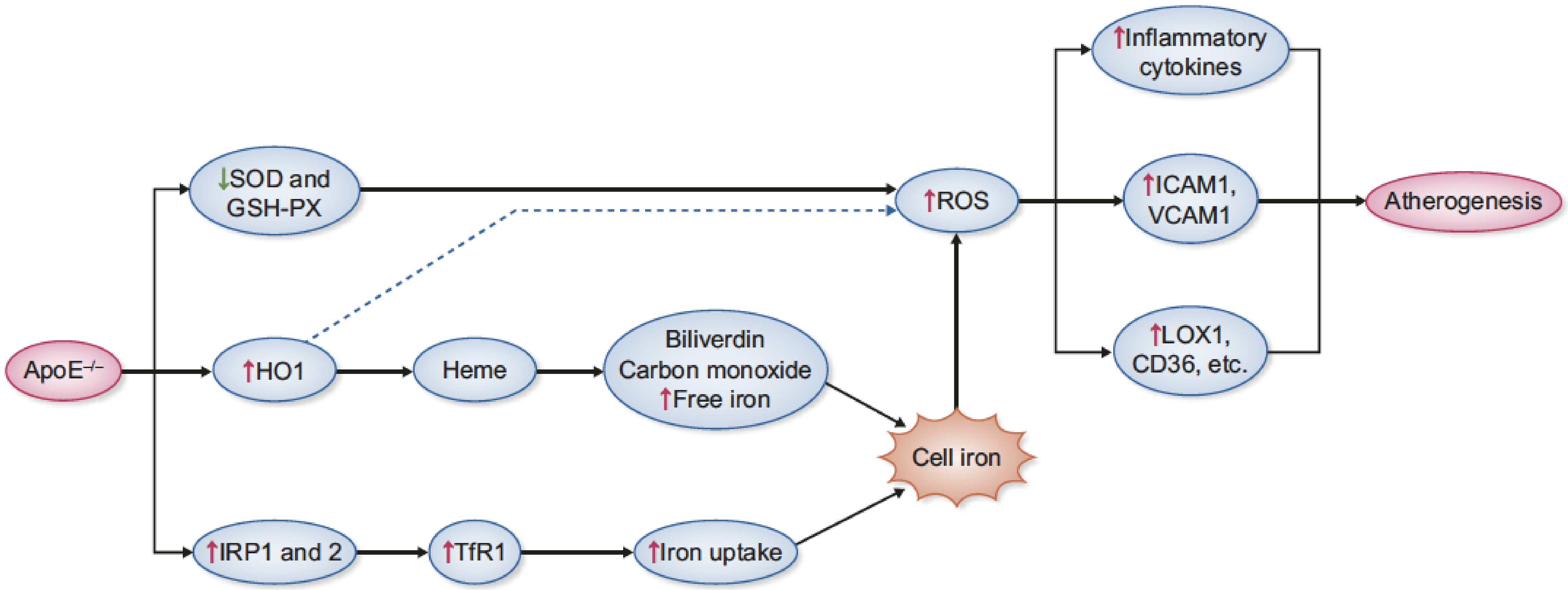
NATURE REVIEWS | MOLECULAR CELL BIOLOGY VOLUME 5 | MAY 2004 | 343

NUOVI ATTORI COINVOLTI NELLA ANEMIA



ANEMIA E INFIAMMAZIONE



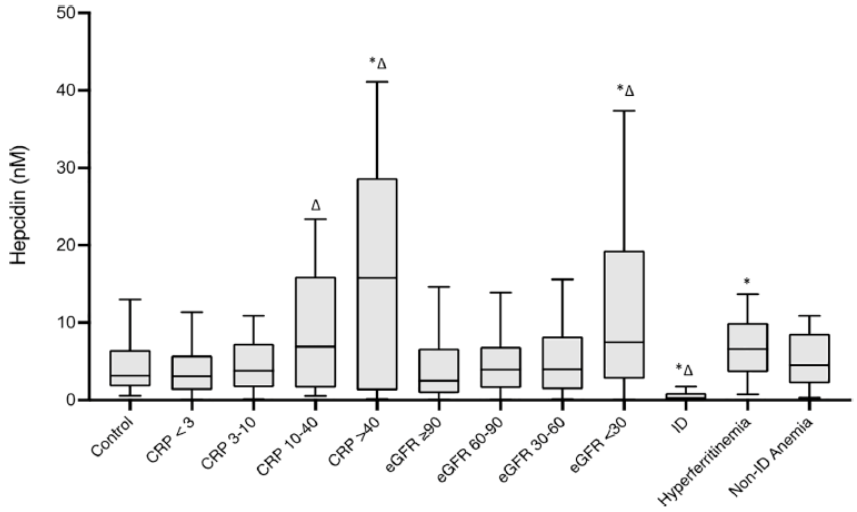


Nephrol Dial Transplant, 2024, 39, 1404–1415

https://doi.org/10.1093/ndt/gfae095

Advance access publication date: 24 April 2024

EPCIDINA.E INFIAMMAZIONE



Journal of Mass Spectrometry and Advances in the Clinical Lab 24 (2022) 43–49

TABLE 4 Multivariate linear regression models of factors associated with log hepcidin-25 levels stratified by ESAs treatment

	ESAs-free (N = 39)	*P* value	ESAs therapy (N = 64)	*P* value
Adjusted *R* square	0.746	<.001	0.606	<.001
	Standardized β		Standardized β	
log ferritin (μg/L)	0.765	<.001	0.677	<.001
log RTC ($\times 10^9$/L)	−0.239	.008	−0.199	.022
hs CRP above 5 mg/L	0.125	.161	0.214	.016

Abbreviations: ESAs, erythropoiesis-stimulating agents; hs CRP, high-sensitivity C-reactive protein; RTC, reticulocytes.

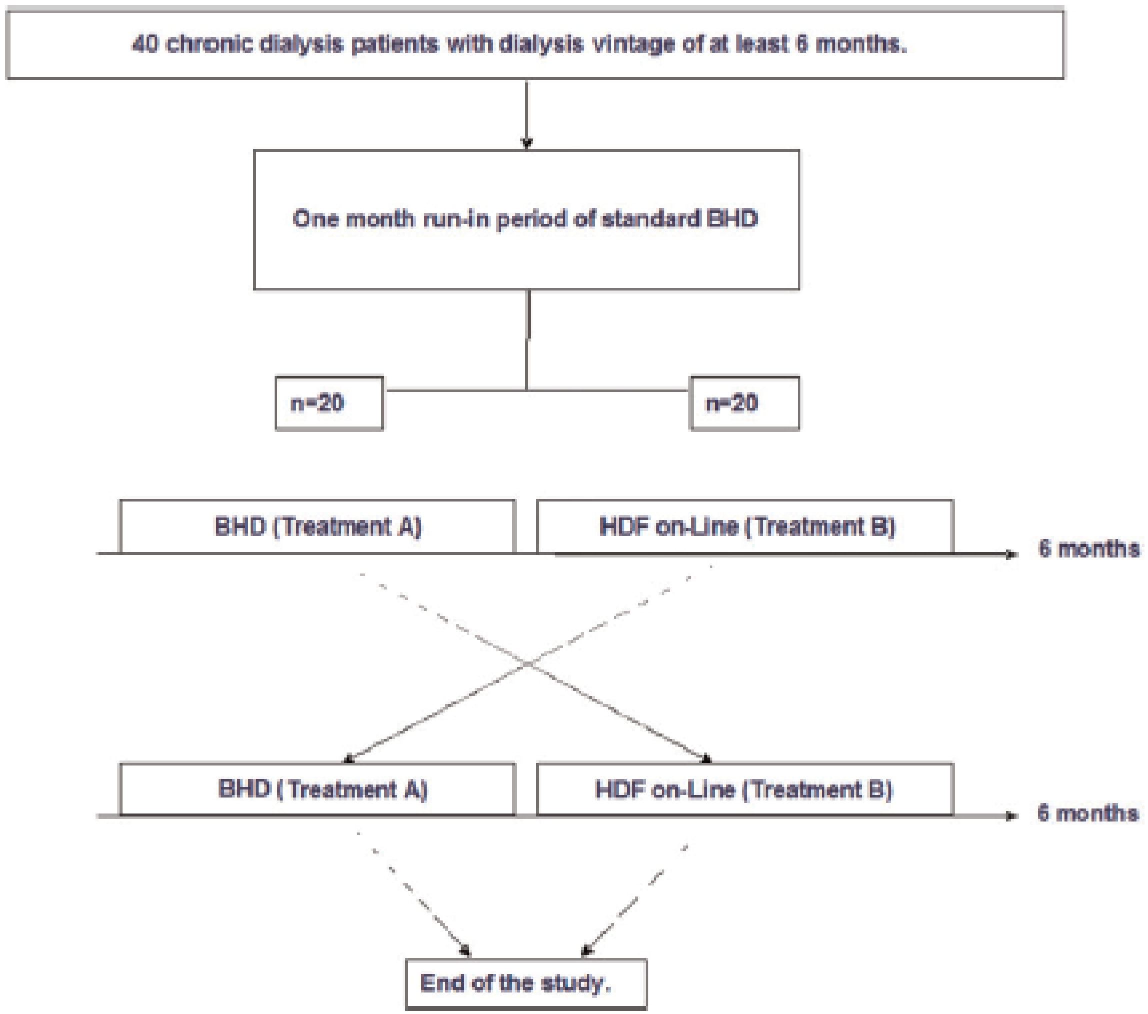
Received: 9 August 2020 | Revised: 25 November 2020 | Accepted: 22 December 2020
DOI: 10.1111/1744-9987.13617

ORIGINAL ARTICLE

WILEY

Factors associated with hepcidin-25 levels in maintenance hemodialysis patients

Miljan Savković[1] | Sanja Simić-Ogrizović[2,3] | Violeta Dopsaj[1,4]



Nephrol Dial Transplant (2015) 30: 682–689
doi: 10.1093/ndt/gfu345
Advance Access publication 10 November 2014

High-volume online haemodiafiltration improves erythropoiesis-stimulating agent (ESA) resistance in comparison with low-flux bicarbonate dialysis: results of the REDERT study

Vincenzo Panichi[1], Alessia Scatena[1], Alberto Rosati[2], Riccardo Giusti[2], Giuseppe Ferro[3], Erasmo Malagnino[2], Alessandro Capitanini[4], Adriano Piluso[4], Paolo Conti[5], Giada Bernabini[5], Massimiliano Migliori[1], David Caiani[3], Ciro Tetta[6], Aldo Casani[7], Giancarlo Betti[7] and Francesco Pizzarelli[3]

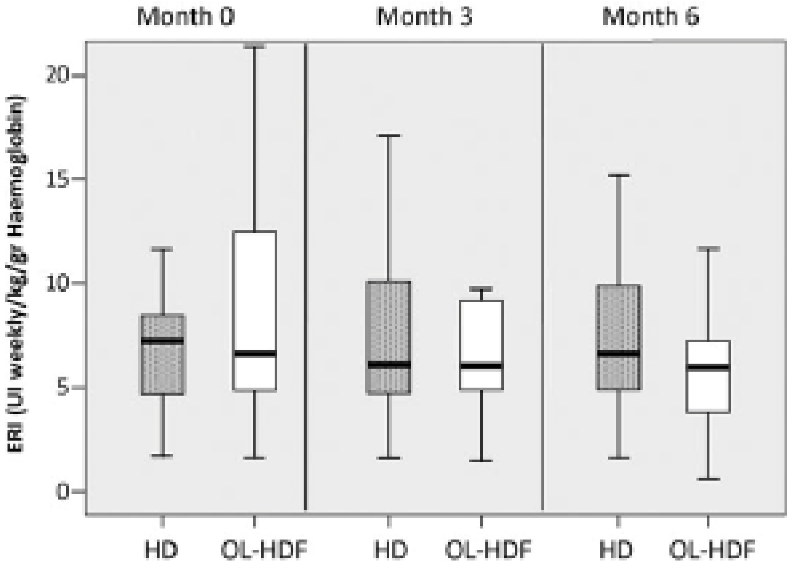


FIGURE 2: ERI was significantly reduced in HV-OL-HDF at Months 3 and 6 with respect to BHD. Number of patients = 36; $P < 0.05$, evaluated by the paired-samples *t*-test or by the Wilcoxon signed-rank test for non-normally distributed data.

Table 1. Mean, SD, median and interquartile range of dry weight, albumin, CRP, b2MG, Hb, ERI, ESA weekly dosage and iron metabolism parameters during BHD and HV-OL-HDF treatments

	HD Mean	HD SD	HD Median	HD IQR	HDF Mean	HDF SD	HDF Median	HDF IQR	
ERI (UI/weekly/kg/g Hb)									
M0	9.0	6.9	7.4	8.0	9.1	6.4	6.7	8.6	0.5715
M3	9.4	7.2	6.5	9.6	6.2	5.1	6.1	4.4	*0.0312
M6	9.7	7.3	6.7	9.7	6.7	5.3	6.1	4.3	*0.0390
ESA dose (UI/weekly)									
M0	5625	3597	4500	5750	5600	4051	6000	5200	0.886
M3	5769	4160	5500	6000	4892	3424	4000	4500	0.197
M6	6030	4318	5000	6000	5083	3623	4000	6000	0.194
HEP (ng/mL)									
M0	48.3	27.6	45.1	37.2	44.3	33.3	37.8	37.1	0.6216
M3	58.3	33.3	48.5	36.1	43.0	31.5	34.4	13.2	*0.0395
M6	62.1	34.7	57.5	50.4	49.5	29.9	43.2	32.8	*0.0556

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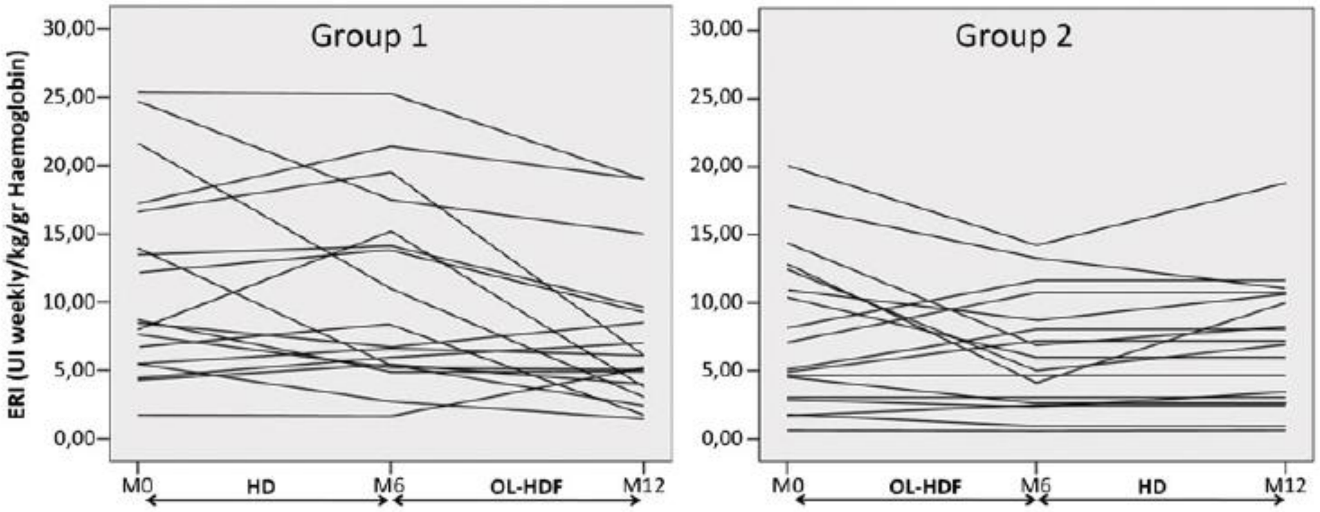
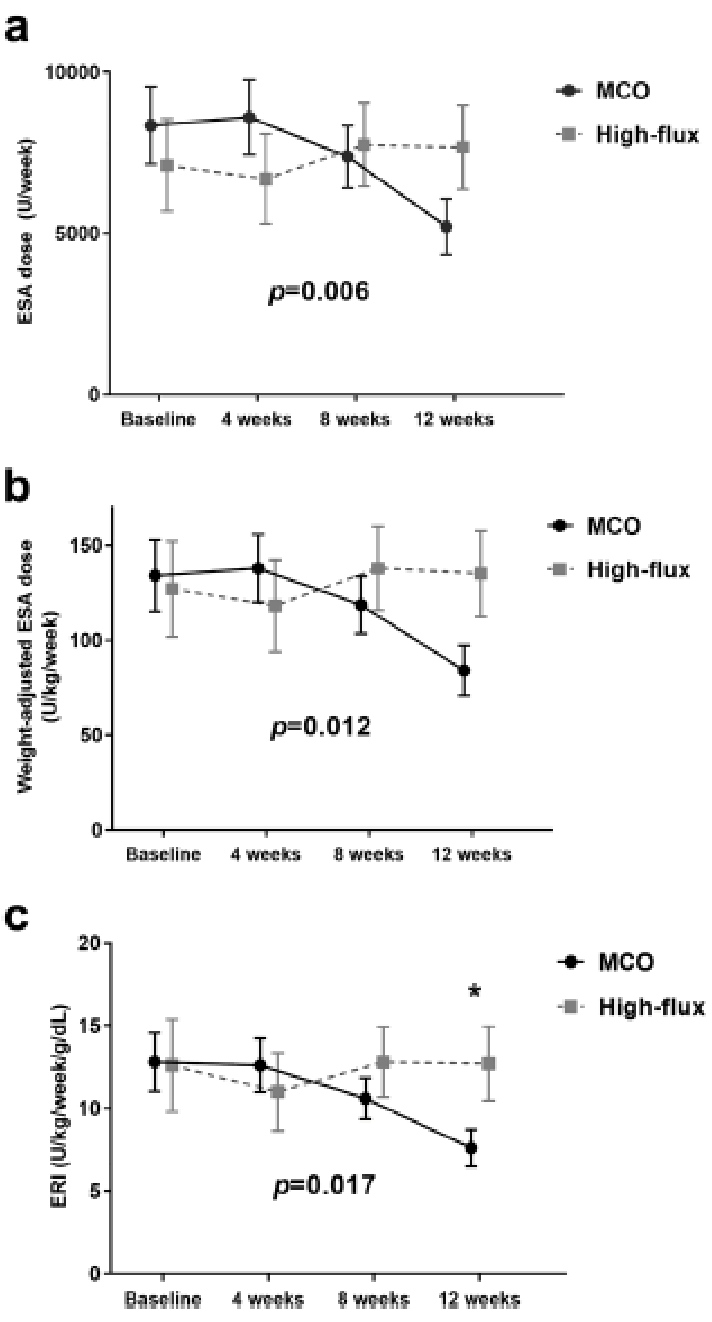
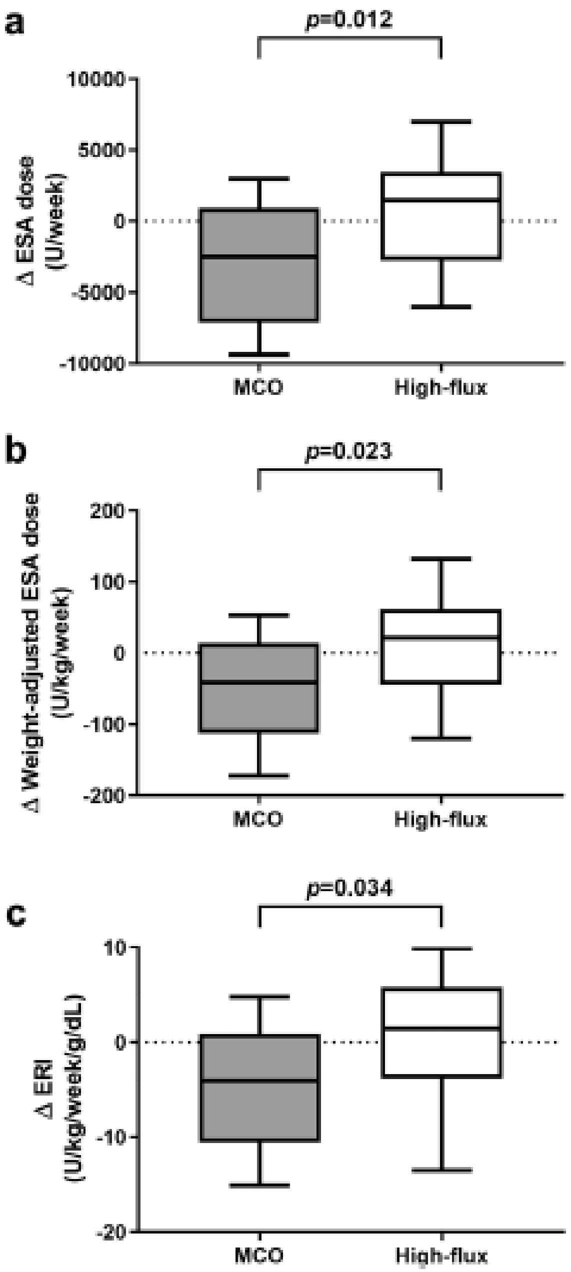




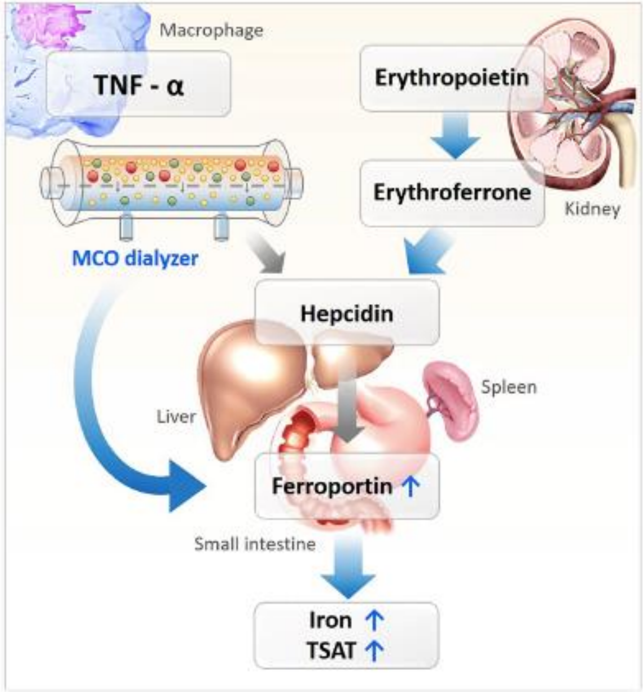


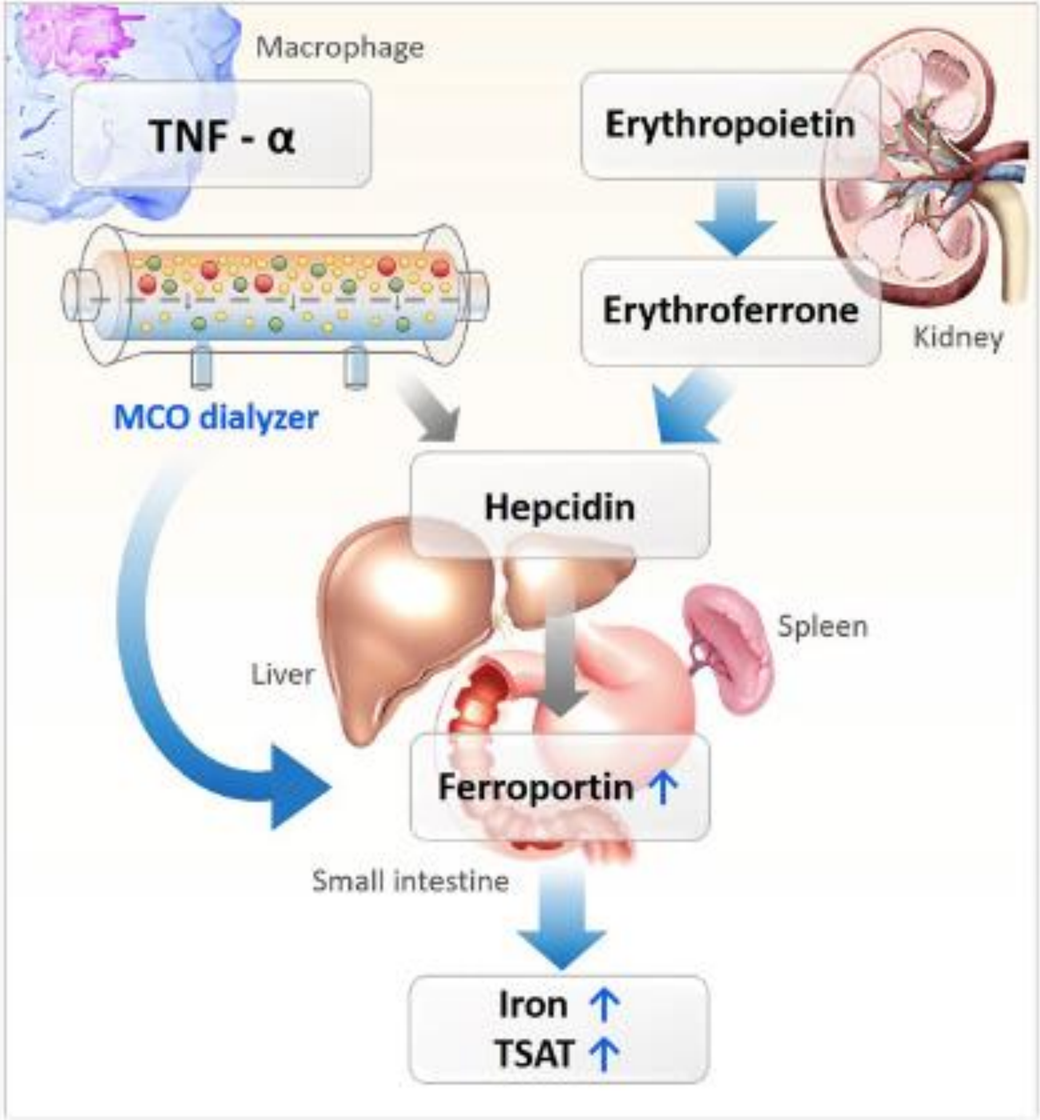
SCIENTIFIC REPORTS
natureresearch

OPEN

Medium cut-off dialyzer improves erythropoiesis stimulating agent resistance in a hepcidin-independent manner in maintenance hemodialysis patients: results from a randomized controlled trial

Jeong-Hoon Lim[1], Yena Jeon[2], Ju-Min Yook[1], Soon-Youn Choi[1], Hee-Yeon Jung[1], Ji-Young Choi[1], Sun-Hee Park[1], Chan-Duck Kim[1], Yong-Lim Kim[1] & Jang-Hee Cho[1]





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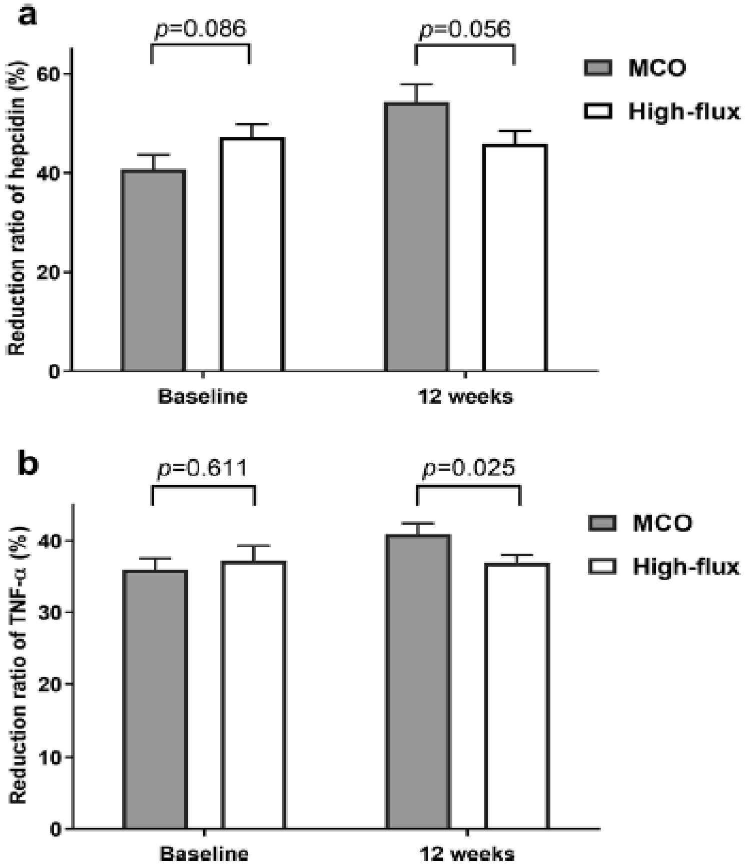
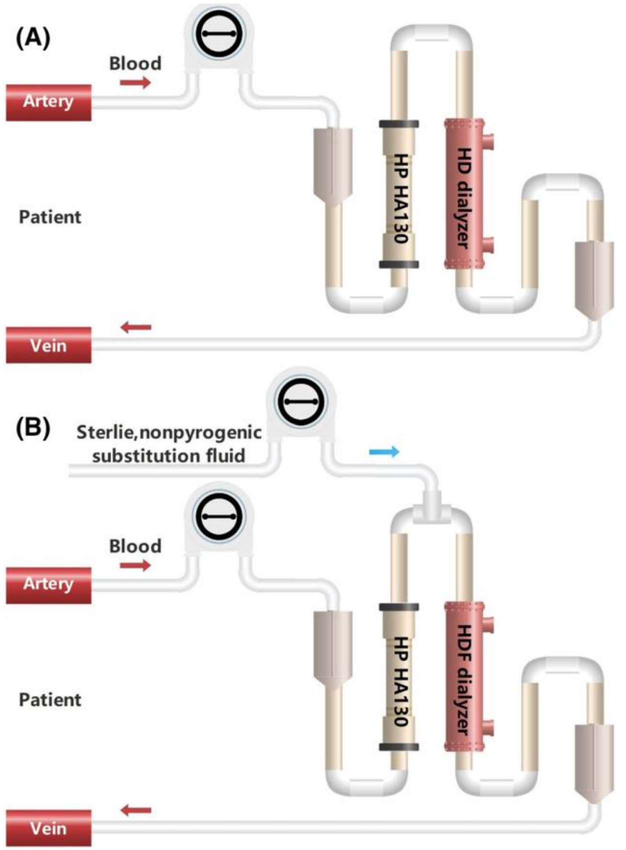


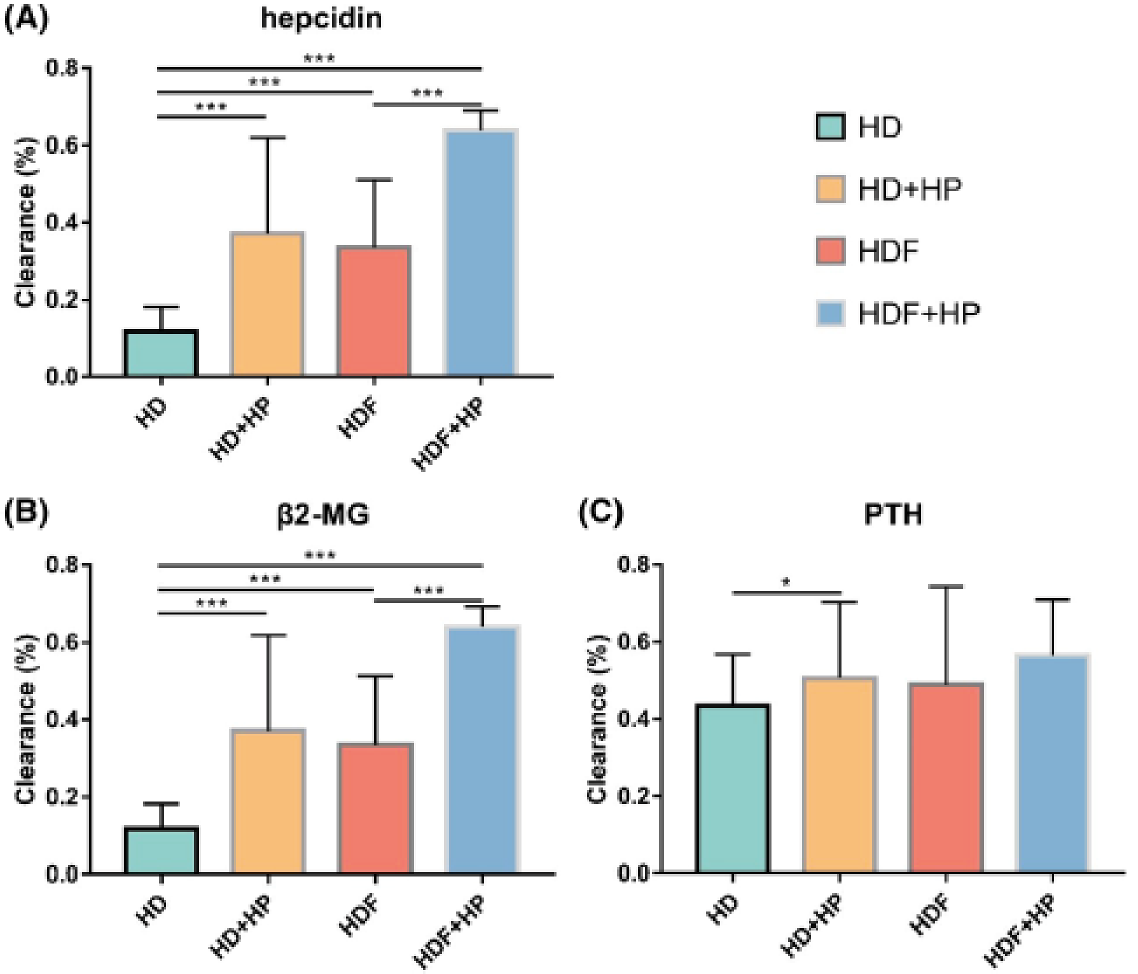
Received: 21 February 2022 | Accepted: 2 June 2022
DOI: 10.1111/sdi.13110
ORIGINAL ARTICLE
Seminars in Dialysis WILEY

Effect of different hemodialysis modalities on hepcidin clearance in patients undergoing maintenance hemodialysis

Ling Sun[1] | Rui-Xue Hua[2] | Yu Wu[2] | Lu-Xi Zou[2]



RUOLO DELL'ADSORBIMENTO

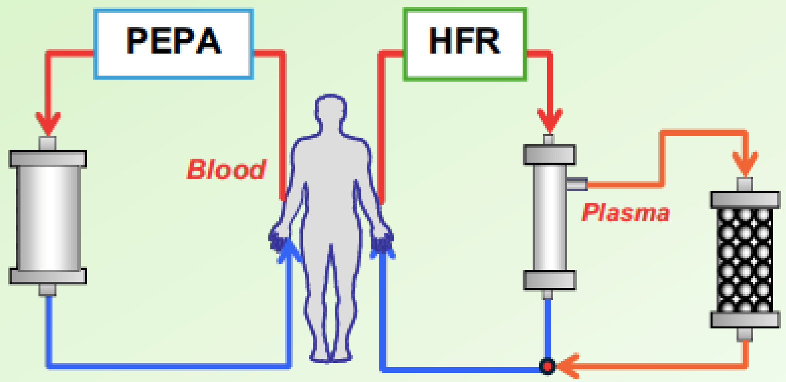


Hemoadsorption and plasma adsorption: two current options for the 3rd dimension of dialysis purification

Niccolò Morisi[1,2], Gaetano Alfano[1,2], Marco Ferrarini[2], Camilla Ferri[2], Francesco Fontana[1], Marco Ballestri[1], Gabriele Donati[1, 2]
[1]Nephrology Dialysis and Kidney Transplant Unit, Azienda Ospedaliero Universitaria di Modena
[2]Department CHIMOMO, University of Modena and Reggio Emilia, Modena Italy

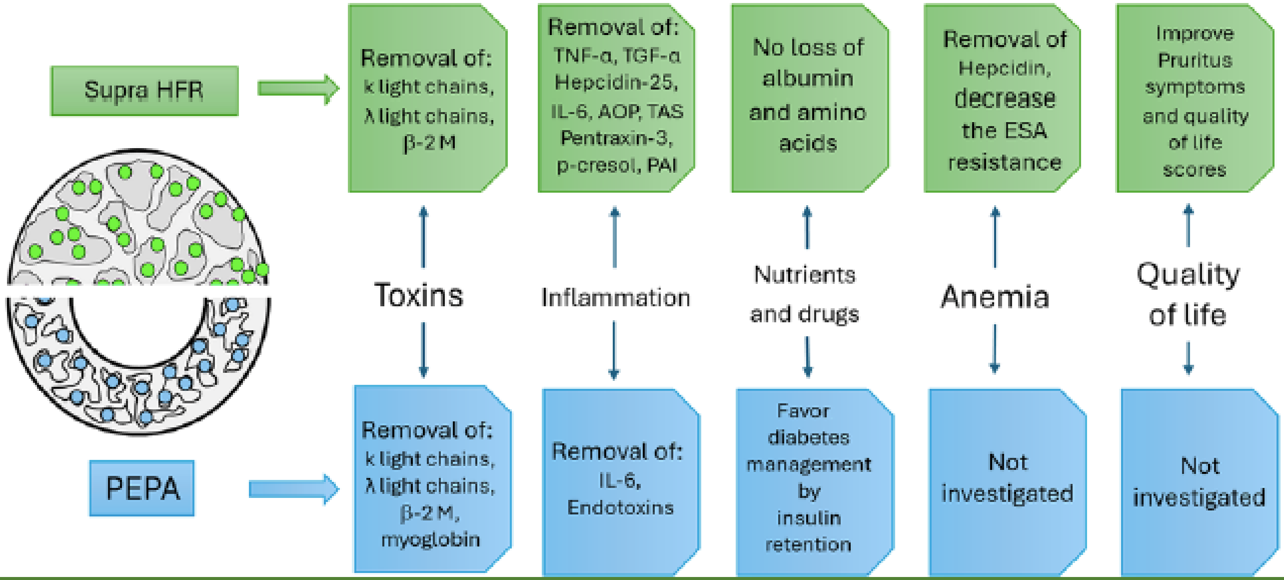
Background

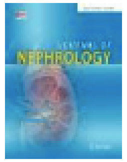
The application of adsorption has enabled the removal of previously non-removable toxins, including those of medium molecular weight and protein-bound toxins. The objective of this review is to provide a more comprehensive account of the role of PEPA and Supra HFR as adsorption techniques.



Main results

Hemadsorption and plasma adsorption are mainly indicated for patients who need the boosting of dialysis purification but for whom online hemodiafiltration (OL-HDF) is not feasible. This group of patients does not achieve the therapeutic convective volume prescribed as they have problems with their vascular access or have dialysis intolerance. Limits to Supra HFR use are the availability of a specific dialysis machine. The PEPA dialyzer is suitable for every dialysis machine, the only technical limitation is the need to use two filters in the same HD session to counteract the saturation of the filter and boost free light chains removal.



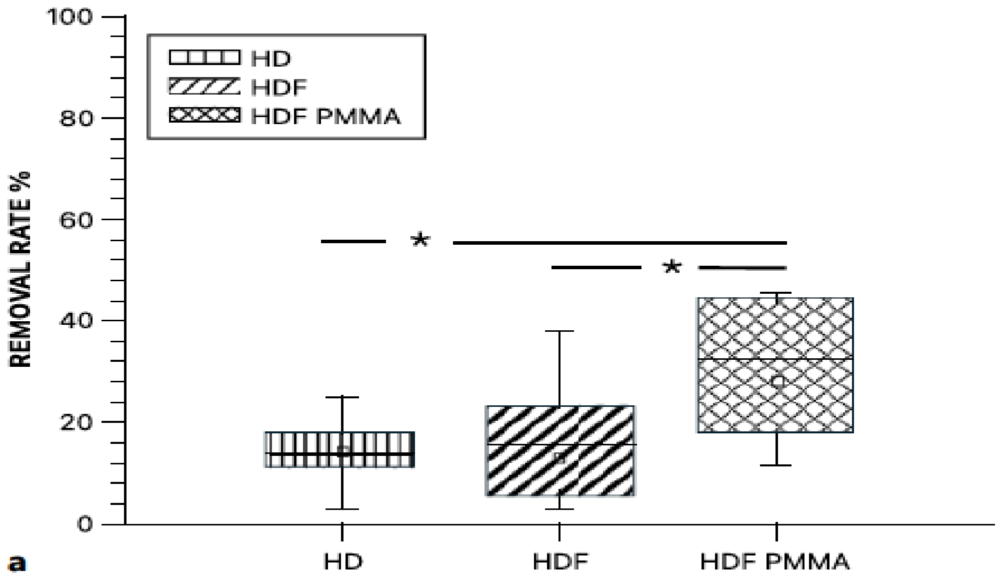


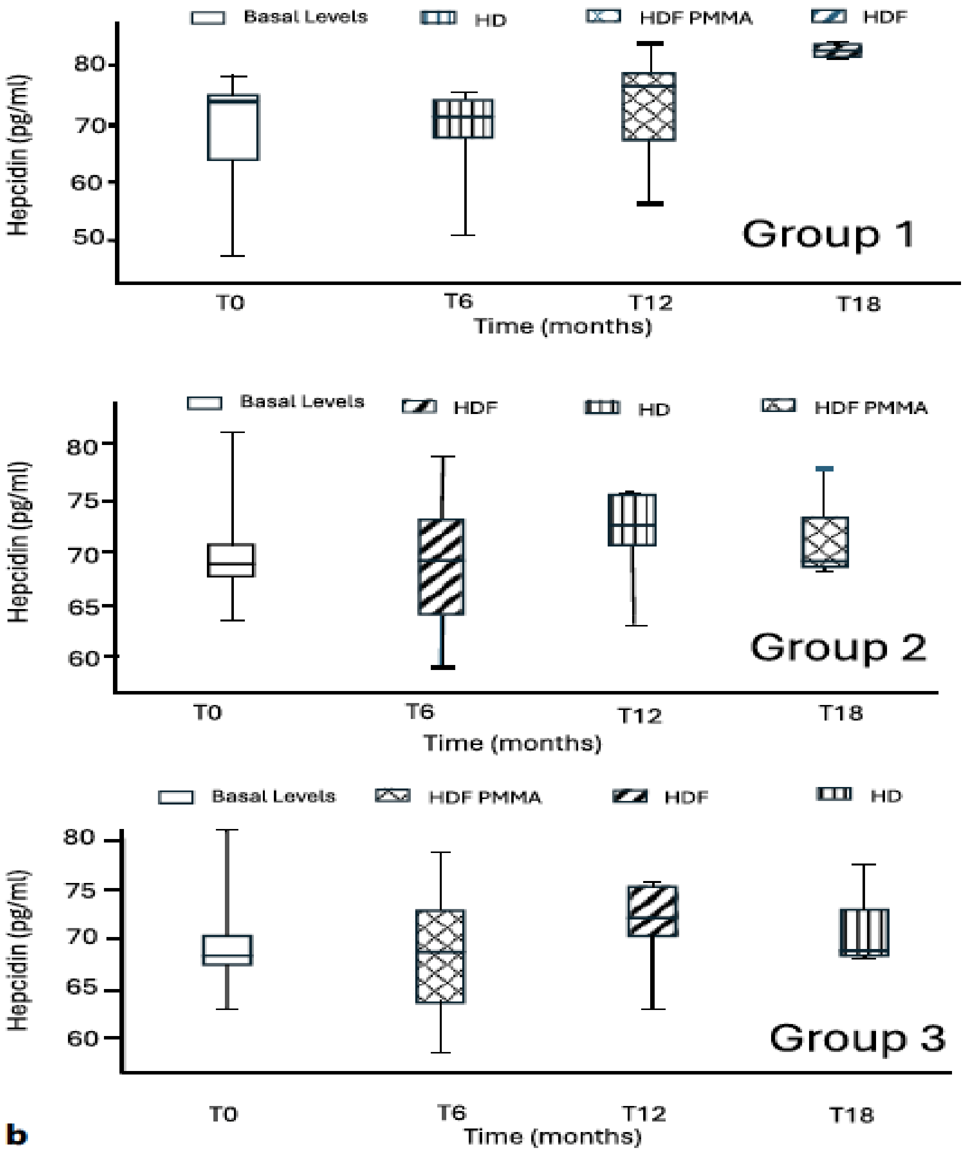
Journal of NEPHROLOGY
official journal of the Italian Society of Nephrology

Conclusions. Supra HFR and PEPA remove uremic toxins by plasma adsorption and hemoadsorption, respectively. For malnutrition or intradialytic hypotension HFR is preferred. For diabetics or young patients, free light chain removal PEPA can be the choice.

Table 2 Study summary for HFR and Supra-HFR

Country	References	Year	N° patients/n° centers	Technique	Treatment modality	Main results
Uremic toxins						
Italy	Murgia et al. [35]	2022	13/1	Supra-HFR in MM patients	3.30 h, Qb 250 mL/min, Qd 500 mL/min	Decrease free-light chain (RR for k 85%, for λ 45%) in ten sessions
Spain	Pendón-Ruiz de Mier et al. [34]	2020	9/1	Supra-HFR in MM patients	4 h, Qb 300–350 mL/min, Qd 500 mL/min; EU 13.2–14.4 L	Decrease free-light chain (RR for k 57%, for λ 44%) per session
Italy	Donati et al. [33]	2016	20/1	HFR vs. standard HD	4 h, Qb 310 mL/min, Qd 500 mL/min, EU rate 2.3 mL/h	Decrease free-light chain (RR for k 44%, for λ 30%). Decrease of β2M (RR 42%)
Inflammation and oxidative stress						
Italy	Donati et al. [31]	2022	9/1	Supra-HFR vs. OL-HDF	Qb 290 mL/min, Qd 500 mL/min, EU 13 L	Significant reduction of FGF23 with both techniques. IL-6 is not modified. Significant decrease of TNF-α and TGF-α with Supra-HFR, IL-8 is not modified
Italy	Tessitore et al. [36]	2018	28/1	Supra-HFR vs. low-flux HD	4 h, Qb 280 mL/min, Qd 500 mL/min	Significant decrease of TNF-α and Hepcidin-25 in HFR. A similar change in IL-6, CRP and Pentraxin-3 between methodics
Spain	Esquivias-Motta et al. [37]	2017	17/1	Supra-HFR vs. OL-HDF in non-inflamed patients		Decrease of all 13 biomarkers of inflammation as IL-6, TNF-α, the proportion of activated proinflammatory monocytes, p-Cs, IS
Italy	Palleschi et al. [38]	2016	41/19	Supra-HFR vs. OL-HDF	4 h, Qb> 300 mL/min, Qd 500 mL/min, EU 13L, CV 12L	Decrease in oxidative stress markers such as AOPP and TAS
Italy	Riccio et al. [39]	2014	12/11	Supra-HFR vs. OL-HDF in inflamed patients	4 h, Qb 330 mL/min, Qd 500 mL/min, EU rate 60 mL/min,	Increased adsorption of IL-6 and p-Cs on the Supra-HFR resin cartridge
Spain	González-Diez et al. [29]	2014	40/multicenter	Supra-HFR vs. standard HD in patients with ferritin< 600 μg/l		HFR show modest changes of oxidative parameters than HD
Italy	Calò et al. [28]	2010	14/6	HFR vs. standard HD in non-inflamed patients		Decrease in oxidative stress markers as OxLDL, PAI-1 mRNA and $p22^{phox}$
Anemia						
Italy	Tessitore et al. [36]	2018	28/1	HFR vs. low-flux HD	4 h, Qb 280 mL/min, Qd 500 mL/min	Significant hepcidin decrease
Italy	Bolasco et al. [40]	2011	30/14	HFR vs. standard HD in non-inflamed patients	3.30–4 h, Qb 300–350 mL/min, Qd 500 mL/min, CV rate 3L/hour	Increased hemoglobin and decreased ESA requirements
Nutrition and albumin losses						
Italy	Murgia et al. [35]	2022	13/1	Supra-HFR	3.30 h, Qb 250 mL/min, Qd 500 mL/min	No loss of albumin per session
Italy	Palleschi et al. [38]	2016	41/19	Supra-HFR vs. HFR and OL-HDF	4 h, Qb> 300 mL/min, Qd 500 mL/min, EU 13L, CV 12L	Sorbent resins do not remove Vitamin C. Supra- HFR decreases RPB. No differences in Vitamin A and E





Blood
Purification

Research Article

Blood Purif 2023;52(suppl 1):85–94
DOI: 10.1159/000540402

Received: April 12, 2023
Accepted: July 7, 2024
Published online: July 24, 2024

Protein-Bound Uremic Toxins and Inflammation Process in Hemodialysis Patients: Is There a Role for Adsorption Hemodiafiltration?

Paolo Fabbrini[a] Denise Vergani[b] Anna Malinverno[b] Federico Pieruzzi[b]
Marita Marengo[c] Guido Merlotti[e] Claudio Medana[d]
Alessandro Domenico Quercia[c] Vincenzo Cantaluppi[e]

cells

Review

Uremic Toxins Affect Erythropoiesis during the Course of Chronic Kidney Disease: A Review

Eya Hamza [1], Laurent Metzinger [1,*] and Valérie Metzinger-Le Meuth [1,2]

Table 2. The pathophysiological roles of Indoxyl sulfate.

The Pathophysiological Role of Indoxyl Sulfate	Reference
Inhibition of endothelial proliferation and wound repair	[2]
Progressive deterioration of renal function	[34,46,50–54]
Induction of oxidative stress	[55]
Increase of circulating EMPs release	[56]
Induces TF production via the AhR pathway	[57,58]
Development of uremic symptoms	[46,59]
Associated with pathogenesis of atherosclerosis	[60]
Increases mortality	[61]
Cardiovascular disease	[54,61–63]
Peripheral arterial disease	[61,64,65]

Abbreviations: EMPs, endothelial microparticles; TF, tissue factor; AhR, aryl hydrocarbon receptor.

Eya Hamza [1], Laurent Metzinger [1,*] and Valérie Metzinger-Le Meuth [1,2]

Table 3. Role of IS in the regulation of renal anemia.

The Pathophysiologic Roles of IS	Molecular Mechanisms	References
Impairment of erythropoiesis in a HIF dependent manner	Suppression of the EPO gene transcription during hypoxia	[43]
Stimulates eryptosis	Extracellular Ca^{2+} entry with subsequent stimulation of cell shrinkage and cell membrane scrambling	[66]
Might contribute to EPO resistance and endothelial dysfunction	IS inhibits EPO-Induced Phosphorylation of EPOR IS inhibits TSP-1 expression through suppression of the AKT phosphorylation	[67]
Suppression of HIF activation	IS-induced AhR activation	[70]
Increased PCA in RBCs	Due to PS exposure and RBCs-derived microparticles release	[71]
EPO decrease	IS negatively regulates the EPO expression	[73]
IS-induced RBCs death	Through OAT2, and NADPH oxidase activity-dependent, and a GSH-independent mechanism	[75]

Abbreviations: HIF, hypoxia-inducted factor; EPO, erythropoietin; EPOR, erythropoietin receptor; IS, indoxyl sulfate; TSP-1, Thrombospondin-1; AhR, the aryl hydrocarbon receptor; PCA, Procoagulant Activity; PS, Phosphatidylserine; RBCs, red blood cells; OAT2, Organic Anion Transporter 2; GSH, glutathione.

Blood Purification

Research Article

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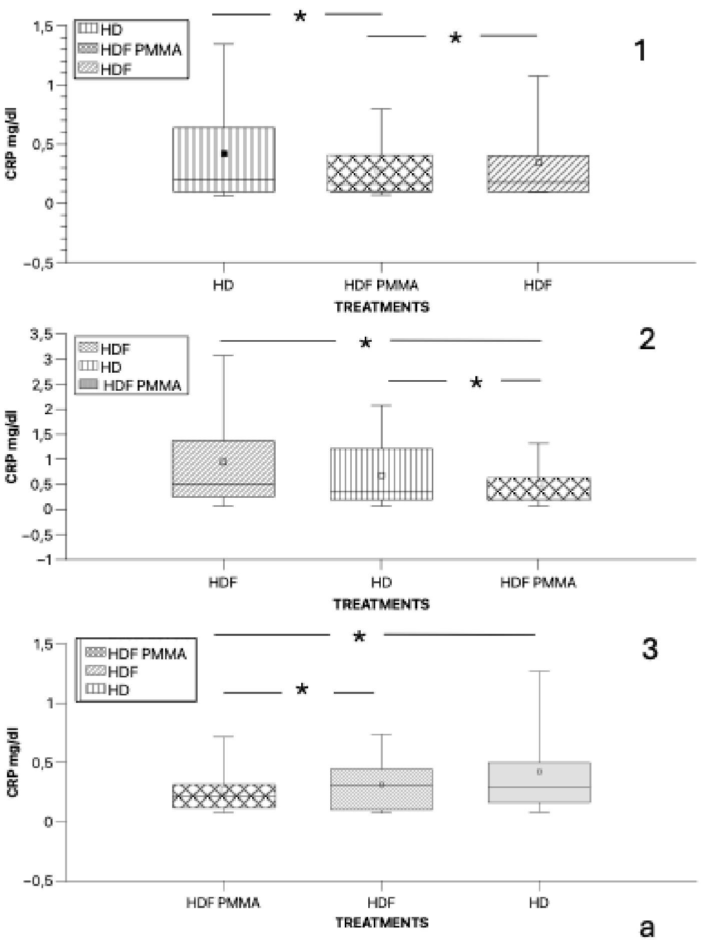
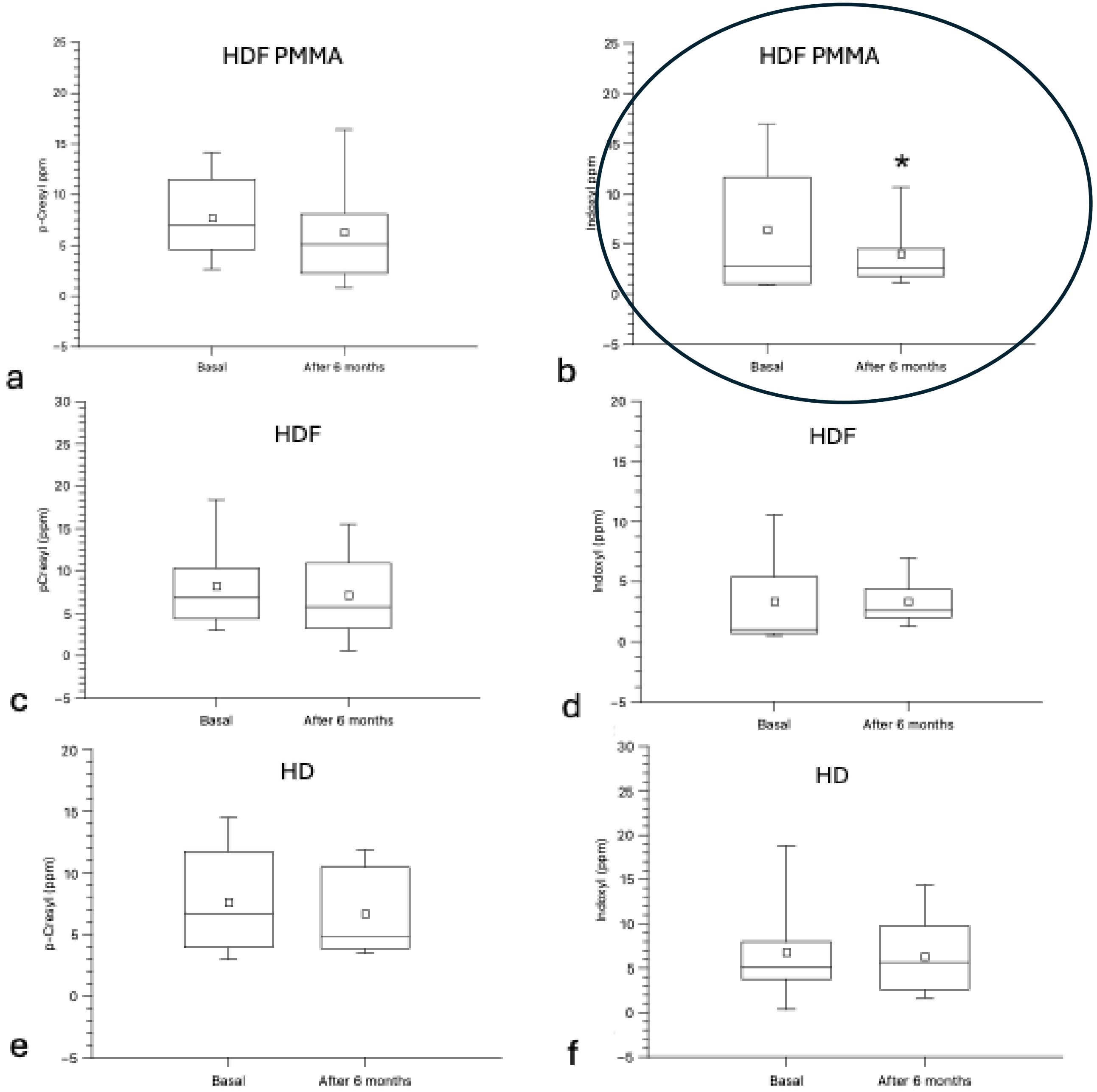




Nephrol Dial Transplant, 2024, 39, 1404–1415
https://doi.org/10.1093/ndt/gfae095
Advance access publication date: 24 April 2024

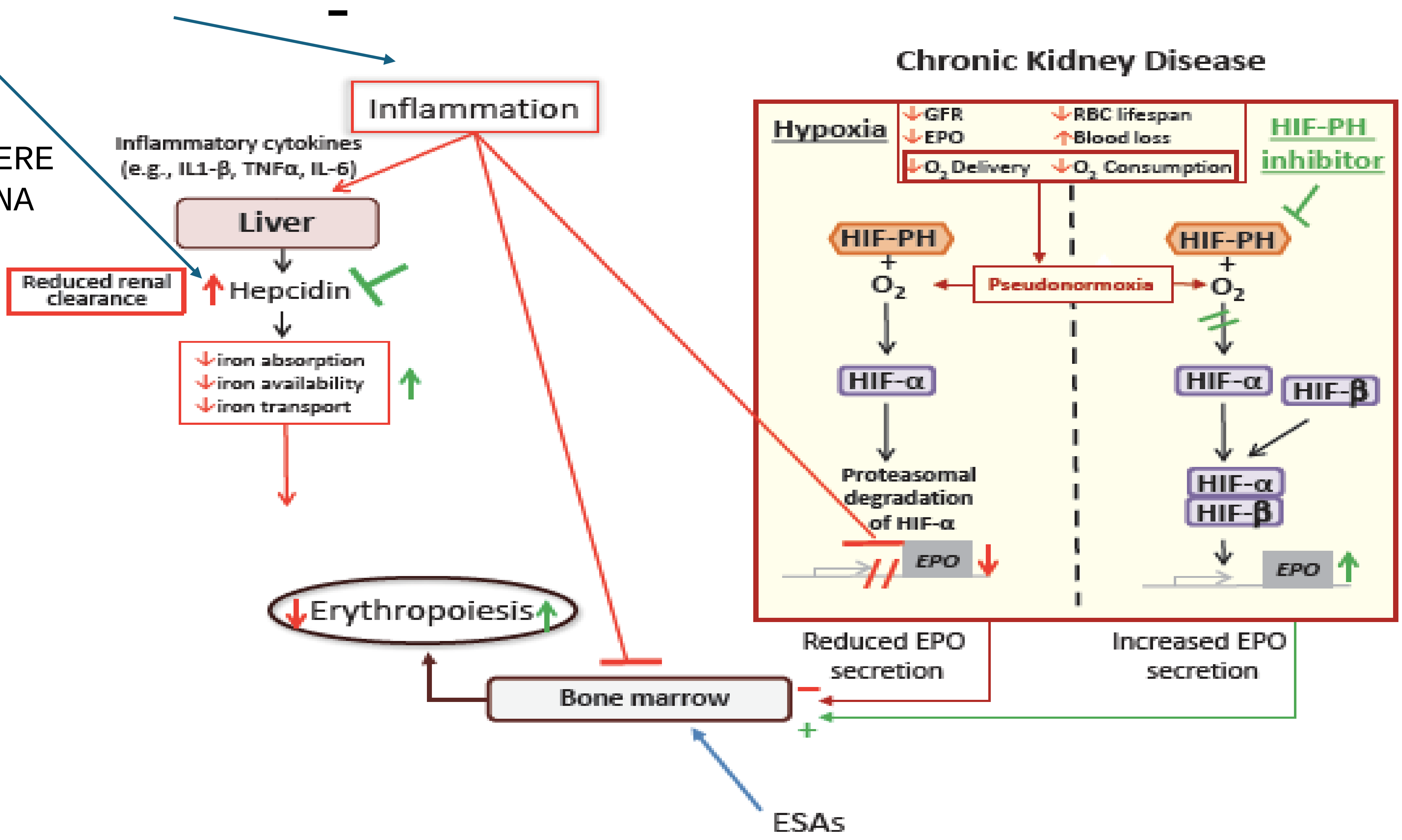
Table 1: New treatments of possible interest for CKD patients with anaemia.

Agent	ClinicalTrials.gov	Company	Mechanism of action	Development phase	Setting	Notes
Agents stimulating erythropoiesis						
Pegmolesatide	NCT03903809	Hansoh Pharmaceutical, China	Small peptide stimulating the EPO receptor	Phase 3	ND and DD CKD and dialysis	
Luspatercept	NA	Bristol Myers Squibb, USA	Targeting the SMAD2 and SMAD3 signalling	Approved for clinical use	Beta thalassemia or myelodysplastic syndromes	No clinical development for CKD
Targeting the growth of early progenitor cells						
Thrombopoietin	NA	Merck, USA	Increase early bone marrow progenitors to counterbalance their depletion due to intensive ESA use	Preclinical for anaemia. Available for clinical use in China. Thrombopoietin receptor agonists used worldwide	EPO-resistant anaemia in rats	Combination therapy with ESAs
Targeting serum hepcidin						
NOX-H94	NCT01372137, NCT02079896	NOXXON Pharma, Germany	Spiegelmer of the molecule	Preclinical, phase 1 and 2	Chronic inflammation and dialysis patients with ESA-hyporesponsive anaemia	No further development
PRS-080	NCT03325621	Pieris Pharmaceutical, USA	Anticalin antibody	Preclinical, phase 2a	Cynomolgus monkey, haemodialysis	No further development
Ab12B9m	NA	Amgen, USA	Anti-hepcidin antibody	Preclinical	Cynomolgus monkeys	No further development
LY2787106	NCT01340976	Eli Lilly, USA	Anti-hepcidin antibody	Phase 1	Patients with cancer and anaemia	No further development
KY1070	NA	Kymab, UK	Anti-BMP-6 antibody	Preclinical	Rodent models of ACD	No further development
CSJ137	NCT02570854	Novartis, Switzerland	Anti-BMP-6 antibody	Phase 2	Haemodialysis patients with anaemia	Unpublished data
h5F9.23, h5F9-AM8	NA	NA	Anti-RGMc/HJV	Preclinical	Mouse and a rat model of ACD, genetic mouse model of IRIDA	No further clinical development
Momelotinib	NA	GSK, UK	JAK1/2 and ALK2 receptor	Approved for clinical use	Myelofibrosis	No data in CKD
Sevuparin	NCT03853421	Novo Nordisk, Denmark; Modus Therapeutics, Sweden	Heparinoid	Preclinical	CKD mouse model of high hepcidin anaemia, healthy volunteers	Phase 2 planned
LY2928057	NCT01991483	Eli Lilly, USA	Inhibition of hepcidin binding to ferroportin	Phase 2	Haemodialysis	No further clinical development
Targeting TfR2						
Anti-sense oligonucleotide	NA	Ionis Pharmaceutical, USA	To reduce hepatic TfR2	Preclinical	Mouse model of anaemia of chronic inflammation	Transient improvement of anaemia
Targeting interleukins						
Ziltivekimab	NCT03926117, NCT02868229	Novo Nordisk, Denmark	Anti-IL-6	Phase 1 and 2	ND CKD and haemodialysis	Phase 3 (ZEUS trial, NCT05021835; HERMES, NCT05636176)
Clazakizumab	NCT03744910	Bristol Myers Squibb, USA; Alder Biopharmaceuticals, USA	Anti-IL-6	Phase 3	Chronic active antibody-mediated rejection in kidney transplant recipients; ESKF	Phase 2b/3, study on CV outcome in DD CKD (NCT05485961)
P2D7KK	NA	NA	Anti-IL-1β	Preclinical	RaKO mice with CKD	NA

ACD, anaemia of chronic disease; IRIDA, iron-refractory iron deficiency anaemia; ESKF, end-stage kidney failure; CV, cardiovascular; DD, dialysis dependent; ND, non-dialysis dependent.

METODICA DIALITICA

RIMUOVERE PECIDINA



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