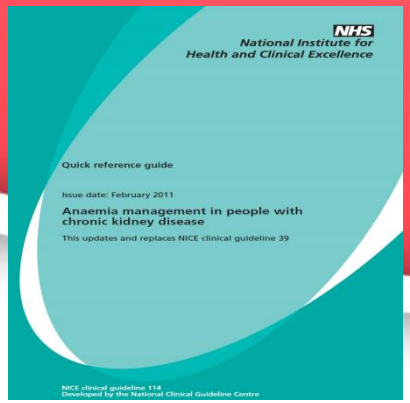
Νέα δεδομένα στην αντιμετώπιση της αναιμίας σε ασθενείς με Χρόνια Νεφρική Νόσο

Ιωάννης Γ. Γριβέας, MD,PhD
Νεφρολόγος

athens-NEPHROLOGY



- **Anaemia** is a state in which the quality and/or quantity of circulating red blood cells are below normal; it is associated with progression of CKD.

- Hb levels fall as kidney function declines.

- Adverse effects associated with anaemia include:
  - tiredness
  - shortness of breath
  - lethargy
  - palpitations
  - increased sensitivity to the cold
  - reduced cognition and concentration.

A Primary Care Approach to CKD Management

Stage	Description	Classification by Severity	Classification by Treatment
1	Kidney damage with normal or increased GFR	GFR ≥ 90	
2	Kidney damage with mild decrease in GFR	GFR of 60-89	T if kidney transplant
3	Moderate decrease in GFR	GFR of 30-59	recipient
4	Severe decrease in GFR	GFR of 15-29	D if dialysis
5	Kidney failure	GFR < 15	D if dialysis

Note: GFR is given in mL/min/1.73^2

National Kidney Foundation. KDOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Am J Kidney Dis 2002;39(suppl 1):S1-S266

KDIGO, Kidney Disease: Increasing Global Outcomes

Οδηγίες – Guidelines

UK Renal Association

Caring for Australasians with Renal Impairment

ERBP guidelines (Europe)

NICE guidelines

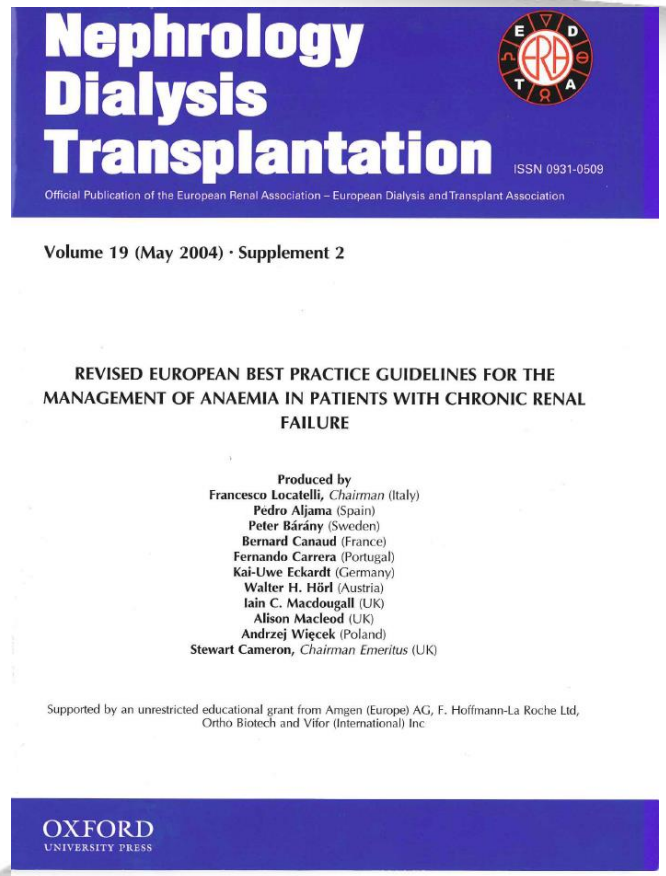
NKF-KDOQI (USA)

International Society of Peritoneal Dialysis

Canadian Society of Nephrology

Οδηγίες – Guidelines

EBPG 2004



	EBPG 2004
Definition of anaemia	Hb <11. 5 in women Hb <13.5 in men ≤70 years Hb <12 in men >70 years
Haemoglobin target	Hb >11 g/dl; Hb >14 g/dl not desirable (>12 g/dl in CVD)
Targets for iron therapy	TSAT (%) Lower limit: 20 Target: 30–50 Ferritin (ng/ml) Lower limit: 100 Target 200–500

EBPG Guidelines. *Nephrol Dial Transplant* 2004;19(Suppl 2):ii1-ii47

	Normal HCT (Besarab et al 1998, NEJM)	CHOIR (Singh et al 2006, NEJM)	CREATE (Drueke et al 2006, NEJM)
Πλήθος ασθενών	1.233	1.432	603
Στάδιο νόσου	ΧΝΝ – 5 με καρδιολογικό νόσημα	ΧΝΝ 3 – 4	ΧΝΝ 3 – 4
Στόχος μελέτης	Ποιες είναι οι επιπτώσεις της φυσιολογικοποίησης των τιμών Hb σε ασθενείς με ΧΝΝ και καρδιά	Ποιά είναι τα βέλτιστα επίπεδα Hb;	Αν θα υπάρξει βελτίωση της καρδιακής λειτουργίας με τη διόρθωση της αναιμίας
Στόχοι Hb			
Χαμηλό όριο	10 g/dl	11.3 g/dl	10.5 – 11.5 g/dl
Υψηλό όριο	14 g/dl	13.5 g/dl	13 – 15 g/dl
Follow up	30 μήνες	16 μήνες	35 μήνες
Αποτέλεσμα	Σε ασθενείς με ΧΝΝ-5 και συμφορητική καρδιακή ανεπάρκεια ή ισχαιμικό επεισόδιο, η πλήρης διόρθωση της αναιμίας δεν συστήνεται	Ο υψηλός στόχος οδήγησε σε αύξηση των κινδύνων σε σχέση με τον χαμηλό, χωρίς βελτίωση της QoL	Η διόρθωση της αναιμίας δεν φαίνεται να διορθώνει τον κίνδυνο εμφάνισης καρδιαγγειακών συμβαμάτων

KDOQI Guidelines 2006\7

"3.2.3 Targets of iron therapy:

In the opinion of the Work Group, sufficient iron should be administered to generally maintain the following indices of iron status during ESA treatment:

3.2.3.1 HD-CKD:

- Serum ferritin>200 ng/mL *AND* TSAT >20%, or CHr >29 pg/cell.

3.2.3.2 ND-CKD and PD-CKD:

- Serum ferritin>100 ng/mL *AND* TSAT >20%.

3.2.4 Upper level of ferritin:

In the opinion of the Work Group, there is insufficient evidence to recommend routine administration of IV iron if serum ferritin level is greater than 500 ng/mL. When ferritin level is greater than 500 ng/mL, decisions regarding IV iron administration should weigh ESA responsiveness, Hb and TSAT level, and the patient's clinical status".

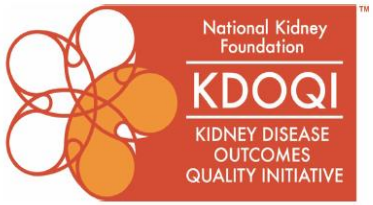
National Kidney Foundation
KDOQI
KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE

KDOQI CLINICAL PRACTICE GUIDELINE AND CLINICAL PRACTICE RECOMMENDATIONS FOR ANEMIA IN CHRONIC KIDNEY DISEASE:

2007 UPDATE OF HEMOGLOBIN TARGET

Οδηγίες – Guidelines

KDOQI Guidelines 2006\7



KDOQI CLINICAL PRACTICE GUIDELINE AND CLINICAL PRACTICE RECOMMENDATIONS FOR ANEMIA IN CHRONIC KIDNEY DISEASE:

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"3.2.5 Route of administration:

3.2.5.1 The preferred route of administration is IV in patients with HD-CKD. (*STRONG RECOMMENDATION)*

3.2.5.2 In the opinion of the Work Group, the route of iron administration can be either IV or oral in patients with ND-CKD or PD-CKD".

KDOQI Guidelines. *Am J Kidney Dis 2006*;47(5):S58-S70
KDOQI Guidelines. *Am J Kidney Dis* 2006;47(5):S33-S53
KDOQI Guidelines. *Am J Kidney Dis* 2007;50(3):474-530

Οδηγίες – Guidelines

ERBP Position Paper 2009

Nephrol Dial Transplant (2009) 24: 348–354
doi: 10.1093/ndt/gfn653
Advance Access publication 26 November 2008

Anaemia management in patients with chronic kidney disease: a position statement by the Anaemia Working Group of European Renal Best Practice (ERBP)

Francesco Locatelli[1], Adrian Covic[2], Kai-Uwe Eckardt[3], Andrzej Wiecek[4] and Raymond Vanholder[5] on behalf of the ERA-EDTA ERBP Advisory Board

[1]Department of Nephrology, Dialysis and Renal Transplantation, 'A. Manzoni' Hospital, Lecco, Italy, [2]Department of Nephrology, Dialysis and Transplantation, C. I. Parhon University Hospital, University of Medicine Gr. T. Popa, Iasi, Romania, [3]Department of Nephrology and Hypertension, University of Erlangen-Nuremberg, Nuremberg, Germany, [4]Department of Nephrology, Endocrinology and Metabolic Diseases, Medical University of Silesia, Katowice, Francuska, Poland and [5]Nephrology Section, University Hospital, Ghent, Belgium

Keywords: anaemia; erythropoiesis stimulating agents; biosimilars; guidelines; pure red cell aplasia

Introduction

Over the last few years, much has been done to develop guidelines on the basis of the strongest possible evidence because this allows an accurate description of the quality and/or degree of uncertainty of the recommendations and provides physicians with a valuable tool for judicious decisions. However, creating and updating evidence-based guidelines is extremely costly, and so the nephrological community has been trying to build up a single set of international guidelines under the aegis of Kidney Disease Improving Global Outcomes (KDIGO) [1]. As part of this unifying effort, the working group responsible for the 2006 update of the National Kidney Foundation–Kidney Disease Outcome Quality Initiative (NKF-KDOQI) guidelines on anaemia management in patients with chronic kidney disease (CKD) [2], and the 2007 update on haemoglobin (Hb) targets [3], included members from Europe, Middle East, Mexico and Canada. However, this international effort may not be correctly perceived by European nephrologists, who sometimes feel that differences in practice patterns make it difficult to apply guidelines developed outside Europe; on the other hand, the latest update of the European Best Practice Guidelines (EBPG) [4] may appear outdated in some respects.

A specially appointed ERA-EDTA Work Group met in Paris to discuss European guideline planning in early January 2008, and agreed that the Association should continue producing and updating guidelines in collaboration with KDIGO [5]. It also agreed that ERA-EDTA should issue suggestions for clinical practice in areas in which evidence is lacking or weak, which will be presented as 'position statements' rather than clinical guidelines [5]. It was also decided to issue position statements about guidelines (recommendations issued by other bodies, of which the current publication is the first result). Finally, the group opted to change the name EBPG to European Renal Best Practice (ERBP) as a means of acknowledging that, especially in nephrology, it is difficult to generate real 'guidelines' because of the lack of sufficient evidence.

In this context, and while awaiting the publication of the KDIGO anaemia guidelines possibly in 2011, an *ad hoc* work group was commissioned by the ERBP Advisory Board to give its opinion on the 'hot topic' of Hb targets, including recently raised issues that were not covered by KDOQI in 2006 [2]. These points are summarized in the present position paper, which is not intended to represent a set of new guidelines as it is not the result of a systematic review of the evidence.

NKF-KDOQI update, 2006

In May 2006, the NKF published a revised set of guidelines on managing anaemia in CKD [2]. The Guideline Committee attempted to integrate new evidence using the 2004 EBPG revision [4] and the 2000 KDOQI guidelines as a starting point [6]. The update also involved a systematic review of the evidence based on an extensive search of the literature and the grading of the strength of the evidence, and separated evidence-based guidelines, which could be used to measure clinical performance when appropriate, and clinical practice recommendations primarily based on expert judgement. The result was a solid document summarizing the evidence available up until September 2005.

Correspondence and offprint requests to: Francesco Locatelli, Department of Nephrology, Dialysis and Renal Transplantation, 'Alessandro Manzoni' Hospital, Via Dell' Eremo 9/11, 23900 Lecco, Italy. Tel: +39-0341-489850; Fax: +39-0341-489860; E-mail: nefrologia@ospedale.lecco.it

ERBP: anaemia group position, 2008

Definition of anaemia	Hb <12 in females Hb <13.5 in males
Haemoglobin target	Generally Hb 11–12 g/dl target Hb should not be >13 g/dl
Targets for iron therapy	TSAT (%) Lower limit: ≥20 Ferritin Lower limit: 100 in non-HD, 200 in HD Do not routinely exceed 500

ERBP Guidelines. *Nephrol Dial Transplant* 2009;24:348-354

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Ουσιαστικά η Ευρωπαϊκή Ομάδα έκδοσης κλινικών οδηγιών ασπάζεται τις θέσεις και τις απόψεις της αντίστοιχης Αμερικάνικης, χωρίς καμία διαφοροποίηση

ERBP Guidelines. *Nephrol Dial Transplant* 2009;24:348-354

The NEW ENGLAND JOURNAL of MEDICINE

A Trial of Darbepoetin Alfa in Type 2 Diabetes and Chronic Kidney Disease

Marc A. Pfeffer, M.D., Ph.D., Emmanuel A. Burdmann, M.D., Ph.D., Chao-Yin Chen, Ph.D., Mark E. Cooper, M.D., Dick de Zeeuw, M.D., Ph.D., Kai-Uwe Eckardt, M.D., Jan M. Feyzi, M.S., Peter Ivanovich, M.D., Reshma Kewalramani, M.D., Andrew S. Levey, M.D., Eldrin F. Lewis, M.D., M.P.H., Janet B. McGill, M.D., John J.V. McMurray, M.D., Patrick Parfrey, M.D., Hans-Henrik Parving, M.D., Giuseppe Remuzzi, M.D., Ajay K. Singh, M.D., Scott D. Solomon, M.D., and Robert Toto, M.D., for the TREAT Investigators*

ABSTRACT

BACKGROUND

Anemia is associated with an increased risk of cardiovascular and renal events among patients with type 2 diabetes and chronic kidney disease. Although darbepoetin alfa can effectively increase hemoglobin levels, its effect on clinical outcomes in these patients has not been adequately tested.

METHODS

In this study involving 4038 patients with diabetes, chronic kidney disease, and anemia, we randomly assigned 2012 patients to darbepoetin alfa to achieve a hemoglobin level of approximately 13 g per deciliter and 2026 patients to placebo, with rescue darbepoetin alfa when the hemoglobin level was less than 9.0 g per deciliter. The primary end points were the composite outcomes of death or a cardiovascular event (nonfatal myocardial infarction, congestive heart failure, stroke, or hospitalization for myocardial ischemia) and of death or end-stage renal disease.

RESULTS

Death or a cardiovascular event occurred in 632 patients assigned to darbepoetin alfa and 602 patients assigned to placebo (hazard ratio for darbepoetin alfa vs. placebo, 1.05; 95% confidence interval [CI], 0.94 to 1.17; P=0.41). Death or end-stage renal disease occurred in 652 patients assigned to darbepoetin alfa and 618 patients assigned to placebo (hazard ratio, 1.06; 95% CI, 0.95 to 1.19; P=0.29). Fatal or nonfatal stroke occurred in 101 patients assigned to darbepoetin alfa and 53 patients assigned to placebo (hazard ratio, 1.92; 95% CI, 1.38 to 2.68; P<0.001). Red-cell transfusions were administered to 297 patients assigned to darbepoetin alfa and 496 patients assigned to placebo (P<0.001). There was only a modest improvement in patient-reported fatigue in the darbepoetin alfa group as compared with the placebo group.

CONCLUSIONS

The use of darbepoetin alfa in patients with diabetes, chronic kidney disease, and moderate anemia who were not undergoing dialysis did not reduce the risk of either of the two primary composite outcomes (either death or a cardiovascular event or death or a renal event) and was associated with an increased risk of stroke. For many persons involved in clinical decision making, this risk will outweigh the potential benefits. (ClinicalTrials.gov number, NCT00093015.)

The affiliations of the authors are listed in the Appendix. Address reprint requests to Dr. Pfeffer at the Cardiovascular Division, Brigham and Women's Hospital, 75 Francis St., Boston, MA 02115, or at mpfeffer@rics.bwh.harvard.edu.

*The Trial to Reduce Cardiovascular Events with Aranesp Therapy (TREAT) committees and teams are listed in the Appendix, and investigators and individual sites are listed in the Supplementary Appendix, available with the full text of this article at NEJM.org.

This article (10.1056/NEJMoa0907845) was published on October 30, 2009, at NEJM.org.

N Engl J Med 2009;361.

Οδηγίες – Guidelines

ERBP Position Paper 2010

NDT Advance Access published June 29, 2010

Nephrol Dial Transplant (2010) 1 of 5
doi: 10.1093/ndt/gfq336

NDT Nephrology Dialysis Transplantation

Editorial Review

Target haemoglobin to aim for with erythropoiesis-stimulating agents: a position statement by ERBP following publication of the Trial to Reduce Cardiovascular Events with Aranesp® Therapy (TREAT) Study

Francesco Locatelli[1], Pedro Aljama[2], Bernard Canaud[3], Adrian Covic[4], Angel De Francisco[5], Iain C. Macdougall[6], Andrzej Wiecek[7], Raymond Vanholder[8] and On behalf of the Anaemia Working Group of European Renal Best Practice (ERBP)

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Abstract

The European Renal Best Practice (ERBP), which are issued by ERA–EDTA, are suggestions for clinical practice in areas in which evidence is lacking or weak, together with position statements on recently published randomized controlled trials, or on existing guidelines and recommendations. In 2009, the Anaemia Working Group of ERBP published its first position statement about the haemoglobin target to aim for with erythropoietin-stimulating agents (ESA) and on issues that were not covered by K-DOQI in 2006–07. This second position paper of the group follows the publication of the Trial to Reduce Cardiovascular Events with Aranesp® Therapy (TREAT) Study. This multi-centre, placebo-controlled trial compared cardiovascular and renal outcomes in 4038 patients with type 2 diabetes, chronic kidney disease not on dialysis, and anaemia who were randomized to complete anaemia correction (haemoglobin target of 13 g/dL using darbepoetin alfa) or placebo (with a haemoglobin rescue value of 9 g/dL).
Following the findings of the TREAT study, the Anaemia Working Group of ERBP maintains its view that 'Hb values of 11–12 g/dL should be generally sought in the CKD population without intentionally exceeding 13 g/dL' and that the doses of ESA therapy to achieve the target haemoglobin should also be considered. More caution is suggested when treating anaemia with ESA therapy in patients with type 2 diabetes not undergoing dialysis (and probably in diabetics at all CKD stages). In those with ischaemic heart disease or with a previous history of stroke, possible benefits should be weighed up against an increased risk of stroke recurrence, when deciding which Hb level to aim for.

These recommendations are not intended to represent a new guideline as they are not the result of a systematic review of the evidence.

Keyword: anemia; chronic kidney disease; diabetes; erythropoiesis stimulating agents; stroke

Introduction (aim and scope)

Some years ago, the nephrological community planned a single set of international guidelines under the aegis of Kidney Disease Improving Global Outcomes (KDIGO) [1]. Consequently, the ERA–EDTA agreed to issue afterwards only suggestions for clinical practice in areas in which evidence is lacking or weak, together with position statements on recently published randomized controlled trials (RCTs), or on existing guidelines and recommendations issued by other bodies or previous European Best Practice Guidelines (EBPG) [2]. Following the publication of KDOQI guidelines about anaemia in 2006/2007 [3,4], the Anaemia Working Group of European Renal Best Practice (ERBP) published its first position statement [5], giving its opinion on the 'hot' topic of haemoglobin (Hb) targets and on recently raised issues that were not covered by KDOQI in 2006 [3].
The aim of this second position statement on anaemia is to give guidance on the interpretation of the recently published Trial to Reduce Cardiovascular Events with Aranesp® Therapy (TREAT) Study [6], and its possible relevance to recommended treatments and Hb targets to be used when treating chronic kidney disease (CKD) patients with erythropoiesis-stimulating agents (ESA) therapy, while

Haemoglobin target

"The ERBP group also feels that it is reasonable to suggest that:

(i) In patients with type 2 diabetes not undergoing dialysis (and probably in diabetics at all CKD stages), more caution is needed when treating anaemia with ESA therapy. In diabetic patients with a history of stroke, a lower target is more sensible (10–12 g/dL), balancing the risk–benefit of treatment and the desired Hb target in the individual patient. It is also of paramount importance to involve the patient in the decision making, and seek their personal views after a discussion about the benefits/risks of treatment. On this respect, the patient's opinion should be carefully taken into consideration.

(ii) The risk–benefit of increased transfusions should also be considered carefully, especially for patients eligible for transplantation."

Locatelli F, et al. Nephrol Dial Transplant 2010;25(9):2846-2850

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Continue…

"**(iii)** In diabetic patients with ischaemic heart disease or with a previous history of stroke, possible benefits of reduced need for coronary revascularization procedures and transfusions should be weighed up against an increased risk of stroke recurrence, when deciding which Hb level to aim for, and use of the lowest possible doses of ESA appears reasonable.

(iv) In patients with CKD and a previous history of cancer, the risk of tumour recurrence and related death should be considered when deciding whether or not to start ESA treatment. Again, in these patients, the lowest possible doses of ESA should be used."

Οδηγίες – Guidelines

ERBP Position Paper 2010

"Treatment of renal anemia

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Editorial Review

Target haemoglobin to aim for with erythropoiesis-stimulating agents: a position statement by ERBP following publication of the Trial to Reduce Cardiovascular Events with Aranesp® Therapy (TREAT) Study

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Abstract

The European Renal Best Practice (ERBP), which are issued by ERA–EDTA, are suggestions for clinical practice in areas in which evidence is lacking or weak, together with position statements on recently published randomized controlled trials, or on existing guidelines and recommendations. In 2009, the Anaemia Working Group of ERBP published its first position statement about the haemoglobin target to aim for with erythropoietin-stimulating agents (ESA) and on issues that were not covered by K-DOQI in 2006–07. This second position paper of the group follows the publication of the Trial to Reduce Cardiovascular Events with Aranesp® Therapy (TREAT) Study. This multi-centre, placebo-controlled trial compared cardiovascular and renal outcomes in 4038 patients with type 2 diabetes, chronic kidney disease not on dialysis, and anaemia who were randomized to complete anaemia correction (haemoglobin target of 13 g/dL using darbepoetin alfa) or placebo (with a haemoglobin rescue value of 9 g/dL). Following the findings of the TREAT study, the Anaemia Working Group of ERBP maintains its view that 'Hb values of 11–12 g/dL should be generally sought in the CKD population without intentionally exceeding 13 g/dL' and that the doses of ESA therapy to achieve the target haemoglobin should also be considered. More caution is suggested when treating anaemia with ESA therapy in patients with type 2 diabetes not undergoing dialysis (and probably in diabetics at all CKD stages). In those with ischaemic heart disease or with a previous history of stroke, possible benefits should be weighed up against an increased risk of stroke recurrence, when deciding which Hb level to aim for.

These recommendations are not intended to represent a new guideline as they are not the result of a systematic review of the evidence.

Keyword: anemia; chronic kidney disease; diabetes; erythropoiesis stimulating agents; stroke

Introduction (aim and scope)

Some years ago, the nephrological community planned a single set of international guidelines under the aegis of Kidney Disease Improving Global Outcomes (KDIGO) [1]. Consequently, the ERA–EDTA agreed to issue afterwards only suggestions for clinical practice in areas in which evidence is lacking or weak, together with position statements on recently published randomized controlled trials (RCTs), or on existing guidelines and recommendations issued by other bodies or previous European Best Practice Guidelines (EBPG) [2]. Following the publication of KDOQI guidelines about anaemia in 2006/2007 [3,4], the Anaemia Working Group of European Renal Best Practice (ERBP) published its first position statement [5], giving its opinion on the 'hot' topic of haemoglobin (Hb) targets and on recently raised issues that were not covered by KDOQI in 2006 [3].

The aim of this second position statement on anaemia is to give guidance on the interpretation of the recently published Trial to Reduce Cardiovascular Events with Aranesp® Therapy (TREAT) Study [6], and its possible relevance to recommended treatments and Hb targets to be used when treating chronic kidney disease (CKD) patients with erythropoiesis-stimulating agents (ESA) therapy, while

(i) Iron administration is an important factor for the successful treatment with any kind of ESA, in order to use the lowest dose for reaching and maintaining the desired Hb target

(ii) ESA treatment should not be started in patients who are iron-deficient

(iii) Iron replacement should be used first in any CKD patient who is proven or likely to be iron-deficient, and only once the iron stores are replete should ESA therapy be initiated

(iv) In CKD patients, ESA treatment should be considered when Hb levels are consistently below 11 g/dL (possibly < 10 g/dL in patients with type 2 diabetes and with a history of strokes), and all other causes of anaemia have been excluded; the threshold for treatment should be decided according to patient characteristics and symptoms, and the desired Hb target"

Locatelli F, et al. Nephrol Dial Transplant 2010;25(9):2846-2850

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KDIGO

KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease

VOLUME 2 | ISSUE 4 | AUGUST (2) 2012

http://www.kidney-international.org

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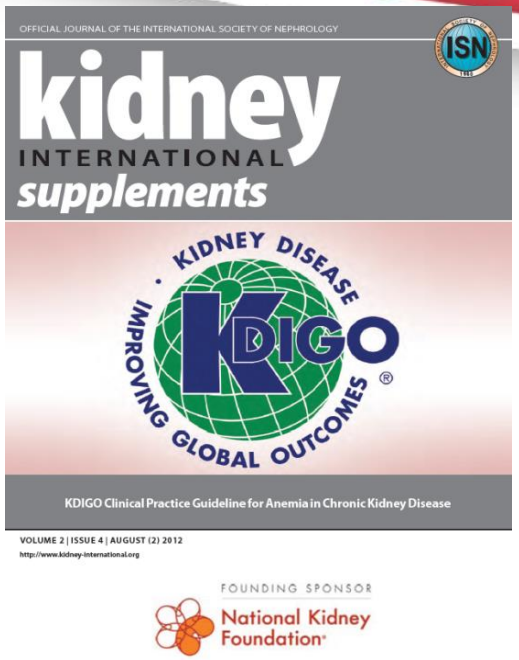
Οδηγίες – Guidelines

KDIGO 2012



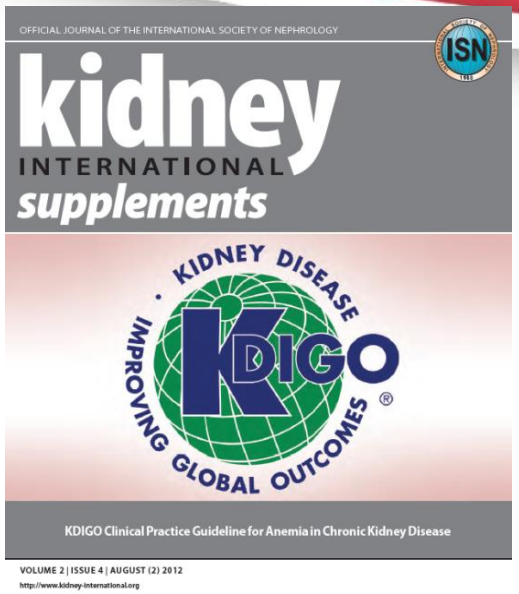
"***Diagnosis of anemia***

1.2.1: Diagnose anemia in adults and children >15 years with CKD when the Hb concentration is <13.0 g/dl (<130 g/l) in males and <12.0 g/dl (,120 g/l) in females. (Not Graded)"

KDIGO Guidelines. *Kidney Int* 2012;2(4):279-335

Οδηγίες – Guidelines

KDIGO 2012



"ESA INITIATION

3.1: Address all correctable causes of anemia (including iron deficiency and inflammatory states) prior to initiation of ESA therapy. (Not Graded)

3.2: In initiating and maintaining ESA therapy, we recommend balancing the potential benefits of reducing blood transfusions and anemia-related symptoms against the risks of harm in individual patients (e.g., stroke, vascular access loss, hypertension). (1B)

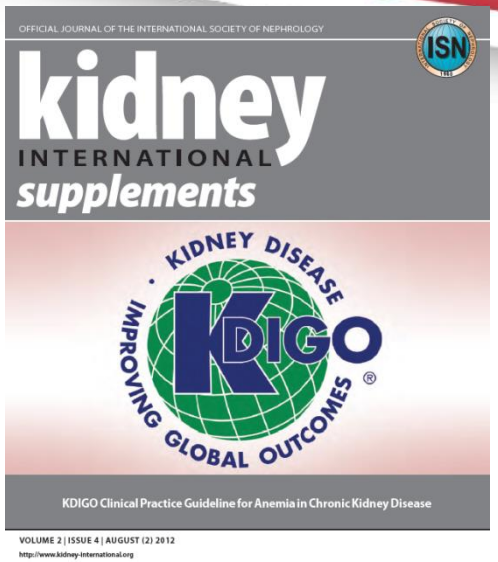
3.3: We recommend using ESA therapy with great caution, if at all, in CKD patients with active malignancy—in particular when cure is the anticipated outcome—(1B), a history of stroke (1B), or a history of malignancy (2C).

3.4.1: For adult CKD-ND patients with Hb concentration >10.0 g/dl (>100 g/l), we suggest that ESA therapy not be initiated. (2D)."

KDIGO Guidelines. *Kidney Int* 2012;2(4):279-335

Οδηγίες – Guidelines

KDIGO 2012



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"***continue…***

3.4.2: For adult CKD-ND patients with Hb concentration <10.0 g/dl (<100 g/l) we suggest that the decision whether to initiate ESA therapy be individualized based on the rate of fall of Hb concentration, prior response to iron therapy, the risk of needing a transfusion, the risks related to ESA therapy and the presence of symptoms attributable to anemia. (2C)

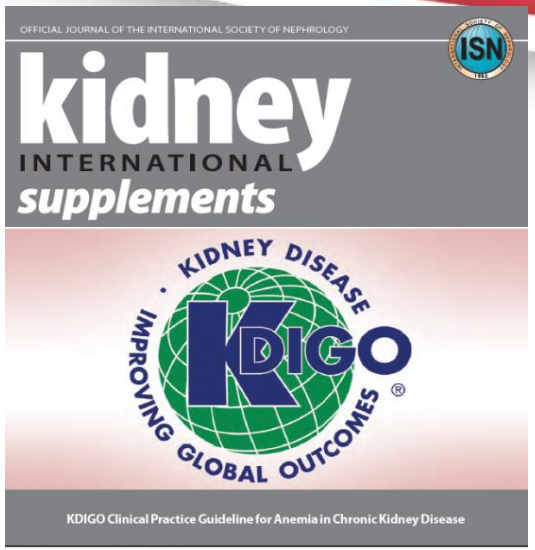
3.4.3: For adult CKD 5D patients, we suggest that ESA therapy be used to avoid having the Hb concentration fall below 9.0 g/dl (90 g/l) by starting ESA therapy when the hemoglobin is between 9.0–10.0 g/dl (90–100 g/l). (2B)

3.4.4: Individualization of therapy is reasonable as some patients may have improvements in quality of life at higher Hb concentration and ESA therapy may be started above 10.0 g/dl (100 g/l). (Not Graded)"

KDIGO Guidelines. *Kidney Int* 2012;2(4):279-335

Οδηγίες – Guidelines

KDIGO 2012



"***Treatment with iron agents***

2.1.1: When prescribing iron therapy, balance the potential benefits of avoiding or minimizing blood transfusions, ESA therapy, and anemia-related symptoms against the risks of harm in individual patients (e.g., anaphylactoid and other acute reactions, unknown long-term risks). (Not Graded)

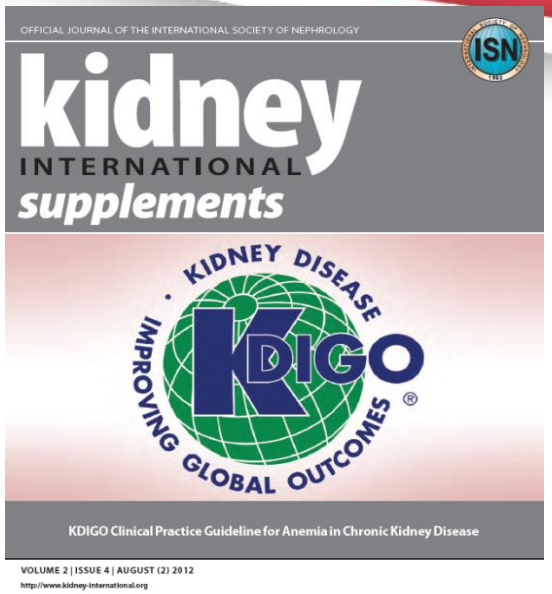
2.1.2: For adult CKD patients with anemia not on iron or ESA therapy we suggest a trial of IV iron (or in CKD-ND patients alternatively a 1–3 month trial of oral iron therapy) if (2C):

- an increase in Hb concentration without starting ESA treatment is desired and
- TSAT is <30% and ferritin is <500 ng/ml (<500 mg/l)"

KDIGO Guidelines. *Kidney Int* 2012;2(4):279-335

Οδηγίες – Guidelines

KDIGO 2012



"***Treatment with iron agents***

2.1.3: For adult CKD patients on ESA therapy who are not receiving iron supplementation, we suggest a trial of IV iron (or in CKD-ND patients alternatively a 1–3 month trial of oral iron therapy) if (2C):

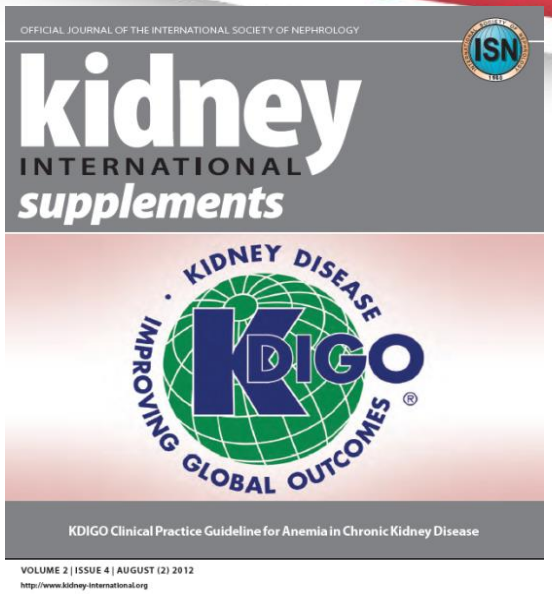
- an increase in Hb concentration or a decrease in ESA dose is desired and
- TSAT is <30% and ferritin is <500 ng/ml (<500 mg/l)

2.1.4: For CKD-ND patients who require iron supplementation, select the route of iron administration based on the severity of iron deficiency, availability of venous access, response to prior oral iron therapy, side effects with prior oral or IV iron therapy, patient compliance, and cost. (Not Graded)."

KDIGO Guidelines. *Kidney Int* 2012;2(4):279-335

Οδηγίες – Guidelines

KDIGO 2012
Σημεία Ενδιαφέροντος



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"In patients with CKD-ND, the available evidence supports an efficacy advantage of IV compared with oral administration of iron although the effect is rather small, with a weighted mean Hb difference of 0.31 g/dl (3.1 g/l). Whether the small Hb benefit of IV iron in CKD-ND patients is clinically meaningful or justifies the small risk of serious adverse events and unknown long-term risks is uncertain."

KDIGO Guidelines. *Kidney Int* 2012;2(4):279-335

Nephrol Dial Transplant (2014) 29: 2075–2084
doi: 10.1093/ndt/gfu201
Advance Access publication 2 June 2014

FIND-CKD: a randomized trial of intravenous ferric carboxymaltose versus oral iron in patients with chronic kidney disease and iron deficiency anaemia

Iain C. Macdougall[1], Andreas H. Bock[2], Fernando Carrera[3], Kai-Uwe Eckardt[4], Carlo Gaillard[5], David Van Wyck[6], Bernard Roubert[7], Jacqueline G. Nolen[7], Simon D. Roger[8] on behalf of the FIND-CKD Study Investigators[†]

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In conclusion, patients with non-dialysis-dependent CKD, anaemia and iron deficiency may benefit from IV iron treatment targeting a higher ferritin level. Both IV and oral iron therapy were effective in increasing Hb, ferritin and TSAT

Assessment and optimisation of erythropoiesis – optimal Hb levels

When determining individual aspirational Hb ranges for people with anaemia of CKD, take into account:

- patient preferences
- symptoms and comorbidities
- the required treatment

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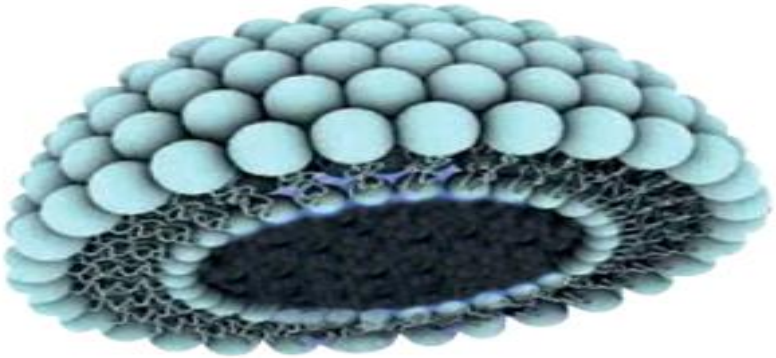
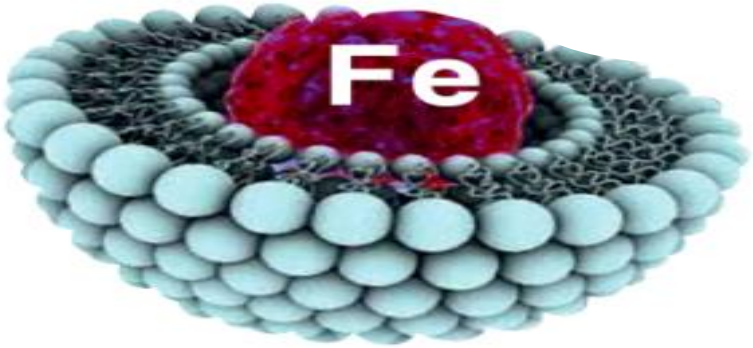
[18–25]; a recent report by Europena Medicines Agency (EMA) (September 2013) clearly points out that IV iron should be prescribed when oral iron cannot be given or does not work, and that should be administered in environments in which resuscitation facilities are present by personnel specifically trained to treat allergic reactions (EMA/579491/2013).





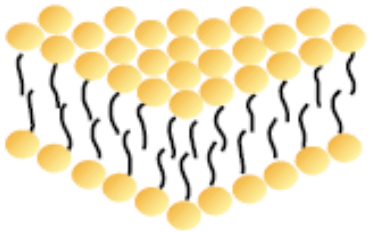
Oral liposomal-sucrosomial iron

- Phospolipid

hydrophilic head

hydrophobic tail

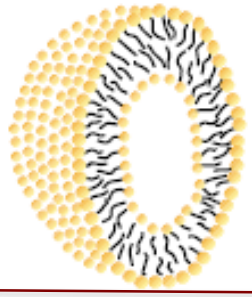
Arrangement of phospholipids in aqueous environment



Phospholipid bilayer

LIPOSOME

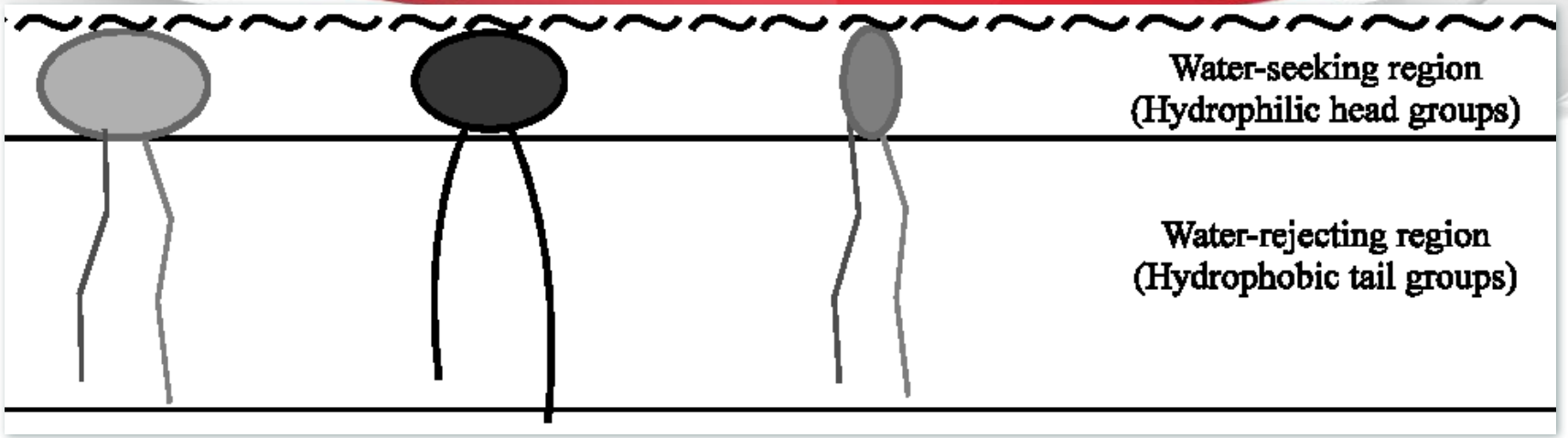
- Longitudinal Section



aqueous environment

- Liposomes are formed by self-aggregation of the phospholipids in an aqueous phase
- The lipid bilayer is similar to cell membranes

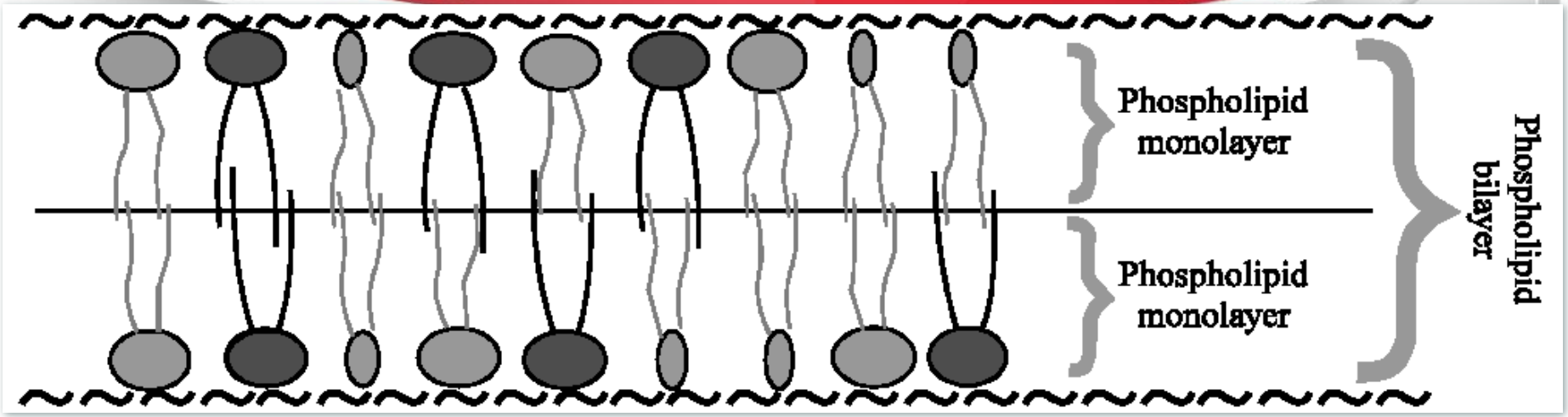
LIPOSOME STRUCTURE



PHOSPHOLIPIDS

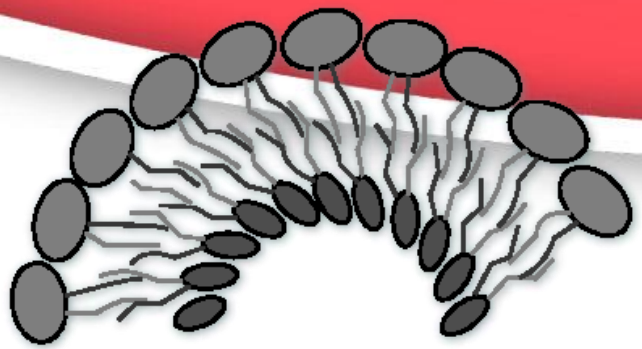
Main constituents of the Liposome (and of cellular membranes)

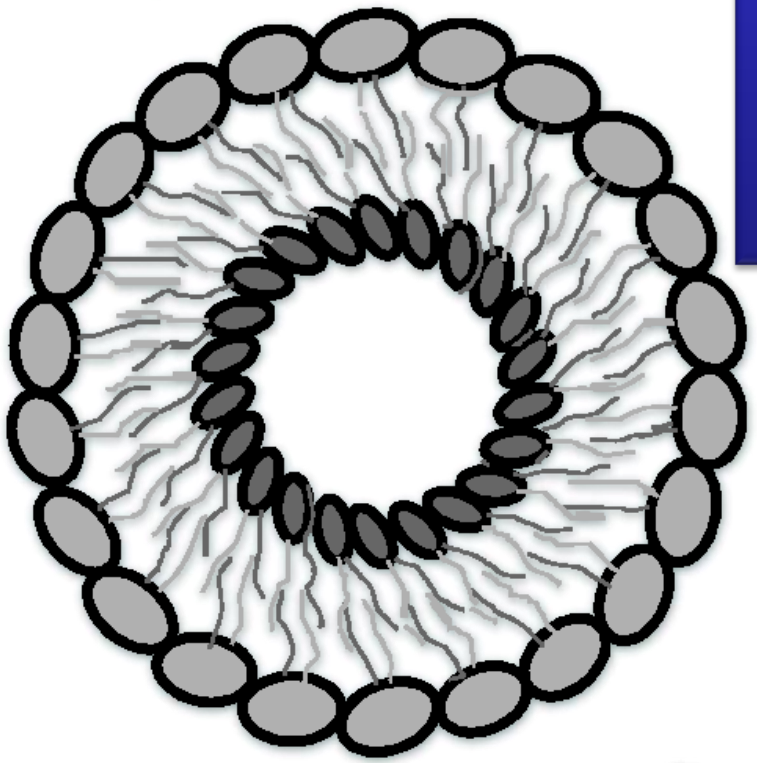
LIPOSOME STRUCTURE



Liposomes form due to the **self-aggregation** of phospholipids in an aqueous phase

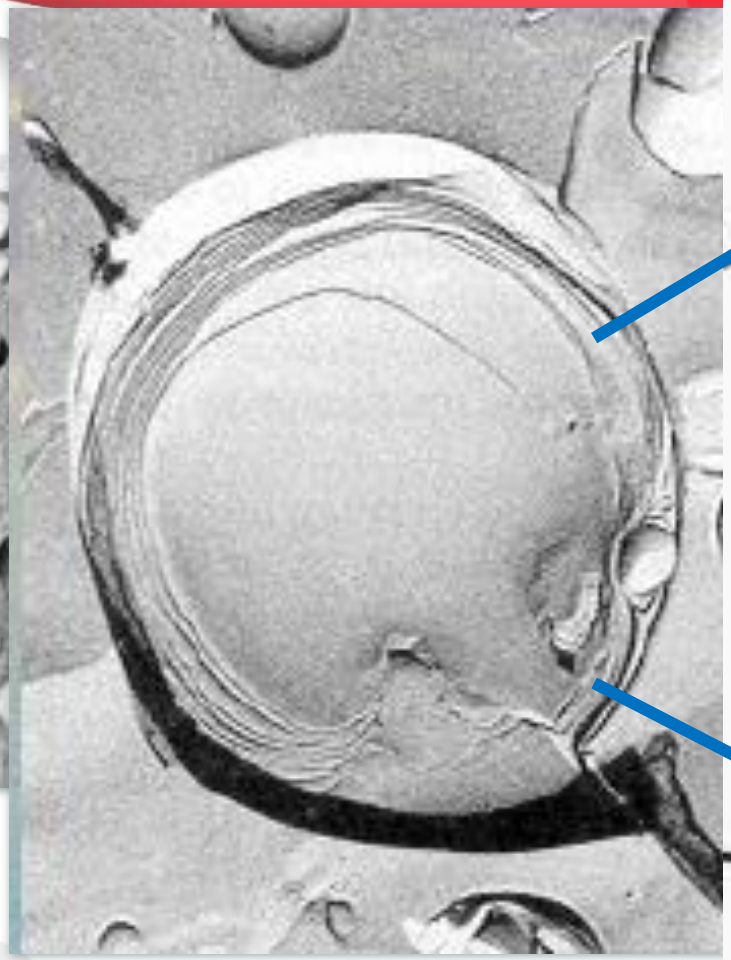
LIPOSOME STRUCTURE

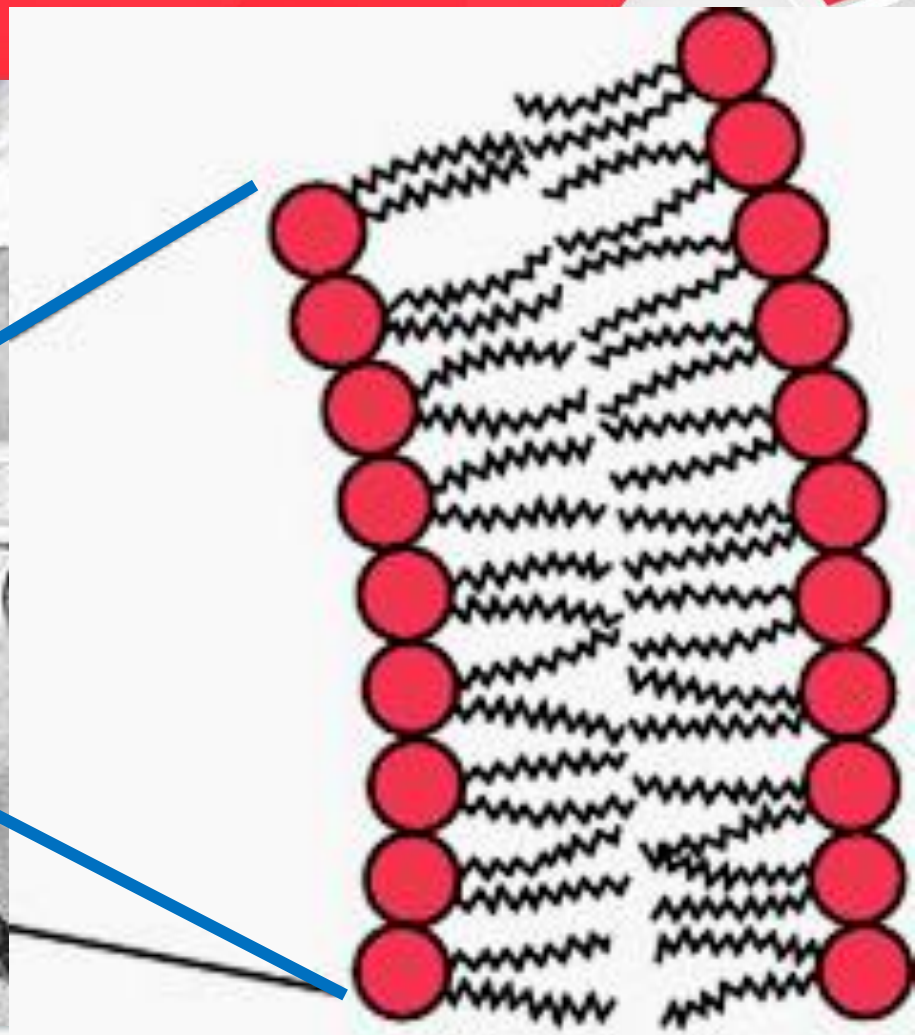




They give spontaneous origin to spherical vesicles (double-layer walls)

LIPOSOMES



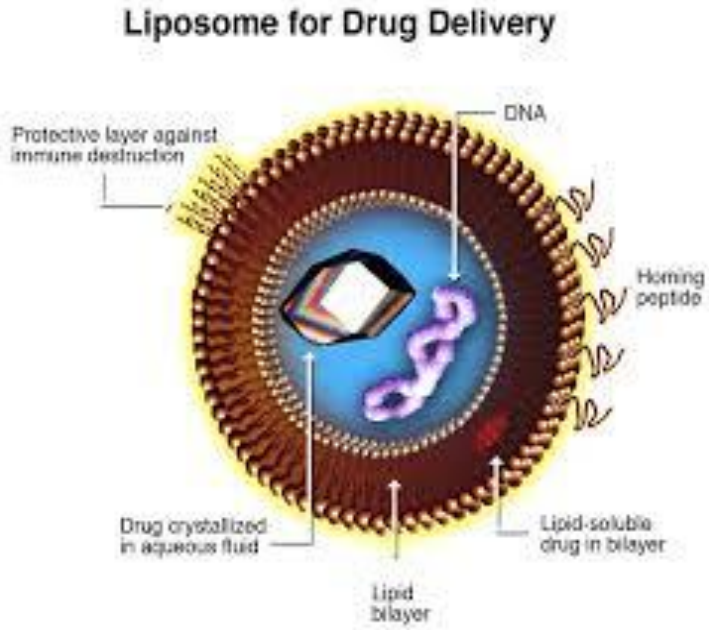


LIPOSOMES
DRUG DELIVERY

"Associating a drug with liposomes markedly changes its pharmacokinetics and lowers systemic toxicity;

Furthermore, the drug is prevented from early degradation and/or inactivation after introduction to the target organism"

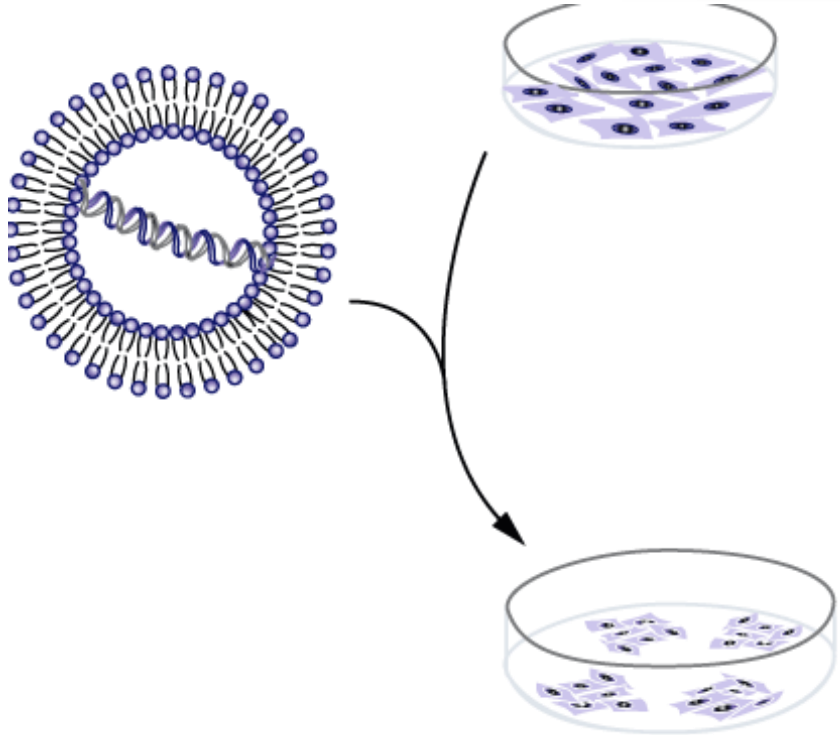
Kozubek - Acta Bioch. 2000



Examples of Liposomal Preparations

Liposomal Drugs	Action
AMPHOTERICIN B	Antifungal
DAUNOMYCIN DOXORUBICIN	Anti-tumor antibiotic
CYTARABINE	Chemotherapy drug
HEPATITIS A VIRUS (INACTIVE)	Hepatitis A Vaccine

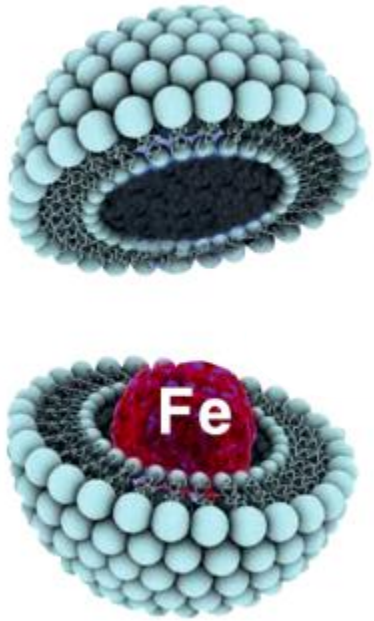
LIPOSOMES AS DNA DELIVERY



It is difficult for “raw” DNA to enter tumor cells or other somatic cells. In fact, it is a highly-polar molecule, with strong negative charge that does not pass the cell membrane.

LIPOSOMIAL IRON

THE ONLY THING WE HAVE DONE IS TO USE LIPOSOMES TO TRANSPORT IRON



LIPOSOMIAL IRON ABSORPTION

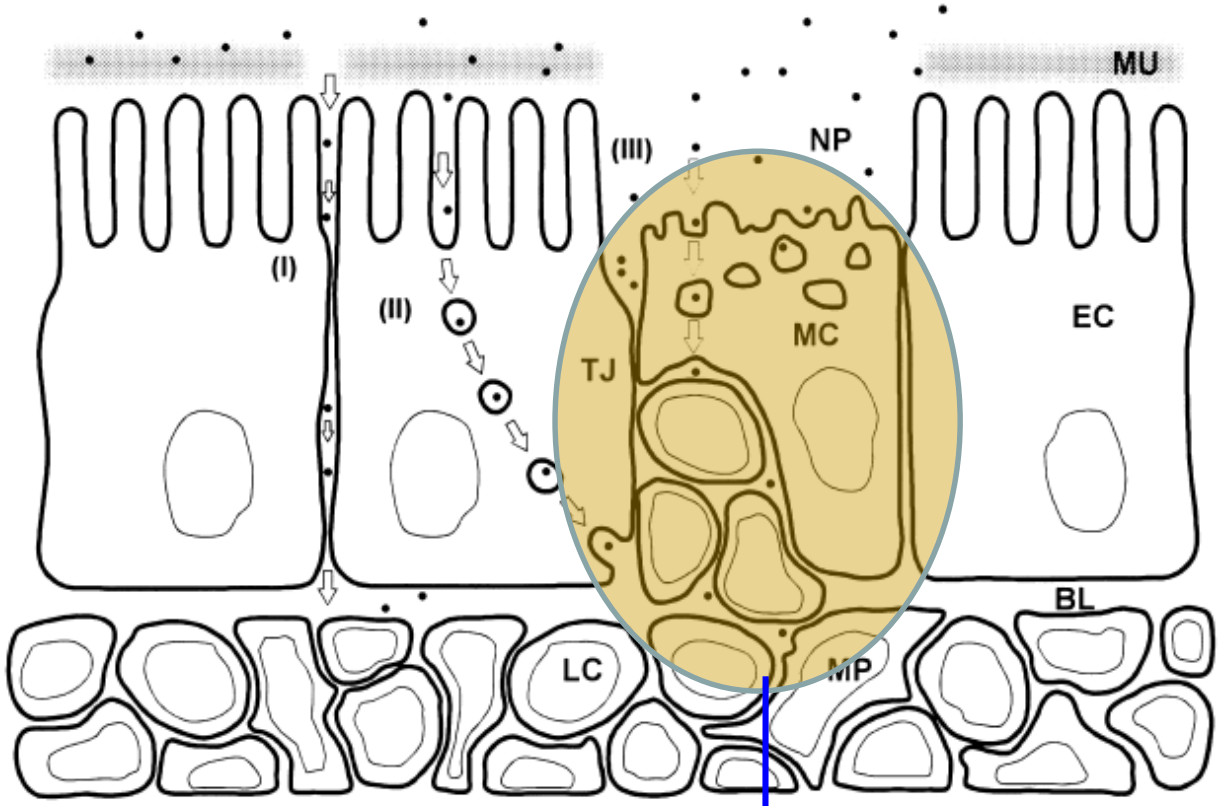
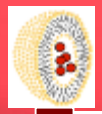
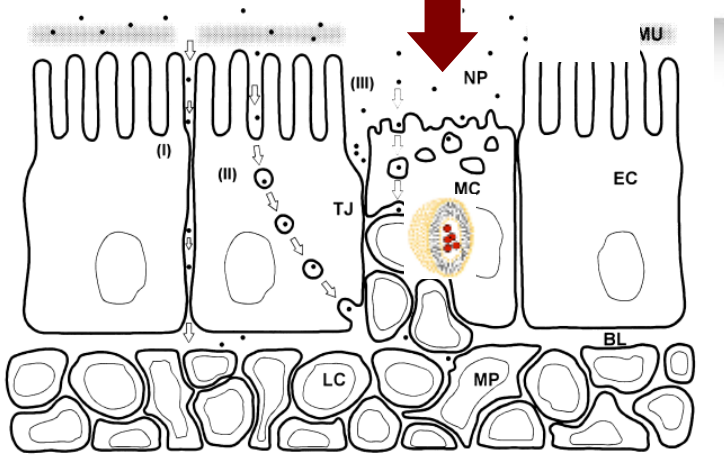
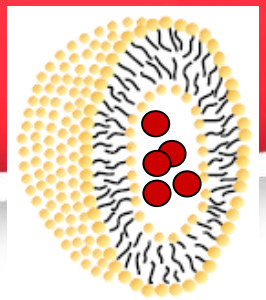


Fig. 1. Schematic drawing of mucus (MU) covered absorptive enterocytes (EC) and M cells (MC) in the small intestine. Lymphocytes (LC) and macrophages (MP) from underlying lymphoid tissue can pass the basal lamina (BL) and reach the epithelial cell layer which is sealed by tight junctions (TJ). Possible translocation routes for NP are (I) paracellular uptake, (II) endocytotic uptake by enterocytes and (III) M cells.

M CELLS



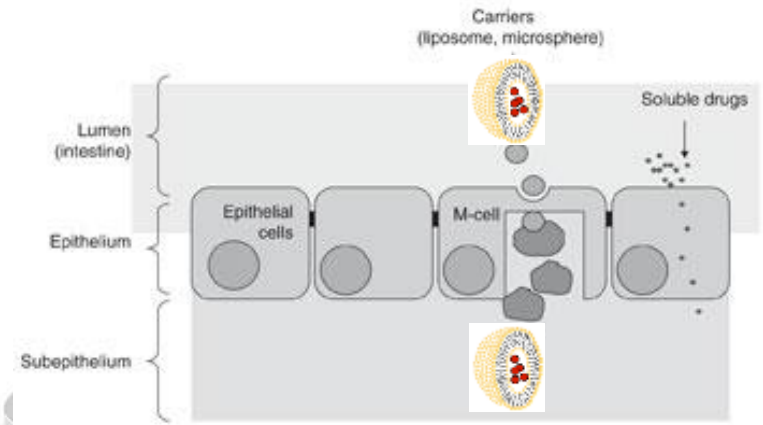




Liposomial Iron

Direct absorption

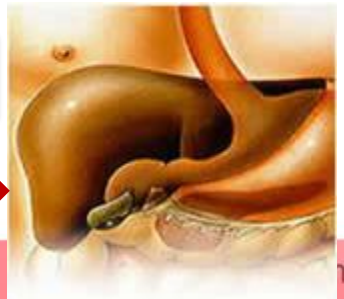
M Cells (endocytosis)



Macrophages

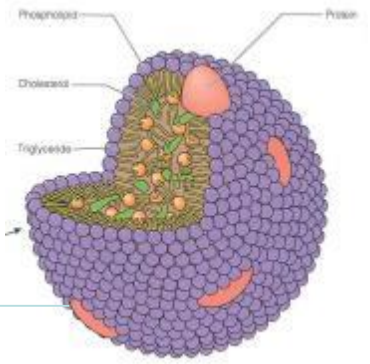
(Peyer's Plaques)

Transport through the lymph

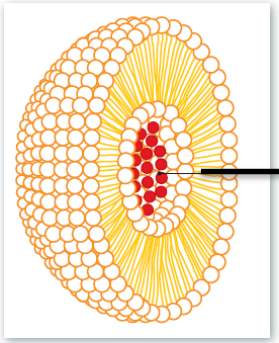


LIPOSOMES ABSORPTION

The iron is enclosed in the liposomes, in this way, passing undamaged through gastric acid environment, Liposomial iron could be recognized as chylomicrons in the intestinal tract and never reacts with mucouse membranes.



Chylomicron



Liposome

New Scientist 27 December 1975

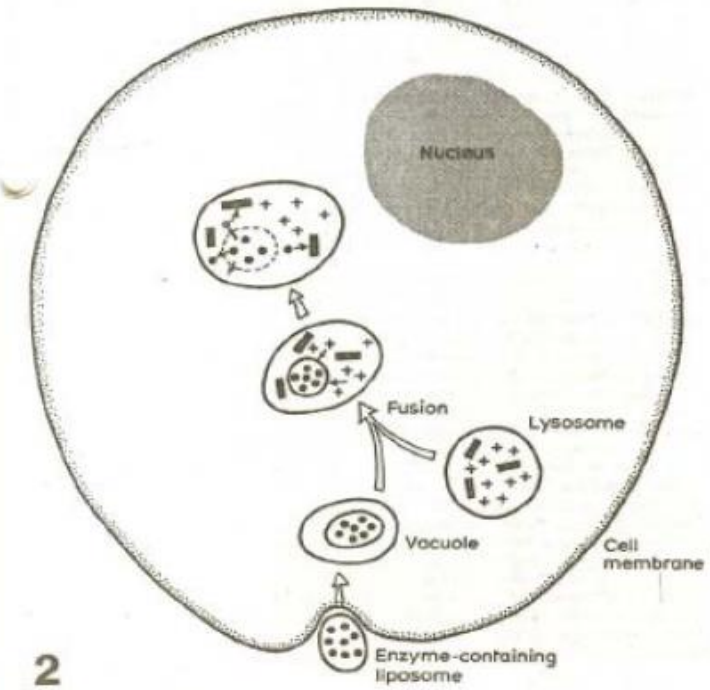
Molecular Trojan horses

With the prospects of genetic engineering in humans still remote, other methods of repairing inborn errors of metabolism have to be sought. Wrapping up enzymes in membrane sacks and injecting them into afflicted patients may be the answer

Dr Gregory Gregoriadis
is a research scientist at the Medical Research Council's Clinical Research Centre, Harrow, near London

The role of enzymes in transforming one substance (substrate) to another (product) is the basis of all biological processes. The existence of enzymes in cells depends on the release of information held in a sequence of nucleic acid, the corresponding structural gene. A faulty gene results in the partial or total absence of its respective enzyme, which in turn leads to the accumulation of the relevant substrate and a deficiency in the product of the reaction. In terms of human suffering, this often means early death, newborns maturing

the lysosomes of cells in different parts of the body does not require any sophisticated effort on our part. Materials near the cell enter the lysosomes by a process known as endocytosis which involves trapping the material within infoldings of the cell membrane which then pinch off to form vacuoles (membrane sacks) inside the cell. These vacuoles subsequently fuse with lysosomes which now contain the endocytosed material, and eventually degrade it by their lysosomal enzymes.

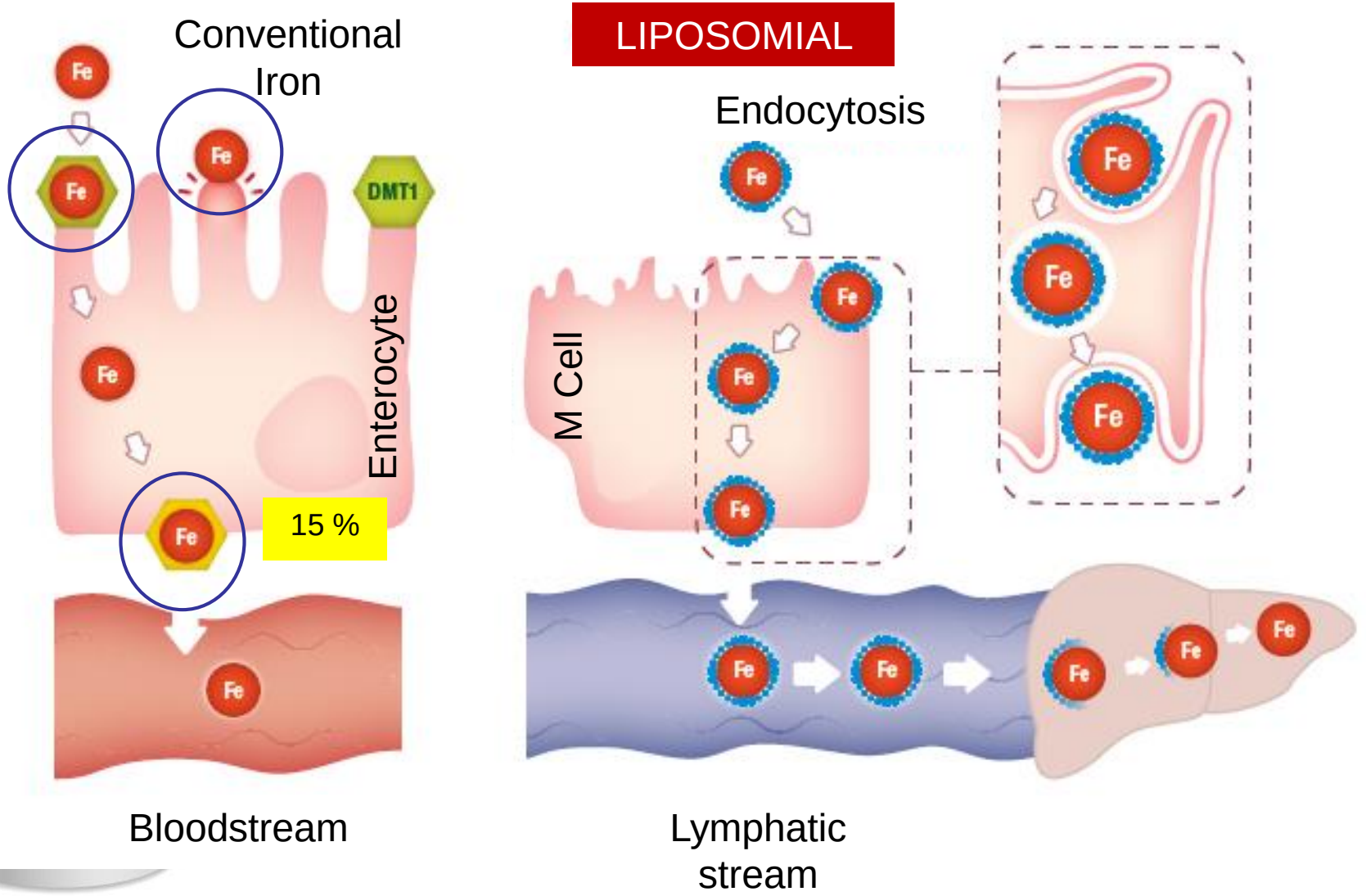


lysosomes or, after diffusion through the membranes surrounding the liposomes, in other cellular compartments (for example, the nucleus).

It is true that at the moment liposomes can be applied only for the liver and the spleen. However, specific manipulations on the liposomal surface can alter both the rate of their removal from the blood and their place of uptake. We have found, for example, that positively charged liposomes will circulate in the blood for much longer than negatively charged liposomes. We hope to be able to exploit this in treating inherited enzyme deficiencies such as phenylketonuria and galactosemia in which excessive levels of phenylalanine or galactose in blood are the cause of severe clinical manifestations. Circulating liposomes containing the appropriate enzymes could help metabolise there substances and therefore lower their level in blood. Asparaginase-containing positive liposomes could be used in treating some forms of leukaemia in which elimination of circulating asparagine has been shown to be beneficial to patients. To increase tissue specificity the attachment on the surface of liposomes of substances (antibodies for instance)

Figure 2 A liposome containing enzyme molecules (dots) is taken up into a cell by endocytosis. The endocytotic vacuole fuses with a lysosome which contains substrate molecules (bars). The lysosomal enzymes (crosses) disrupt the lipid bilayers of the liposome releasing the entrapped enzyme to act on the stored substrate

LIPOSOMIAL IRON ABSORPTION



LIPOSOMIAL IRON

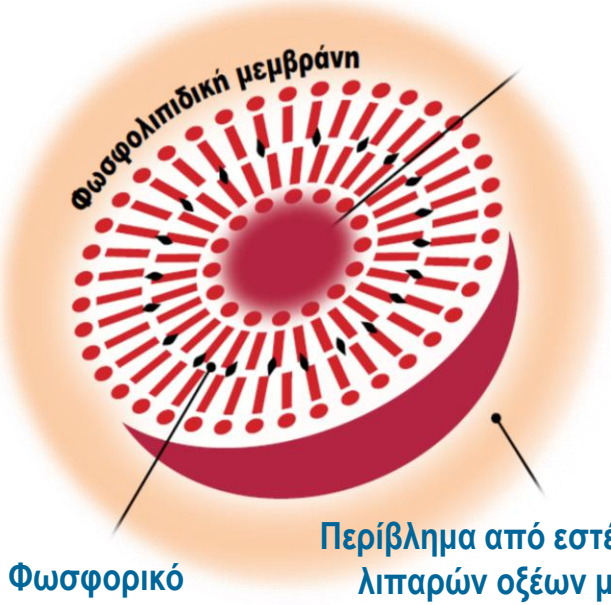
Thanks to liposomial technology, iron never comes in contact with intestinal mucosae

NO SIDE EFFECTS

Sucrosomial® Iron

Χρησιμοποιεί μία προηγμένη τεχνολογία για τη μεταφορά & απόδοσης του σιδήρου στον οργανισμό

Τρισθενής πυροφωσφορικός Fe



Ο Fe βρίσκεται εγκλωβισμένος σε μία δομή από φυσικά συστατικά

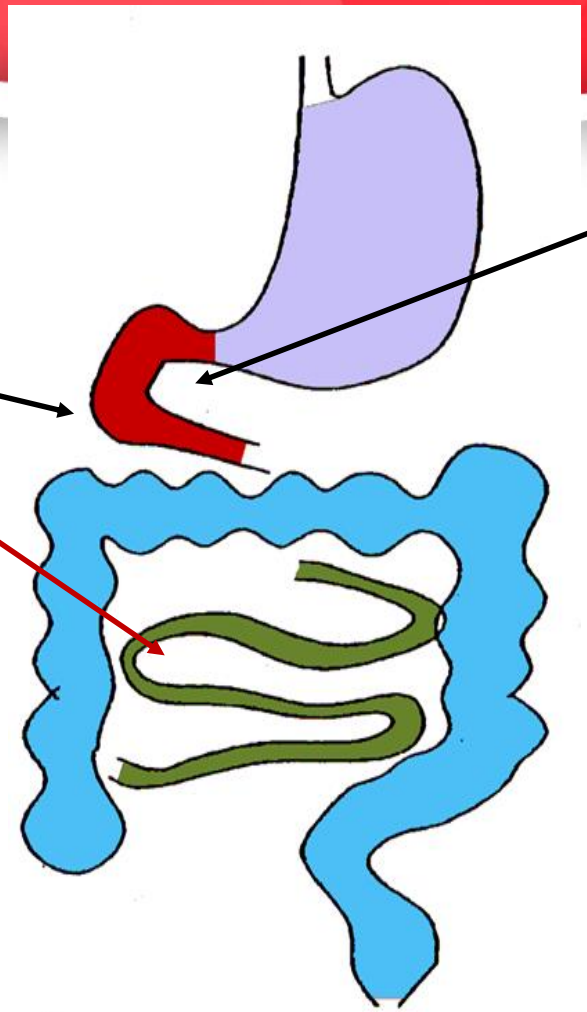
- ✓ **Φωσφολιπίδια**
  Φωσφολιπιδική διπλοστοιβάδα η οποία περιέχει το σίδηρο
  Ο σίδηρος που εμπεριέχεται είναι τρισθενής πυροφωσφορικός
- ✓ **Φωσφορικό ασβέστιο**
  Ενισχύει τους δεσμούς μεταξύ των φωσφολιπιδίων
- ✓ **Εστέρες λιπαρών οξέων με σουκρόζη**
  - Προστατεύουν τη δομή κατά τη διεύλευσή της από το γαστρεντερικό σύστημα
  - Βελτιώνουν την απορρόφηση της

Η δομή προστατεύεται από πατέντα (PCT/1B2013/001659 & PCT/IB2014/001780)

Απορρόφηση σιδήρου

Sucrosomial® Iron

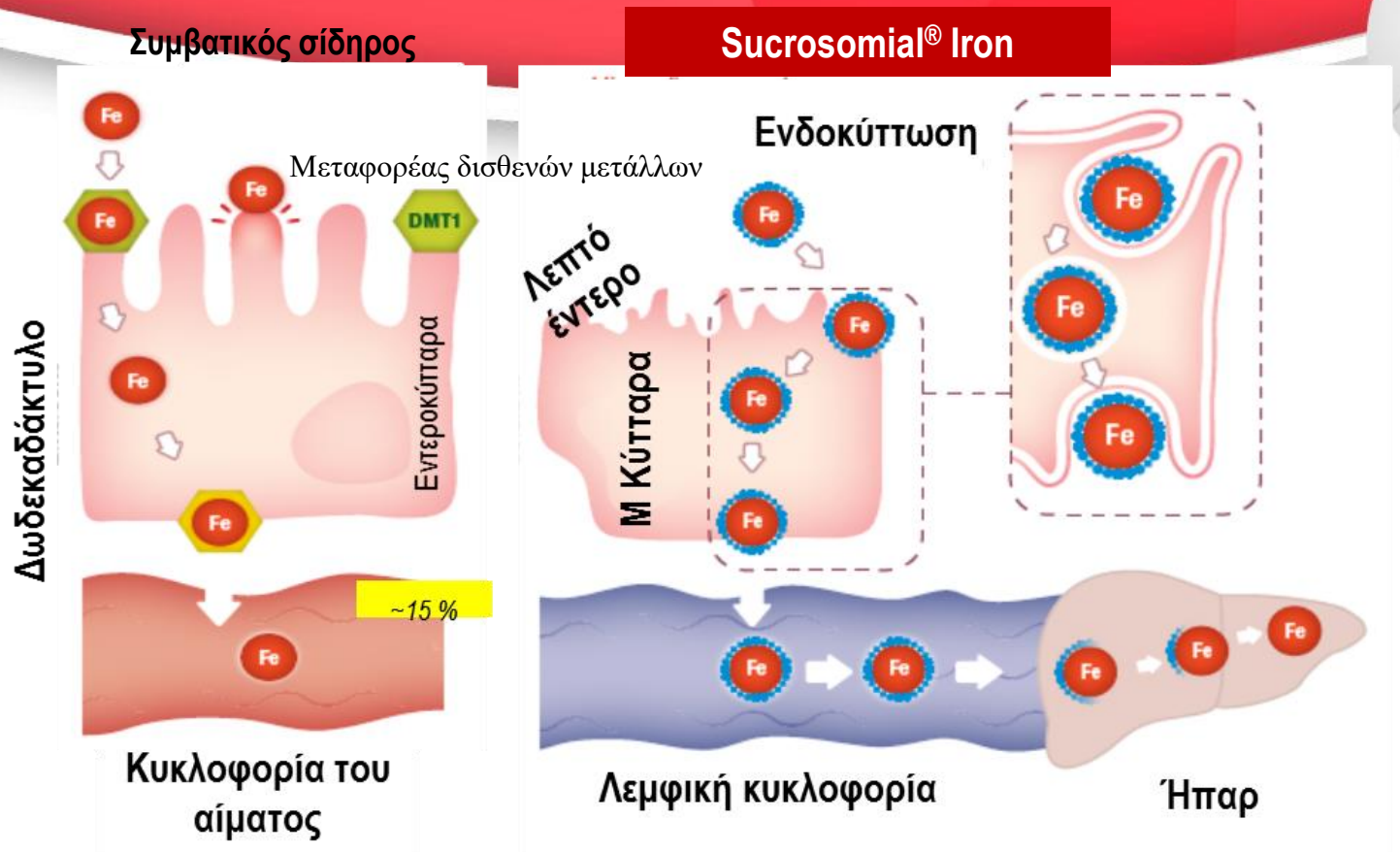
Απορρόφηση συμβατικού σιδήρου



Απορροφάται το 10-20% του χορηγούμενου σιδήρου

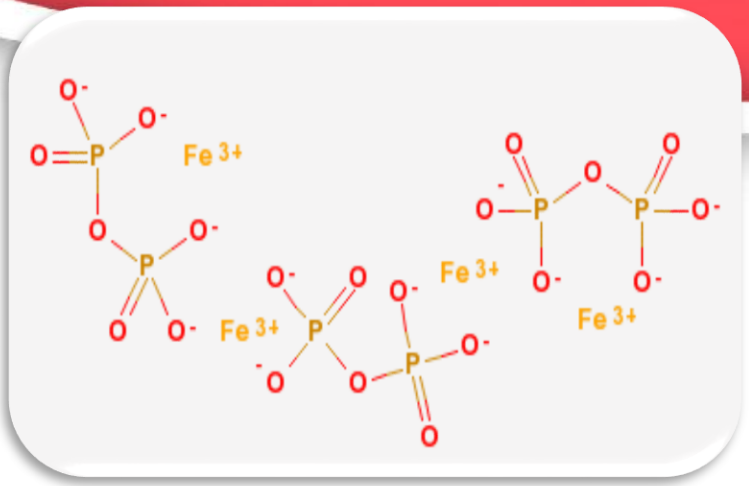
Pisani A. et al Nephrol Dial Transplant,2015;30:645-652

Sucrosomial® Iron: Απορρόφηση

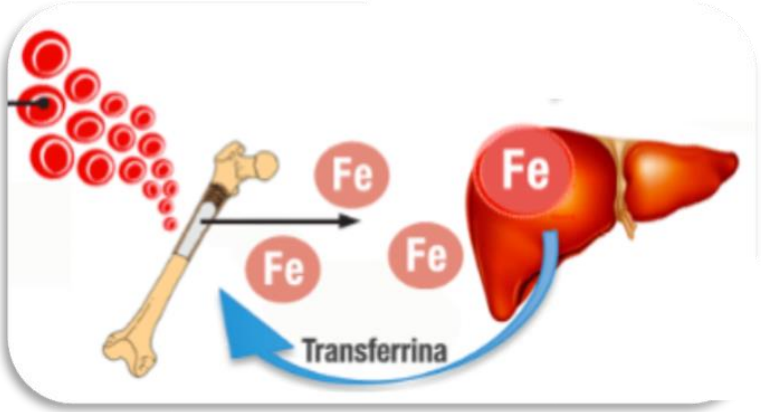


Pisani A. et al Nephrol Dial Transplant,2015;30:645-652

Τρισθενής πυροφωσφορικός σίδηρος

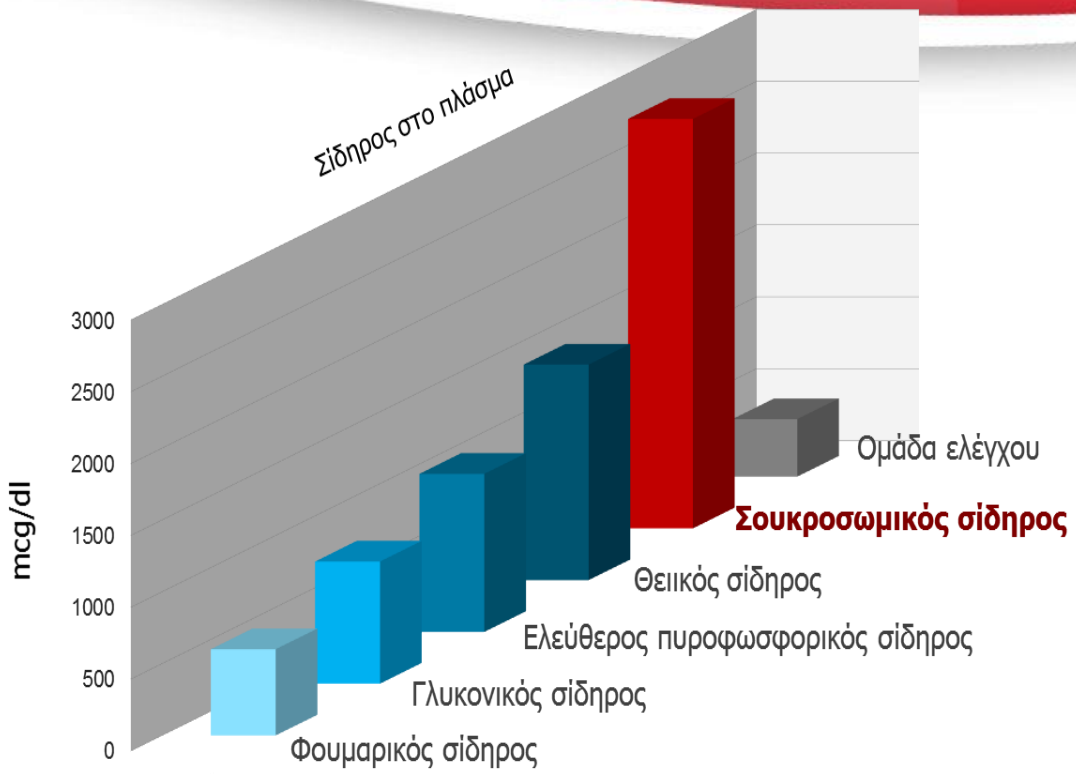


1. Η **πυροφωσφορική ομάδα** έχει υψηλή συγγένεια με την τρανσφερρίνη
2. Η τρανσφερρίνη χρησιμοποιεί τρισθενή σίδηρο



Gupta et al, 1999
Konopka, 1981

Υψηλότερη βιοδιαθεσιμότητα από τα άλατα σιδήρου



+5 vs φουμαρικού σιδήρου

+4,1 vs γλυκονικού σιδήρου

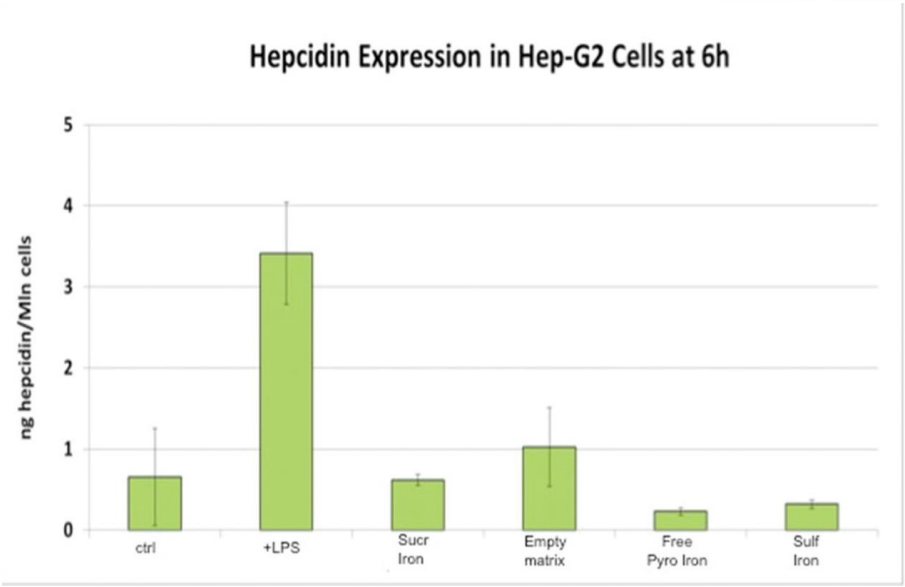
+3,5 vs ελεύθερου πυροφωσφορικού σιδήρου

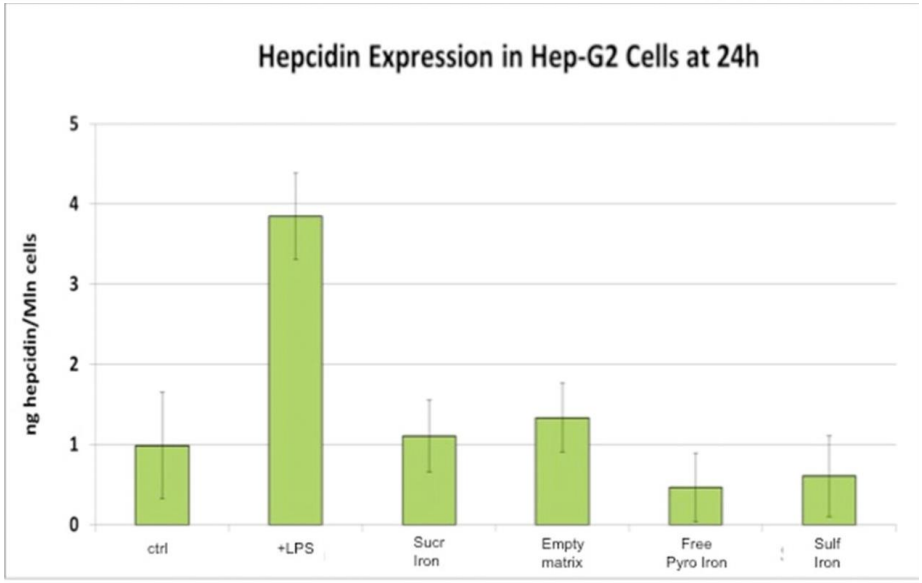
+2,7 vs θειικού σιδήρου

Visciano B et al, G. Ital 1999

blood Volume 126(23):4563-4563 December 3, 2015

Innovative Oral Iron Supplement (Sucrosomial Iron®) Is Able to Downregulate Hepcidin Release during Inflammation: In Vitro Study





Results showed that Sucrosomial Iron® is able to significantly reduce Hepcidin level both 6 and 24 h after treatment in comparison with other iron formulations.

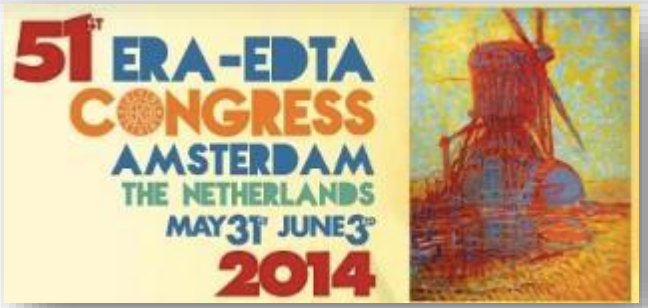
Tarantino G et al. Blood 2015

Liposomial iron for the treatment of iron deficiency anemia in non dialysis Chronic Kidney Disease (CKF) patients: a randomized controlled trial

Bianca Visciano1, Paola Nazzaro1, Elenora Riccio1, Antonio Del Rio2, Giusi Rosaria Mozzillo1, Antonio Pisani1 1Department of Nephrology, University of Naples Federico II, Naples, Italy 2Department of Biochemistry, University of Naples Federico II, Naples, Italy.

Presented as Abstract at 53th National Congress of SIN (Italian Society of Nephrology), 2012

Presented as Abstract at 51st Congress ERA-EDTA (European Renal Association – European Dialysis and Transplant Association) 2014



AIM

To evaluate the efficacy of treatment with liposomial iron, compared to intravenous iron (IV), in the anemic patient with CKD not on dialysis in the presence of an iron deficiency.

Nephrol Dial Transplant (2015) 30: 645–652
doi: 10.1093/ndt/gfu357
Advance Access publication 13 November 2014

Effect of oral liposomal iron versus intravenous iron for treatment of iron deficiency anaemia in CKD patients: a randomized trial

Antonio Pisani[1,†], Eleonora Riccio[1,†], Massimo Sabbatini[1], Michele Andreucci[2], Antonio Del Rio[3] and Bianca Visciano[1]

[1]Department of Public Health, University Federico II of Naples, Naples, Italy, [2]Department of Nephrology, Magna Graecia University, Catanzaro, Italy and [3]Department of Biochemistry and Medical Technology, University Federico II of Naples, Naples, Italy

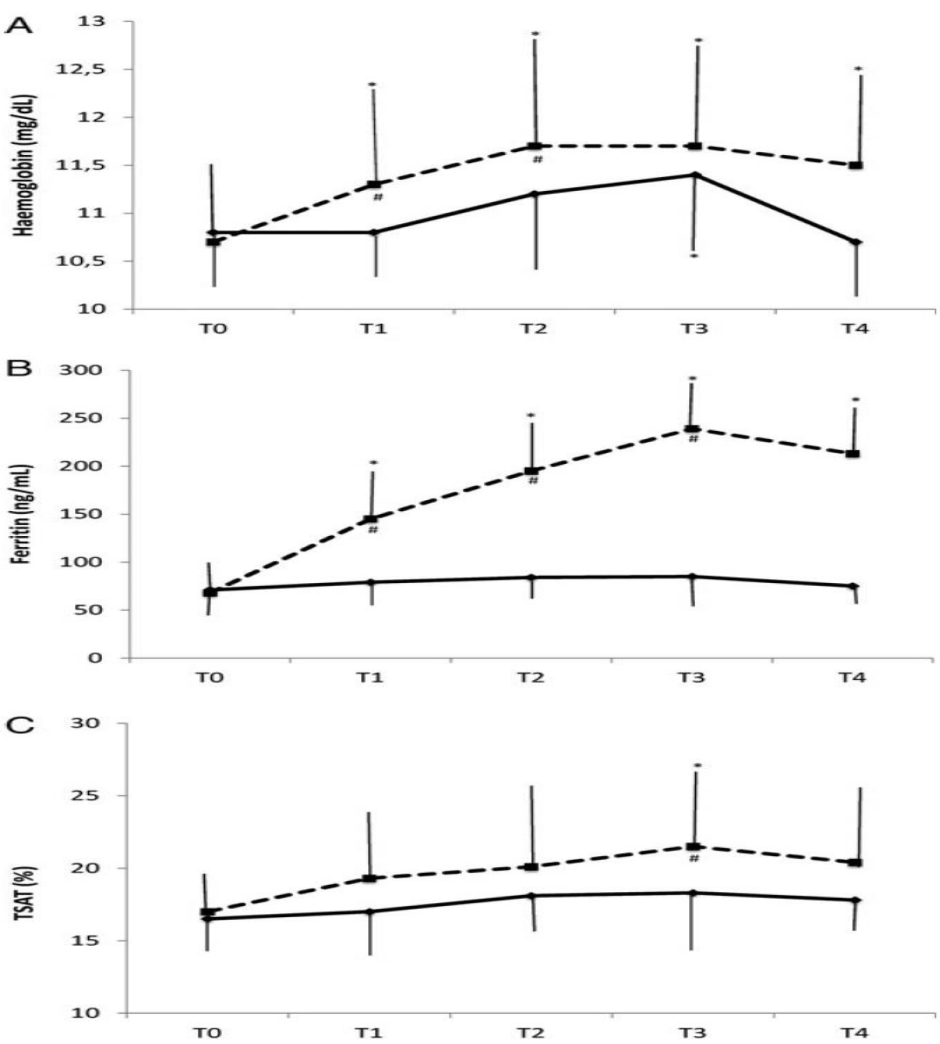
Σουκροσωμικός σίδηρος έναντι ενδοφλέβιου σιδήρου σε ασθενείς με ΧΝΝ (Ι)

- ✓ Τυχαιοποιημένη μελέτη σε 99 ασθενείς με χρόνια νεφρική νόσο (υπολογιζόμενος ρυθμός σπειραματικής διήθησης < 60 ml/min/1,73m^2) και σιδηροπενική αναιμία που δεν υποβάλλονταν σε αιμοκάθαρση
- ✓ Sideral Forte 30 mg ημερησίως από του στόματος ή γλυκονικός σίδηρος σε 8 ενδοφλέβιες εβδομαδιαίες εγχύσεις των 125 mg (συνολική δόση 1.000 mg)
- ✓ Διάρκεια θεραπείας 3 μήνες

Nephrol Dial Transplant 2015;30:645-52

Σουκροσωμικός σίδηρος έναντι ενδοφλέβιου σιδήρου σε ασθενείς με ΧΝΝ (Ι)

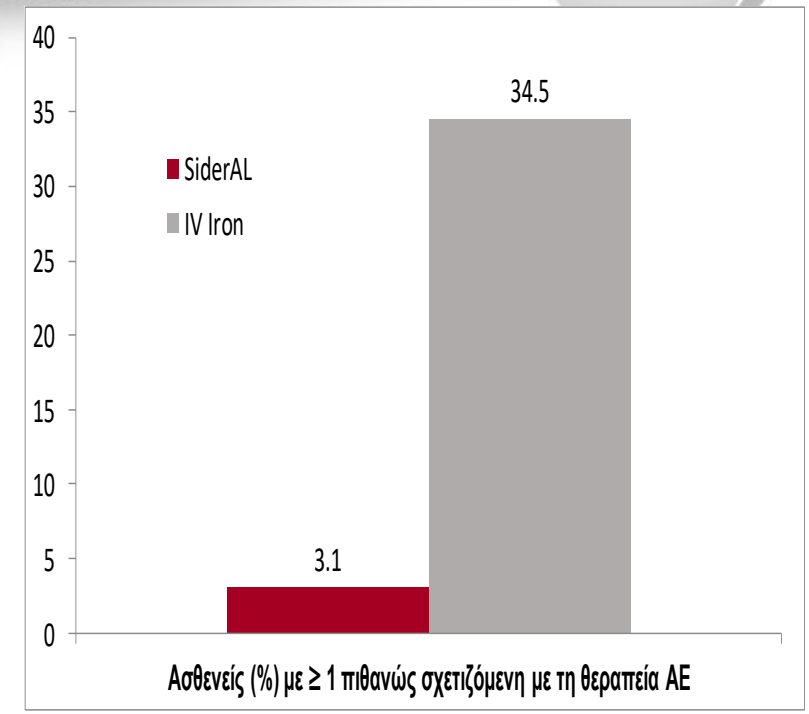
- Ο iv σίδηρος παρουσίασε ταχύτερη αύξηση της Hb
- Μετά από 3 μήνες θεραπεία παρατηρήθηκε παρόμοια
  - αύξηση της Hb
  - Συμμόρφωση στη θεραπεία (96,2% iv vs 95,8% po)



Nephrol Dial Transplant 2015;30:645-52

Σουκροσωμικός σίδηρος έναντι ενδοφλέβιου σιδήρου σε ασθενείς με ΧΝΝ (Ι)

Οι ασθενείς που έλαβαν σουκροσωμικό σίδηρο παρουσίασαν σημαντικά λιγότερες ανεπιθύμητες ενέργειες (3,1 και 34,5% αντίστοιχα, p < 0,001)



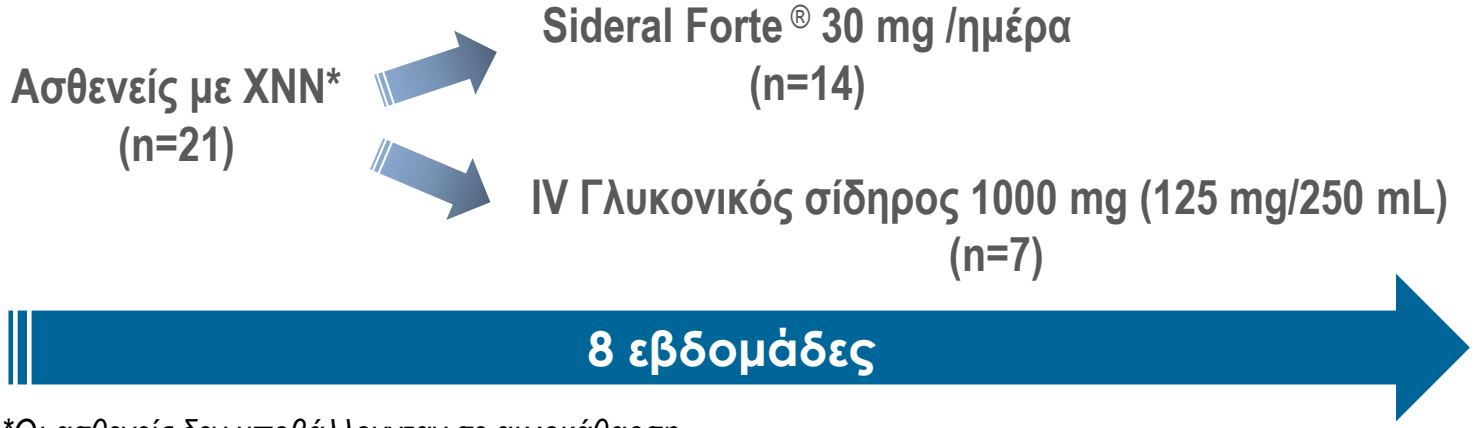
Adverse event, *n* (%)	Group OS	Group IV
Constipation	3 (4.5)	1 (3)
Diarrhoea	3 (4.5)	3 (9.1)
Nausea	2 (3)	2 (6.1)
Infusion site reaction	0 (0)	4 (12.1)
Oedema peripheral	0 (0)	2 (6.1)
Headache	2 (3)	6 (18.2)
Hypotension	0 (0)	4 (12.1)

Nephrol Dial Transplant 2015;30:645-52

Σουκροσωμικός σίδηρος έναντι ενδοφλέβιου σιδήρου σε ασθενείς με ΧΝΝ (II)

Σχεδιασμός μελέτης

Προοπτική, τυχαιοποιημένη μελέτη φάσης IV – 1 ερευνητικό κέντρο



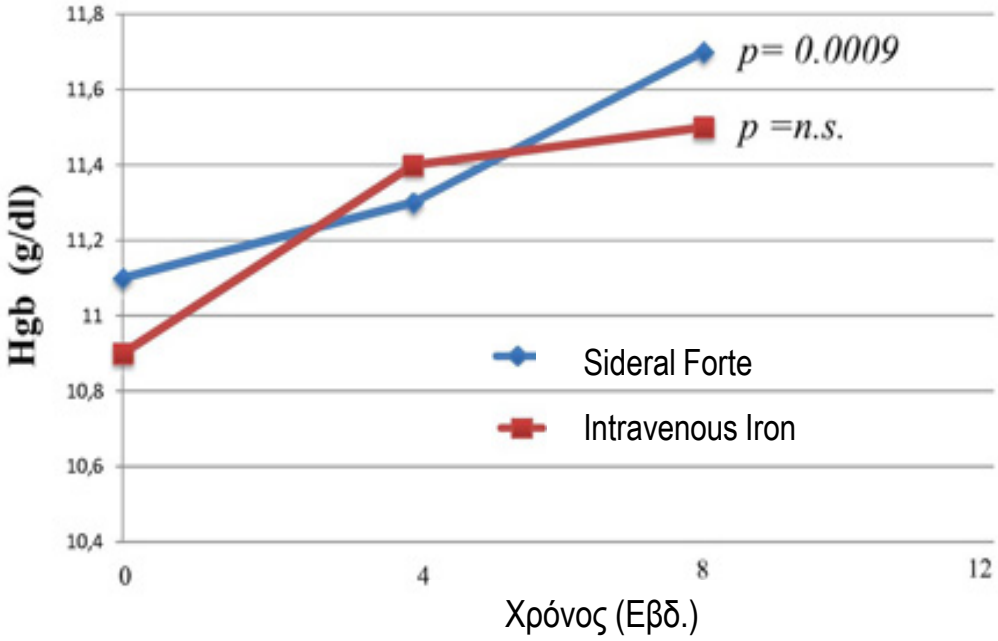
Οι ασθενείς δεν υποβάλλονγταν σε αιμοκάθαρση

- **Κύριο καταληκτικό σημείο**: αύξηση Hb από τα αρχικά επίπεδα
- **Δευτερεύοντα καταληκτικά σημεία** : μείωση της δόσης της EPO κατά ≥ 25 % (ασθενείς υπό αγωγή με EPO) – αύξηση φερριτίνης ορού από αρχικά επίπεδα (> 100 ng/mL)

Visciano B. et al, G Ital Nephrol 2013;30 (5) ISSN 1724-5590

Σουκροσωμικός σίδηρος έναντι ενδοφλέβιου σιδήρου σε ασθενείς με ΧΝΝ (ΙΙ)

- Στατιστικά σημαντική αύξηση της Hb έναντι των αρχικών
- Συγκρίσιμη αποτελεσματικότητα στην αύξηση της Hb με αυτήν του ενδοφλεβίως χορηγούμενου γλυκονικού σιδήρου



Visciano B. et al, G Ital Nephrol 2013;30 (5) ISSN 1724-5590

CONCLUSIONS

In anemic patients suffering from CKF, not on dialysis and with iron deficiency, **the treatment with Liposomial iron produces a significant increase of Hb levels after 8 weeks compared to iv iron**, but not iron repletion.

USE OF LIPOSOMAL IRON IN CKD (CHRONIC KIDNEY DISEASE) PATIENTS NOT TOLERATING FERROUS SULFATE IN CONSERVATIVE THERAPY

Dr. Remo Luciani, Department of Nephrology, Rummo Hospital of Benevento

Presented at the 52° Congress of SIN (Italian Society of Nephrology) 2011 in Genova (Itally)

Σουκροσωμικός σίδηρος έναντι θειικού σιδήρου σε ασθενείς με ΧΝΝ

Σχεδιασμός μελέτης

17 ασθενείς με χρόνια νεφρική νόσο, σιδηροπενική αναιμία και δυσανεξία στο θειϊκό σίδηρο

Ερωτηματολόγιο σχετικά με την ανεκτικότητα του σιδήρου από το πεπτικό

Διακοπή θεραπείας (15 ημέρες wash-out)

Αξιολόγηση αιματολογικών παραμέτρων (Χρόνος 0)

Έλαβαν Sideral® Forte 30mg ημερησίως

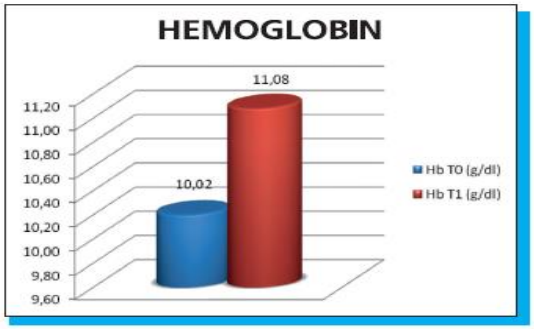
3 μήνες :

- Ερωτηματολόγιο σχετικά με την ανεκτικότητα του σιδήρου από το πεπτικό
- Αξιολόγηση αιματολογικών παραμέτρων (Χρόνος 1)

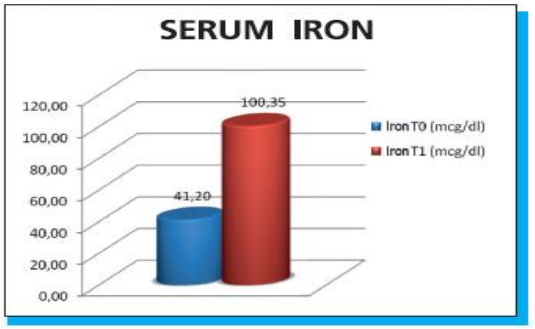
G Ital Nephrol 2011;28(S53):S60-71

Σουκροσωμικός σίδηρος έναντι θειικού σιδήρου σε ασθενείς με ΧΝΝ

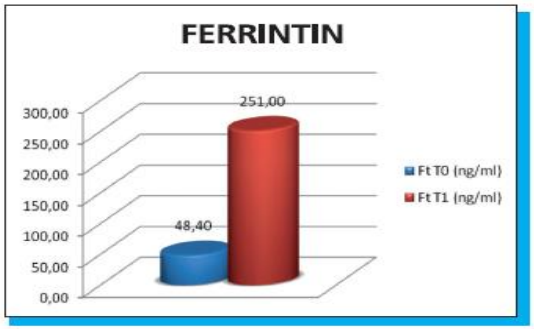
Αποτελέσματα



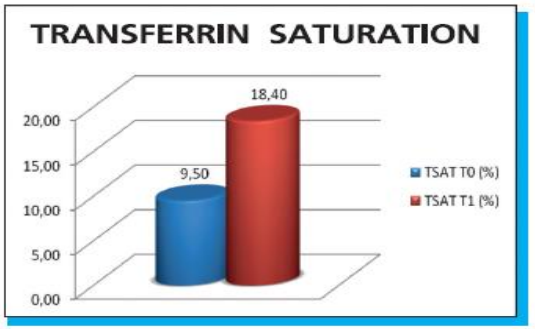
Average increase In Hemoglobin:
+ 1,06 g/dl



Average Increase in Serum Iron
+ 59,15 mcg/dl



Average Increase in Ferritin:
+ 202,6 ng/ml



Average Increase in Transferrin Saturation:
+ 8,9 %

Κανείς ασθενής δεν ανέφερε ανεπιθύμητες ενέργειες από το γαστρεντερικό σύστημα

G Ital Nephrol 2011;28(S53):S60-71

Completed Studies	15
Published Studies	14
Total n. patients treated:	719

Comparative study between Sideral® Forte and intravenous Iron in chronic kidney disease.

Chiara Ralli[1] M.D., Patrizio Imperiali[1] M.D, Elisa Brilli[2] PhD, Germano Tarantino[2*] M.D. and Ennio Duranti[1] M.D.

[1] Nephrology and Dialysis Unit, Ospedale San Donato, Via Pietro Nenni 20, 52100 Arezzo, Italy

[2] Pharmanutra S.p.A., Via delle Lenze 216/b 56122 Pisa, Italy

Presented as Abstract at
55th National Congress of SIN
(Italian Society of Nephrology), 2014

STUDY PROCEDURE

10 anemic patients in HD treated 3 times for 9 months:

3 months with Intravenous iron (iv1) → 3 months with SIDERAL FORTE (1 cps/die) (os) → 3 months with Intravenous iron (iv2)

AIM

To evaluate the effectiveness of treatment with liposomal iron compared to intravenous iron.

RESULTS

Period	Hb (g/dl)	TSAT (%) Sat Fe (%)	Ferritina (mcg/L)	PCR (mg/dl)	Albumina (g/dl)	Epo (UI/sett)	Fe (mg/sett)
IV1							
OS	**10,6** ±1,4	13±6,9	108±103	**0,7** ±0,6	4±0,3	10200±8000	81,2±50
s) IV2	**11,4**±1.1	15±8	102±90	**0,4**±0,3	4,2±0,2	8750±7100	210±0
(Periodo iv2)	**10,1**±1.3	18±12,6	153±198	**0,9**±1,2	3,8±0,3	12200±7200	106±56

RESULTS

SIDERAL FORTE showed a significant increase in terms of Hb concentration and TSAT and a significant decrease regarding CRP values and a weekly dose savings of Erythropoietin (reduction of at least 2000 U/week/PCs) **respect to Intravenous iron**

CONCLUSIONS

SIDERAL FORTE seems to be a valid alternative to intravenous iron therapy.

4TH MEDITERRANEAN MULTIDISCIPLINARY COURSE ON IRON ANEMIA
SUCROSOMIAL® IRON, UPDATE AND RECENT NEW EVIDENCES TO TREAT IRON DEFICIENCY ANEMIA
APRIL 2016 • FRI 29th, SAT 30th
MADRID, SPAIN
POSTER

EFFECT OF ORAL SUCROSOMIAL IRON IN CKD PATIENTS WITH ANEMIA

Ioannis Griveas,
Nephrology Department 417 Veterans Army Administration Hospital (NIMTS), Athens. Greece
Private Dialysis Unit "Nefroiatriki" , Athens, Greece
Private Renal Clinic "Athens-nephrology", Athens, Greece

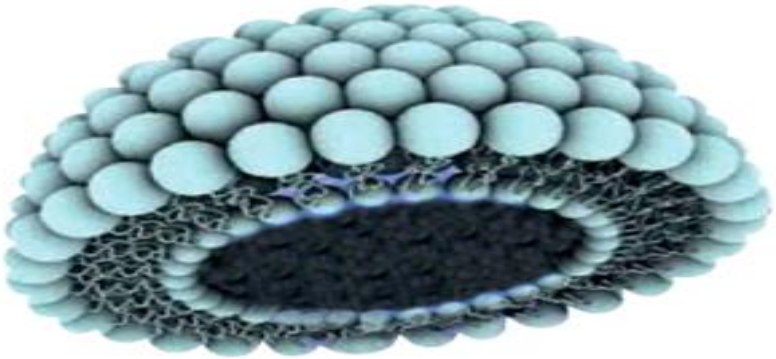
Backround: Anemia is a common manifestation in patients with Chronic Kidney Disease (CKD) and is linked with iron deficiency. The optimum route of administration of iron is controversial in this group of patients since oral administration is easier, safer and less expensive but may be linked to gastrointestinal side effects and suboptimal iron absorption. Sucrosomial iron is a new iron formulation in a phospholipid membrane with reported high bioavailability, low incidence of side effects and satisfactory tolerated.

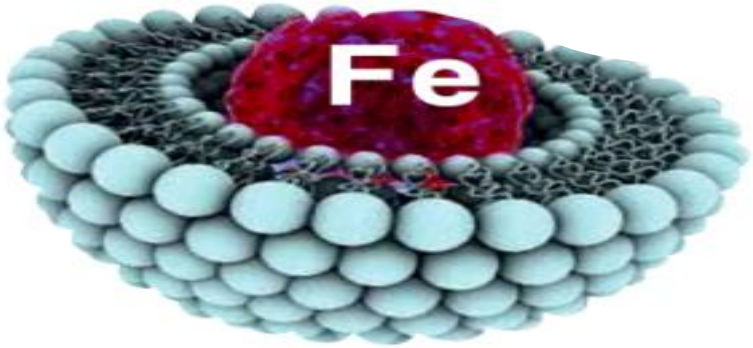
Objectives: The purpose of this study was to investigate the efficacy and tolerability of oral sucrosomial iron in CKD patients with anemia.

Methods: 10 patients with CKD stage 3-5 (e GFR <60 mils/min, range: 12-48) and anemia (Hb<12 gr/dl, ferritin<200 ng/ml) were enrolled in our study. During the 6 months study period, all of the patients had stable renal function, did not need to be transfused or admitted to the hospital for any reason and received oral sucrosomial iron (sideral) once daily. Hematological profile and renal function were recorded at the beginning of the study, 3 months later and in the end of the study protocol. The primary efficacy end points of the study included the change in Hb values from baseline to end of treatment. Adverse effects and compliance data were reported from the day of initial treatment to the end of treatment. Data were analysed using t-test (SPSS).

Results: Hemoglobin levels were 9.82+/-2 g/dl at the beginning of the study and ended to be 10.36+/-0.97 which represented a 5,5% increase (p=NS). At the same time Hct levels increased from 31.4+/-4.92% at the beginning of the protocol to 32.28+/-3.05 in the end (increase 3.12%, p=NS). Ferritin levels which is one index of iron stores also increased from 91.9+/-75.74 to 129.28+/-177.05 (increase 40,67%, p=NS). Oral iron was well tolerated and no significant adverse effects were recorded.

Conclusions: Oral sucrosomial iron seems to be a safe and efficacious alternative in managing CKD patients with anemia. Despite the small amount of patients in our study protocol, the low rate of adverse events with sucrosomial iron and its practicality suggest that this formulation has all the potential to be the first step to correct anemia in stable CKD patients. Further larger studies are needed to investigate iron sucrosomial effects in complicated CKD patients and help scientific community to reach solid conclusions.





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- 10 patients with CKD stage 3-5 (e GFR <60 mils/min, range: 12-48) and anemia (Hb<12 gr/dl, ferritin<200 ng/ml) were enrolled in our study.
- During the 6 months study period, all of the patients had stable renal function, did not need to be transfused or admitted to the hospital for any reason and received oral sucrosomial iron (sideral) once daily.
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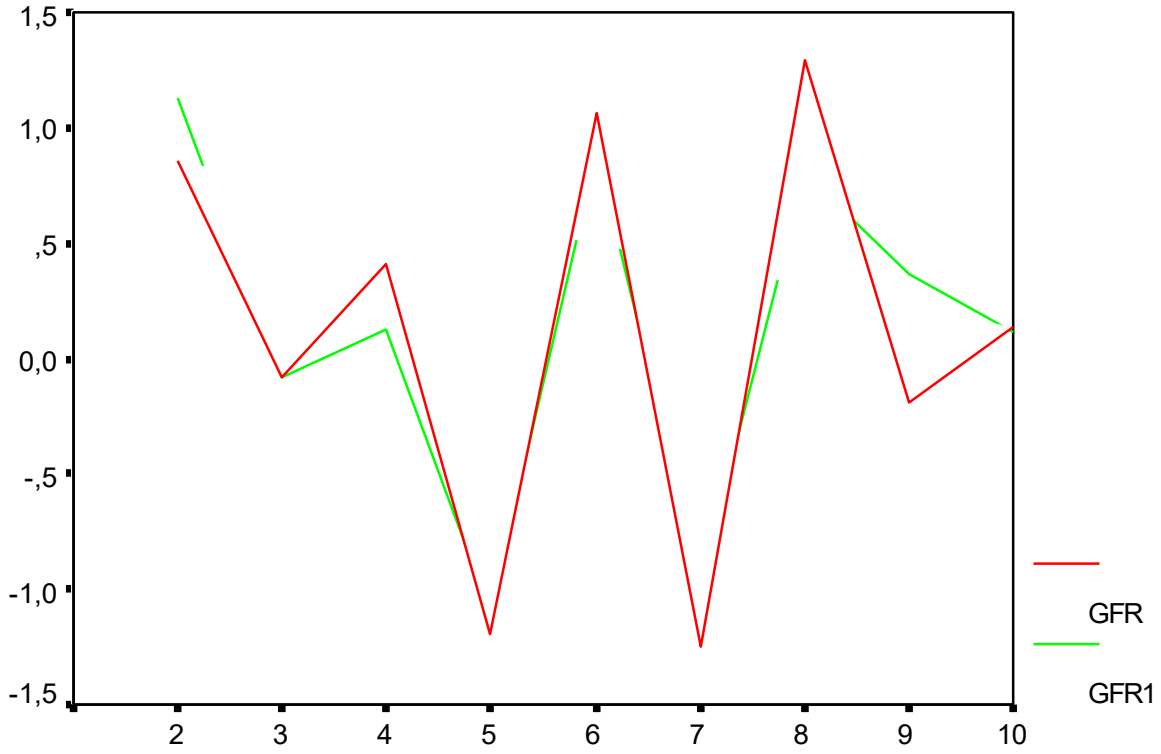
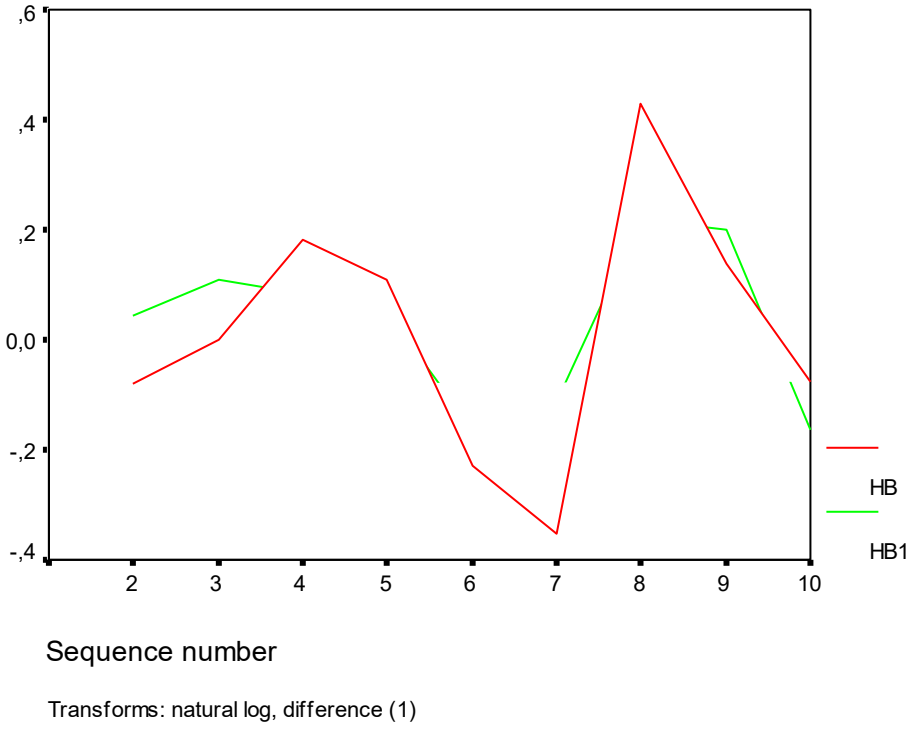
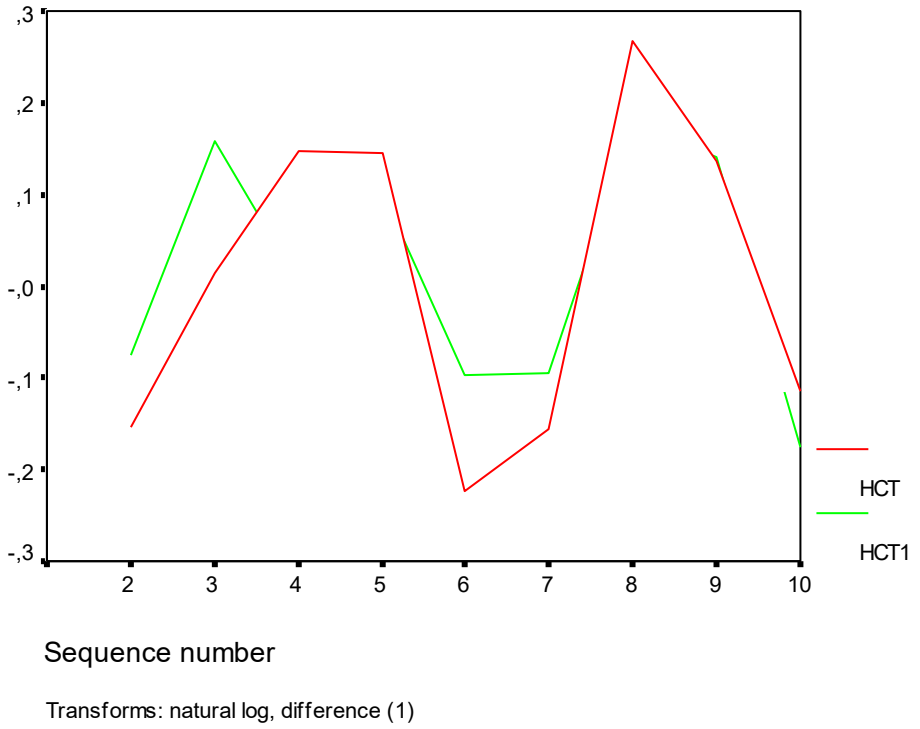

1,5
1,0
,5
0,0
-,5
-1,0
-1,5
2
3
4
5
6
7
8
9
10
GFR
GFR1
Sequence number
Transforms: natural log, difference (1)

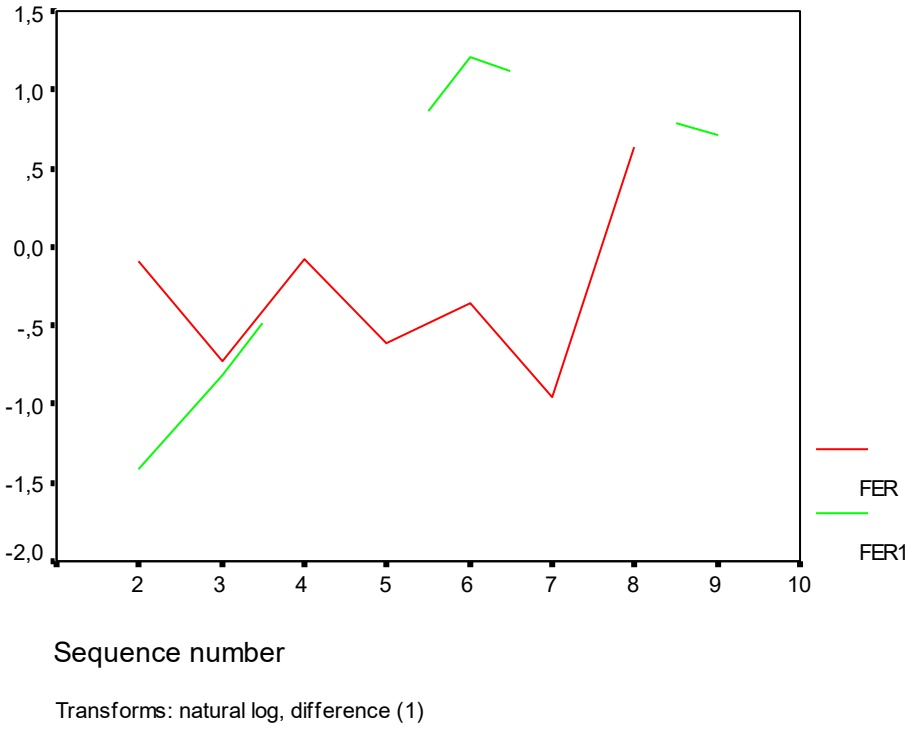
Hemoglobin levels were 9.82+/-2 g/dl at the beginning of the study and ended to be 10.36+/-0.97 which represented a 5,5% increase (p=NS).



Hct levels increased from 31.4+/-4.92% at the beginning of the protocol to 32.28+/-3.05 in the end (increase 3.12%, p=NS).



Ferritin levels which is one index of iron stores also increased from 91.9+/-75.74 to 129.28+/-177.05 (increase 40,67%, p=NS).



Oral iron was well tolerated and no significant adverse effects were recorded.

4TH MEDITERRANEAN MULTIDISCIPLINARY COURSE ON IRON ANEMIA
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APRIL 2016 • FRI 29th, SAT 30th
MADRID, SPAIN
P-018

CLINICAL EXPERIENCE WITH ORAL SUCROSOMIAL IRON IN A SEVERE ANEMIC PATIENT WITH CHRONIC KIDNEY DISEASE

Ioannis Griveas,
Nephrology Department 417 Veterans Army Administration Hospital (NIMTS), Athens. Greece
Private Dialysis Unit "Nefroiatriki" , Athens, Greece
Private Renal Clinic "Athens-nephrology", Athens, Greece

Back round: Iron deficiency is common in patients with Chronic Kidney Disease (CKD). Factors predisposing to the above fact include, among others, increased blood losses, decreased duodenal iron absorption or impaired iron release from tissue stores. Gastrointestinal (GI) causes of increased blood losses are quite common and in many cases difficult to manipulate due to the location of GI tract that bleeds.
Objective: We present the case of a woman with CKD and recurrent GI bleeding with severe and refractory anemia that against all odds remained stable receiving oral sucrosomial iron.

Case history: An 83 year old woman with CKD (e GFR: 35 mils/min) presented with severe anemia (Hb 8.1 gr/dl, Hct 25) and low levels of ferritin (10) despite long stand therapy with oral ferrous iron preparations. Further investigation of anemia and intention to treat attitude guided her to admission at hospital. During her stay she underwent GI endoscopy that revealed gastritis, tubular adenoma of rectum, polypectomy at stomach dome was taken place along with cautery of angiodysplasia in the 2nd fate of duodenum. Patient was transfused and discharged from the hospital with Hct 30.5 and Hb 9.7 gr/dl. Three months later the above patient had Hct 28.7, Hb 9.5 gr/dl with ferritin levels of 177 and started to receive oral sucrosomial iron.

Results: For the next following months patient appeared to have Hct 28, Hb 9.4 gr/dl (3 months with oral sucrosomial iron therapy) and Hct 29.3, Hb 9.8 gr/dl (6 months with oral sucrosomial iron therapy) with ferritin levels 144. During the above period, our patient did not receive i.v Fe infusions, erythropoietin (EPO) or transfusions. Using oral iron treatment had good gastric tolerability. Her clinical condition remained stable, no side effects were reported, she felt well by herself and did not need to be admitted again.

Conclusions: For those of us we have experience of treating old CKD patients with anemia and GI angiodyspasia, it is clear that "achieving" to hold the patients' anaemia without admissions to hospital, transfusions or EPO administration is a major accomplishment. Angiodysplasia may cause slow releasing bleeding in a permanent basis. We showed that using oral sucrosomial iron in a CKD patient with severe anemia that had also other contributing factors as causes of that anemia, may be an effective and reliable option.

P-021

EFFICACY, TOLERANCE AND ADHERENCE TO TREATMENT WITH SUCROSOMIAL® IRON IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGES 3-4 AND IRON DEFICIENCY

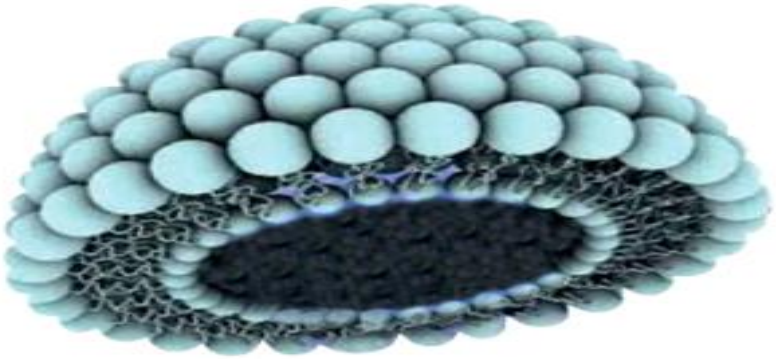
OBJECTIVE:

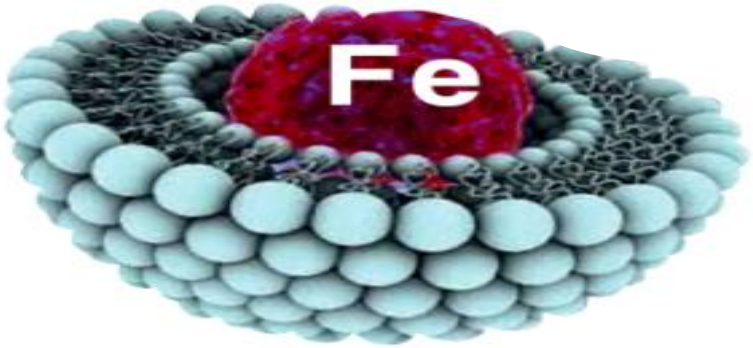
To evaluate the efficacy, tolerance and adherence to treatment with Sucrosomial® Iron in CKD stages 3-4 patients with iron deficiency associated with gastrointestinal tract diseases.

METHOD:

Open-label, single-arm, single-center, prospective, 6 months study, in 24 patients with ND-CKD and iron deficiency treated with Sucrosomial® Iron (Fisiogen Ferro Forte®: 30 mg/day). All patients included in the study had been treated previously, for at least 3 months, with other oral iron preparations and had shown lack of response or bad tolerance. 2 patients left the study since they requested to be treated with medication financed by the National Health Insurance. Therapeutic adherence was estimated by the SMAQ questionnaire. Values are expressed as means (SD: standard deviation) or percentages.

Variables	Baseline	3 months	6 months	p
Ferritin mcg/l	34,0 (22,6)	62,4 (33,6)	75,1 (51,2)	<0,01
Transferrin saturation (%)	13,8 (3,8)	21,5 (3,4)	26,1 (7,3)	<0,05
Hemoglobin (g/dl)	11,1 (0,8)	12,2 (0,9)	12,8 (1,2)	<0,01
Creatinine (mg/dl)	1,9 (0,9)	1,7 (0,6)	1,7 (0,6)	NS
GFR (MDRD IV) ml/min	38,1 (12,1)	39,7 (9,7)	39,2 (8,7)	NS





Oral sucrosomial iron seems to be a safe and efficacious alternative in managing CKD patients with anemia.

The low rate of adverse events with sucrosomial iron and its practicality suggest that this formulation has all the potential to be the first step to correct anemia in stable CKD patients.

Further larger studies are needed to investigate iron sucrosomial effects in complicated CKD patients and help scientific community to reach solid conclusions.