ORDINE DEI MEDICI CHIRURGHI
E DEGLI ODONTOIATRI
DELLA PROVINCIA DI PARMA

LA CORREZIONE DELL'ANEMIA NEL PAZIENTE CON NEFROPATIA CRONICA

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• KEYPOINTS

→ Diagnosis and evaluation of anemia in CKD

→ Use of iron to treat anemia in CKD

→ Use of ESAs and other agents

→ Red cell transfusion

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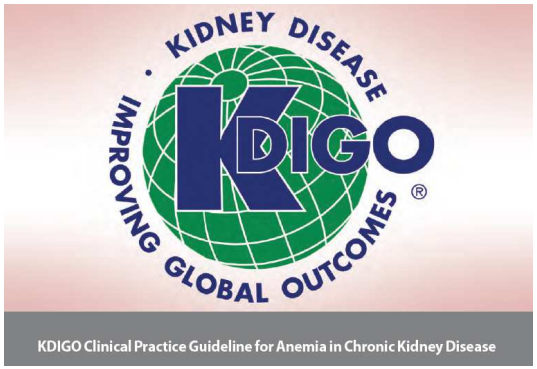


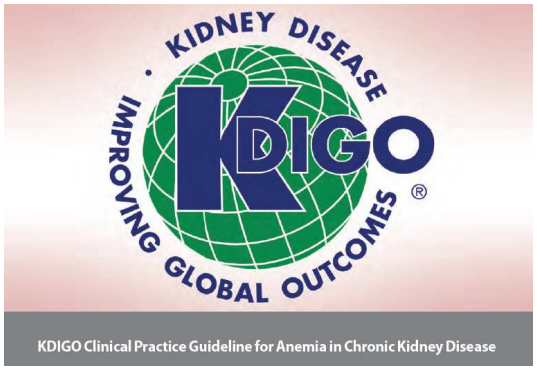
http://www.kidney-international.org

ANEMIA IN CKD: ?

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*)

Diagnose anemia in children with CKD if Hb concentration is <11.0 g/dl (<110 g/l) in children 0.5–5 years, <11.5 g/dl (115 g/l) in children 5–12 years, and <12.0 g/dl (120 g/l) in children 12–15 years. *(Not Graded)*

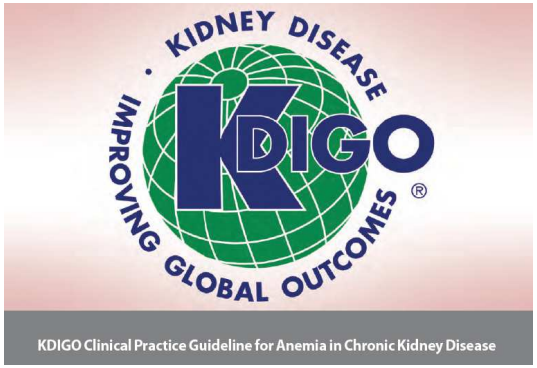
KDIGO Guidelines, Kidney Int 2012



ANEMIA IN CKD: DIAGNOSIS

- Complete blood count (CBC), which should include Hb concentration, red cell indices, white blood cell count and differential, and platelet count
- Absolute reticulocyte count
- Serum ferritin level
- Serum transferrin saturation (TSAT)
- Serum vitamin B_{12} and folate levels

KDIGO Guidelines, Kidney Int 2012



http://www.kidney-international.org

DIAGNOSIS: WHEN?

For CKD patients without anemia measure Hb concentration when clinically indicated and

- at least annually in patients with CKD 3
- at least twice per year in patients with CKD 4–5ND
- at least every 3 months in patients with CKD 5HD and CKD 5PD

For CKD patients with anemia not being treated with an ESA

measure Hb concentration when clinically indicated and

- at least every 3 months in patients with CKD 3–5ND and CKD 5PD
- at least monthly in patients with CKD 5HD

KDIGO Guidelines, Kidney Int 2012

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- **Use of iron to treat anemia in CKD**
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IRON DIAGNOSTIC TESTS

TSAT – TRANSFERRIN SATURATION (%)
(serum iron x 100) / total iron binding capacity)

FERRITIN (ng/mL or µg/L)

- **Evaluate iron status at least every 3 months during ESA therapy, including the decision to start or continue iron therapy**

- **Test iron status more frequently when initiating or increasing ESA dose, when there is blood loss, when monitoring response after a course of IV iron, and in other circumstances where iron stores may become depleted**

why?

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)*

KDIGO Guidelines, Kidney Int 2012

Adult CKD patients with anemia not on iron or ESA therapy

Trial of IV iron (or in CKD-ND patients, alternatively, a 1–3 month trial of oral iron therapy), if:

- **an increase in Hb concentration without starting ESA treatment is desired (symptoms, avoidance of transfusion)**

and

- ***TSAT is ≤ 30% and ferritin is ≤ 500 ng/ml***

KDIGO Guidelines, Kidney Int 2012

Adult CKD patients on ESA therapy who are not receiving iron supplementation

Trial of IV iron (or in CKD-ND patients, alternatively, a 1–3 month trial of oral iron therapy), if:

- **an increase in Hb concentration or a decrease in ESA dose is desired [according ESA recommendations]**

and

- ***TSAT is ≤ 30% and ferritin is ≤ 500 ng/ml***

KDIGO Guidelines, Kidney Int 2012

“Blocked” iron

Iron depletion → ***iron supplementation*** → **Before considering ESA**
Before increasing ESA doses

Normal iron → ***iron supplementation*** → **During ESA treatment**

“Blocked” iron:

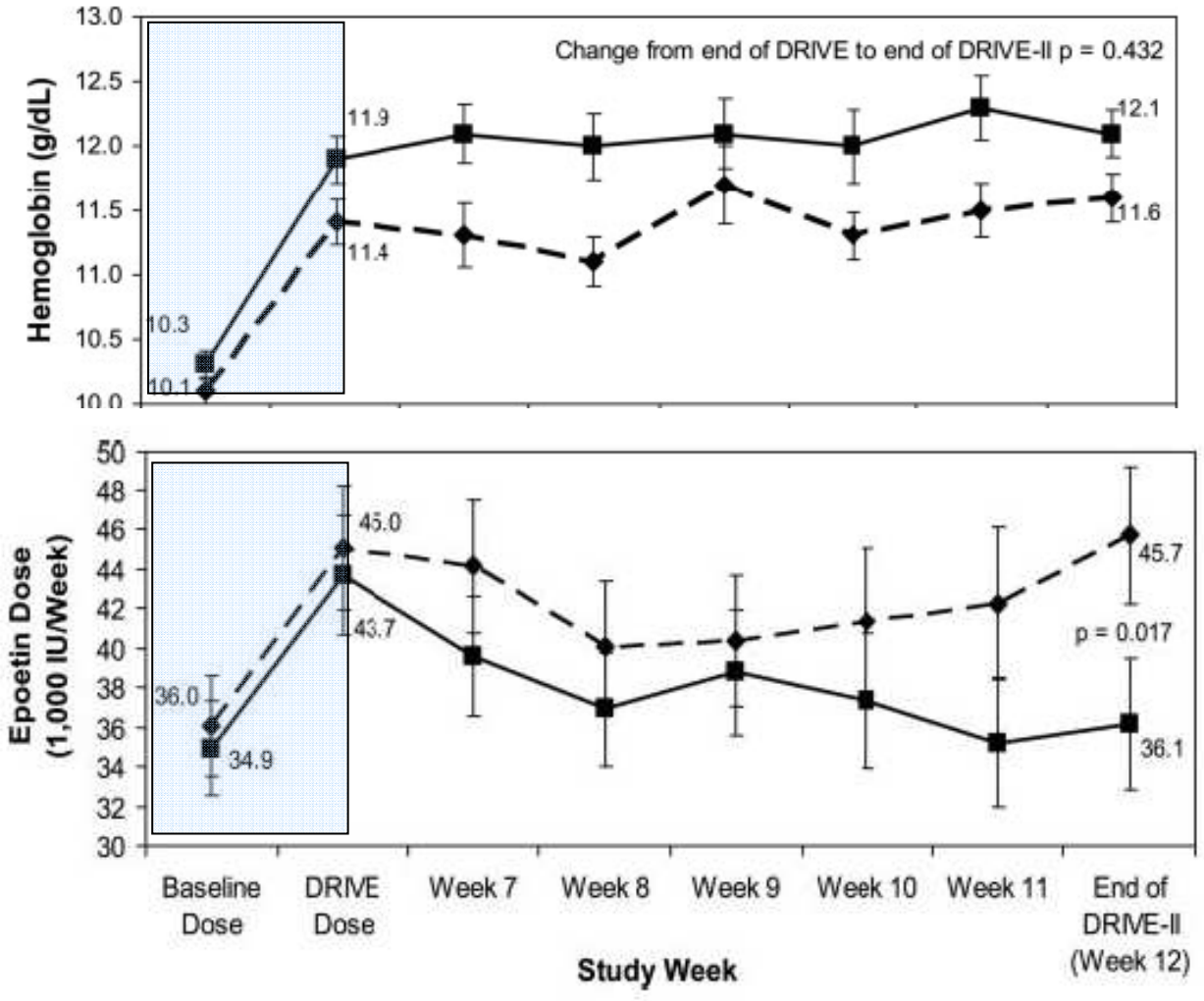
- **Anemia** *(Hb<11 g/dL)*
- **High Ferritin** *(>500 ng/mL)*
- **Low TSAT** *(<20-25%)*

Prevalence: 26.6% → ***iron supplementation?***

Coyne, J Am Soc Nephrol 2007

Ferric Gluconate Reduces Epoetin Requirements in Hemodialysis Patients with Elevated Ferritin

Toros Kapoian,* Neeta B. O'Mara,† Ajay K. Singh,‡ John Moran,§ Adel R. Rizkala,‖ Robert Geronemus,¶ Robert C. Kopelman,** Naomi V. Dahl,‖ and Daniel W. Coyne††



Controlli

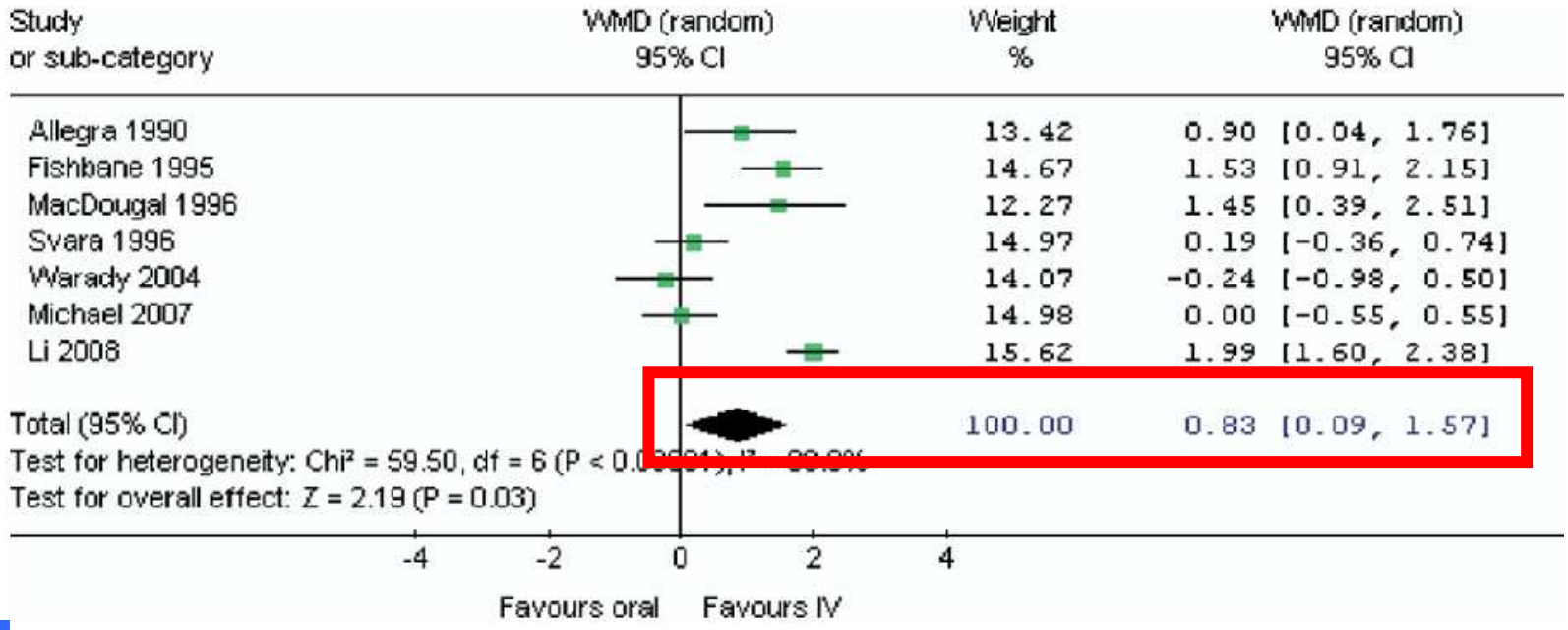
Δ 7527±18,021 IU/wk
***P* 0.003**

Ferro

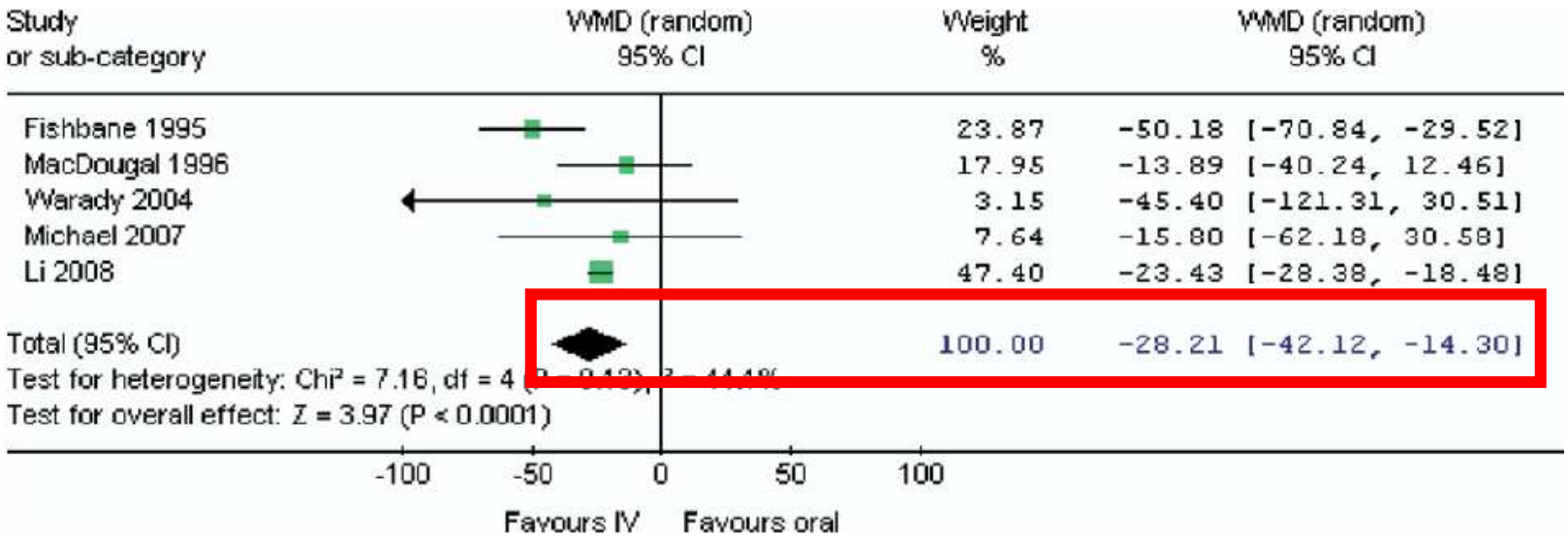
Kapoian, J Am Soc Nephrol 2008

Intravenous *vs* oral iron supplementation

Δ Hb



Δ ESA



Rozen-Zvi, Am J Kidney Dis 2008

• KEYPOINTS

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Step 1

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

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*)

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*).

KDIGO Guidelines, Kidney Int 2012

Step 2 (continue)

Adult CKD, ND patients
Hb ≥ 10.0 g/dL → ***ESA therapy not be initiated (2D)***

Adult CKD, ND patients
Hb < 10.0 g/dL → ***Individualized ESA therapy (rate of fall of Hb, prior response to iron, risk of needing a transfusion, risk ESA related, symptoms) (2C)***

Adult CKD, 5D patients → ***• ESA therapy to avoid having Hb fall < 9.0 g/dL***
• Starting ESA when Hb 9.0 – 10.0 g/dL (2B)
• Individualized therapy

KDIGO Guidelines, Kidney Int 2012

Step 2 (continue)

Anemia trials: lessons for clinicians, politicians, and third-party payers

Kidney International (2010) **77,** 479–480. doi:10.1038/ki.2009.496

Anemia management is getting complex. The evidence that we use to guide anemia therapy is based on observational studies as well as clinical trials. The observational studies have uniformly demonstrated that persons with higher hemoglobin levels enjoy better outcomes, including fewer hospitalizations and longer survival.[1] Randomized controlled trials, on the other hand, paint a different and far more complex picture.

Szczech, Kidney Int 2010

Step 3

In general, we suggest that ESAs not be used to maintain Hb concentration above 11.5 g/dl (115 g/l) in adult patients with CKD. (*2C*)

Individualization of therapy will be necessary as some patients may have improvements in quality of life at Hb concentration above 11.5 g/dl (115 g/l) and will be prepared to accept the risks. (*Not Graded*)

In all adult patients, we recommend that ESAs not be used to intentionally increase the Hb concentration above 13 g/dl (130 g/l). (*1A*)

KDIGO Guidelines, Kidney Int 2012

Step 4

Low Half-Life ESA (iv 10 h, sc 20 h)	Epoetin β (NeoRecormon ®) Epoetin α (Eprex ®)	3 adm / week 1 adm / week (off label)
Long Half-Life ESA (iv 20 h, sc 70 h) **CERA** (continuous erythropoetin receptor activator) (iv 130 h, sc 140 h)	Darbepoetin α (Aranesp ®) Metossi-Polietilenglicole- Epoetin β (Mircera ®)	1 adm / 2 weeks 1 ADM / 4 weeks

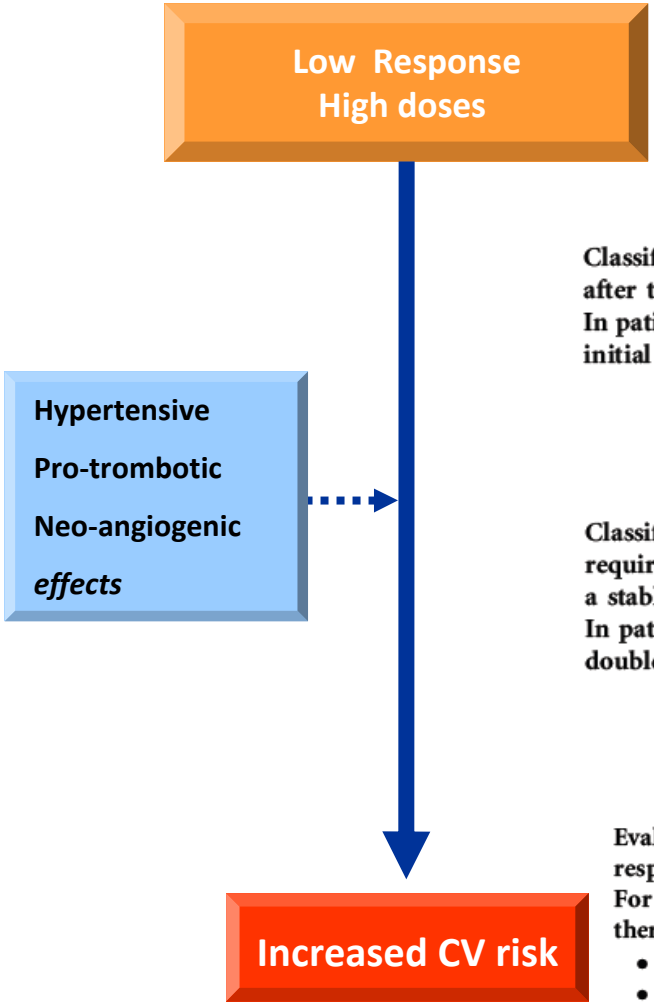
TUTTO IN UNA NOTTE
Revisione Interattiva di Casi Clinici possibili in una Notte di Guardia o non solo

Locatelli, J Nephrol 2008
Mann, Clin Nephrol 2007

Young FADOI

FADOI

Step 5 (continue)



Initial ESA hyporesponsiveness

Classify patients as having ESA hyporesponsiveness if they have no increase in Hb concentration from baseline after the first month of ESA treatment on appropriate weight-based dosing. (*Not Graded*)
In patients with ESA hyporesponsiveness, we suggest avoiding repeated escalations in ESA dose beyond double the initial weight-based dose. (*2D*)

Subsequent ESA hyporesponsiveness

Classify patients as having acquired ESA hyporesponsiveness if after treatment with stable doses of ESA, they require 2 increases in ESA doses up to 50% beyond the dose at which they had been stable in an effort to maintain a stable Hb concentration. (*Not Graded*)
In patients with acquired ESA hyporesponsiveness, we suggest avoiding repeated escalations in ESA dose beyond double the dose at which they had been stable. (*2D*)

Management of poor ESA responsiveness

Evaluate patients with either initial or acquired ESA hyporesponsiveness and treat for specific causes of poor ESA response. (*Not Graded*)
For patients who remain hyporesponsive despite correcting treatable causes, we suggest individualization of therapy, accounting for relative risks and benefits of (*2D*):

- decline in Hb concentration
- continuing ESA, if needed to maintain Hb concentration, with due consideration of the doses required, and
- blood transfusions