

**PREDİYALİZDEN DİYALİZE
DEMİR TEDAVİSİ:
GETİRDİKLERİ VE GÖTÜRDÜKLERİ**

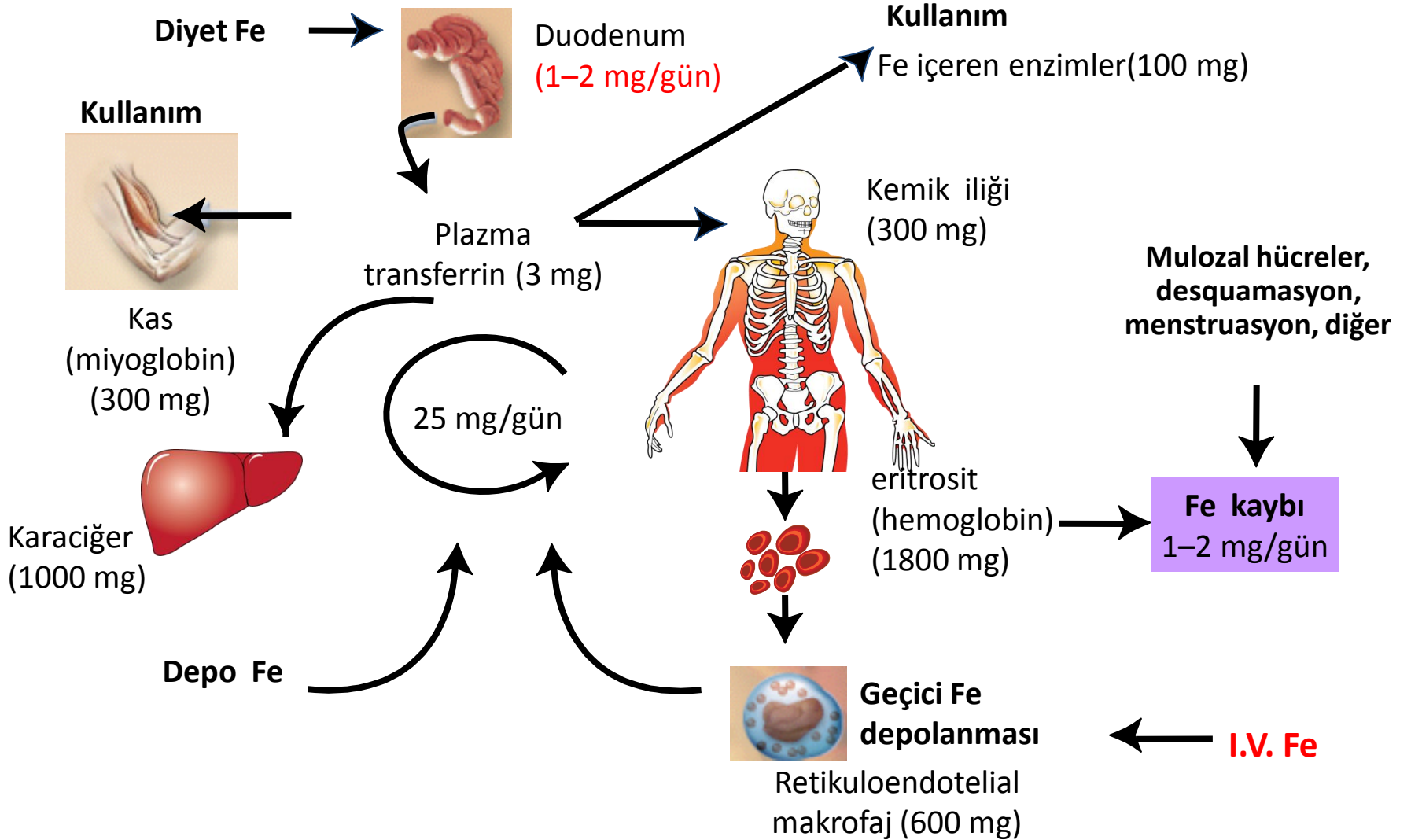
Dr. Aykut SİFİL

Dokuz Eylül Üniversitesi

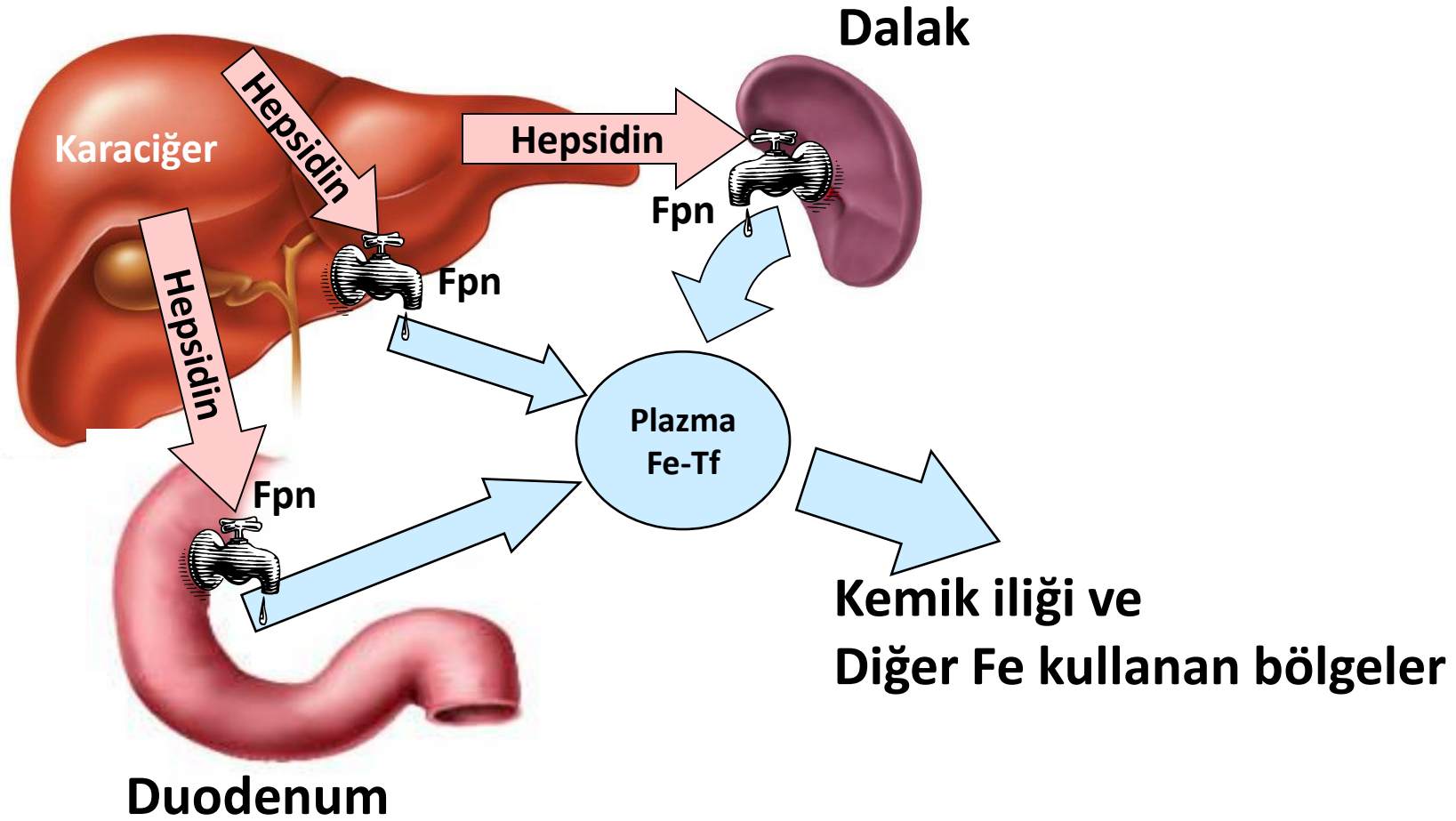
DEMİR

- DNA, RNA ve protein sentezi
- Oksijen taşınması
- Elektron transportu
- Hücre solunumu
- Enzimin yapısında yer alır

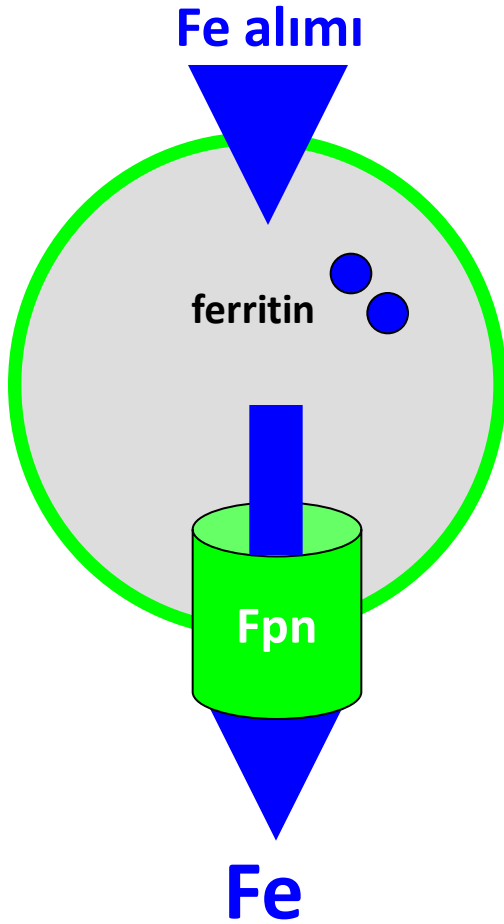
DEMİR DÖNGÜSÜ



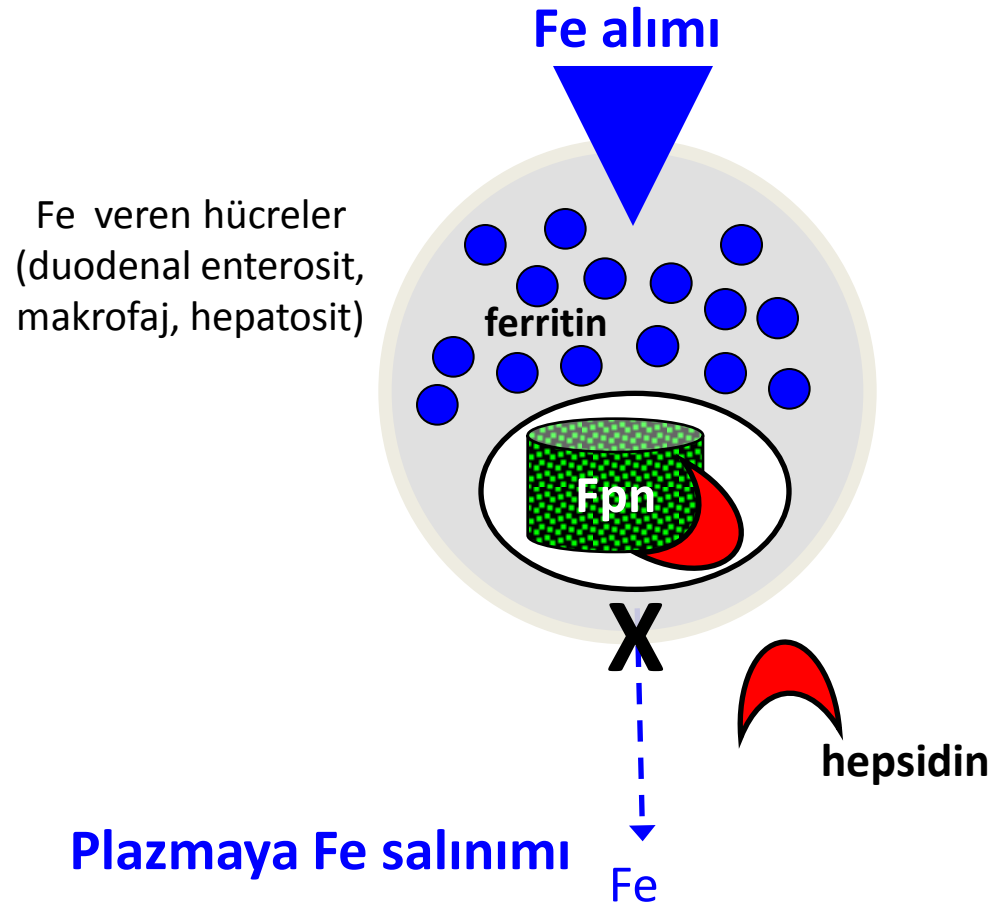
Hepsidin/Fe



Düşük Hepsidin



Yüksek Hepsidin



DEMİR EKSİKLİĞİ

- Alım azlığı (istahsızlık)
- Emilim bozukluğu
- GIS kayıpları (ASA, NSAID)
- Sık kan testleri
- EPO tedavisi (Demir döngüsü artışı)
- Enfeksiyon/Enflamasyon
- Transferrin düşüklüğü

DEMİR EKSİKLİĞİ TANISI

- Serum demir düzeyi
- Serum ferritin düzeyi
- Serum transferrin satürasyonu
- Retikulosit Hb içeriği
- Hipokromik eritrosit yüzdesi
- Soluble transferrin resptör
- Eritrosit zink protoporfirin
- Hepsidin
- Kemik iliği, karaciğer biyopsisi

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KRONİK BÖBREK YETERSİZLİĞİNDE KANSIZLIĞIN DEĞERLENDİRİLMESİ

| | Transferrin satürasyonu (%) | Ferritin (ng/ml) | Hipokromik eritrositler (%) |
|--------------------------------------|-----------------------------|------------------------------|-----------------------------|
| Normal popülasyon Demir eksikliği | < 16 | < 15 | > 10 |
| Kronik böbrek hastalığı | < 20 | < 100 | > 5 |
| Fonksiyonel demir eksikliği | < 25 (ve düşmekte) | > 100 (fakat düşmekte) | > 2.5 |
| İnflamatuar hastalıklar | < 20 (düşmekte) | > 100 (fakat yükselmekte) | |

BÖLÜM

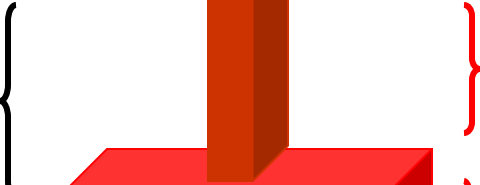
TEST

DOKUDAKİ DEPO



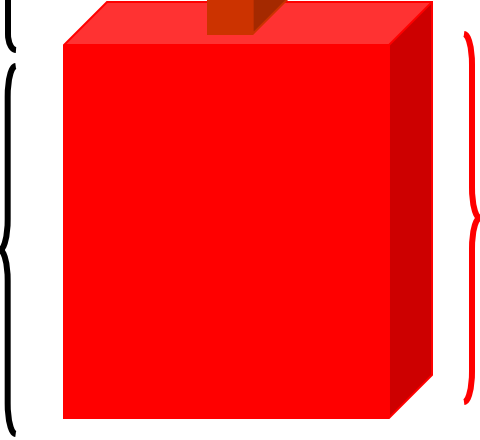
FERRİTİN

EKSRASEL. SIVI



TSAT

ERİTROSİT

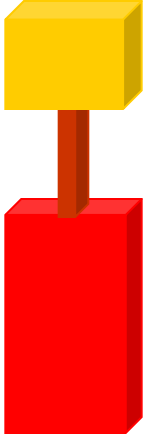


HEMOGLOBİN

DEMİR DAĞILIMI

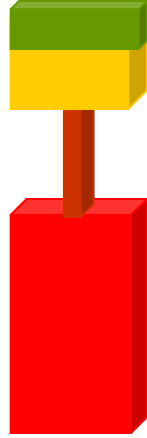
DEMİR EKSİKLİĞİNİN EVRELERİ

NORMAL



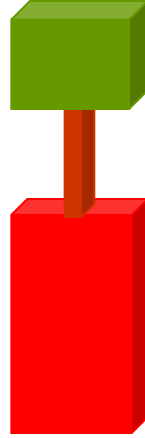
HGB>11
TSAT> %20
FERRİTİN>100

**NEGATİF
DEMİR
DENGESİ**



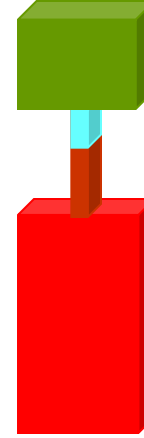
FERRİTİN ↓

**DEMİR
DEPOLARININ
BOŞALMASI**



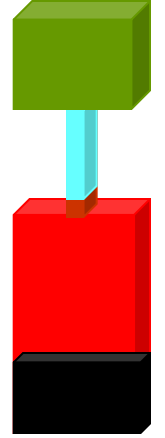
FERRİTİN<100

**DEMİR
YOKLUĞUNDA
ERİTROPOEZ**



FERRİTİN<100
TSAT< %20
EPO ↑

**DEMİR
EKSİKLİĞİ
ANEMİSİ**



FERRİTİN<100
TSAT< %20
HGB<11
EPO ↑

DEMİR EKSİKLİĞİ

- NHANES III



%19



%46

KDIGO DEMİR TEDAVİSİ

- Tedavi planlanırken anemi semptomlarını düzeltmenin ve transfüzyon/ESA kullanmaktan kaçınmanın yararları ve demir tedavisinin olası riskleri göz önünde bulundurulmalıdır.
- **ESA veya demir almayan KBH'li hastalarda TSAT \leq %30 ve Ferritin 500 ng/mL ise**

KDIGO DEMİR TEDAVİSİ

- Erişkin KBH hastalarına damardan
- Diyaliz öncesi hastalara ise 1-3 aylık ağızdan demir tedavisi önerilir.

KDOQI DEMİR TEDAVİSİ

- **HD**
 - Serum ferritin >200 ng/mL
 - TSAT >%20,
- **DIYALİZ ÖNCESİ ve PD:**
 - Serum ferritin >100 ng/mL
 - TSAT >%20.
- **Ferritin 500 ng/mL**

KDOQI DEMİR TEDAVİSİ

- **Hemodiyaliz** hastalarına damardan (güçlü öneri)
- **Diyaliz öncesi ve PD** ağızdan veya damardan demir tedavisi önerilir.

KDIGO DEMİR TEDAVİSİ

- **Diyaliz öncesi KBH'li hastalarda demir tedavisi yolunun seçiminde göz önünde bulundurulması gereken noktalar**
- Hastanın belirtileri
- Demir eksikliğinin şiddeti
- Uygun damar yolu varlığı
- Önceki tedaviye yanıtı
- Önceki tedavinin yan etkileri
- Tedaviye uyum
- Maliyet

DIYALİZ ÖNCESİ KBH

- **Ağızdan demir tedavisinin olumsuzlukları**
Gastrointestinal yan etkiler
Hasta uyumunun iyi olmaması
Demir emiliminin yetersizliği
ESA tedavisi sırasında yetersiz kalma

DIYALİZ ÖNCESİ KBH

- **Ağızdan demir tedavisinin olumlu tarafları**
 - Ekonomik
 - Uygulama kolaylığı
 - Anafilaksi/alerjik yan etki çok az

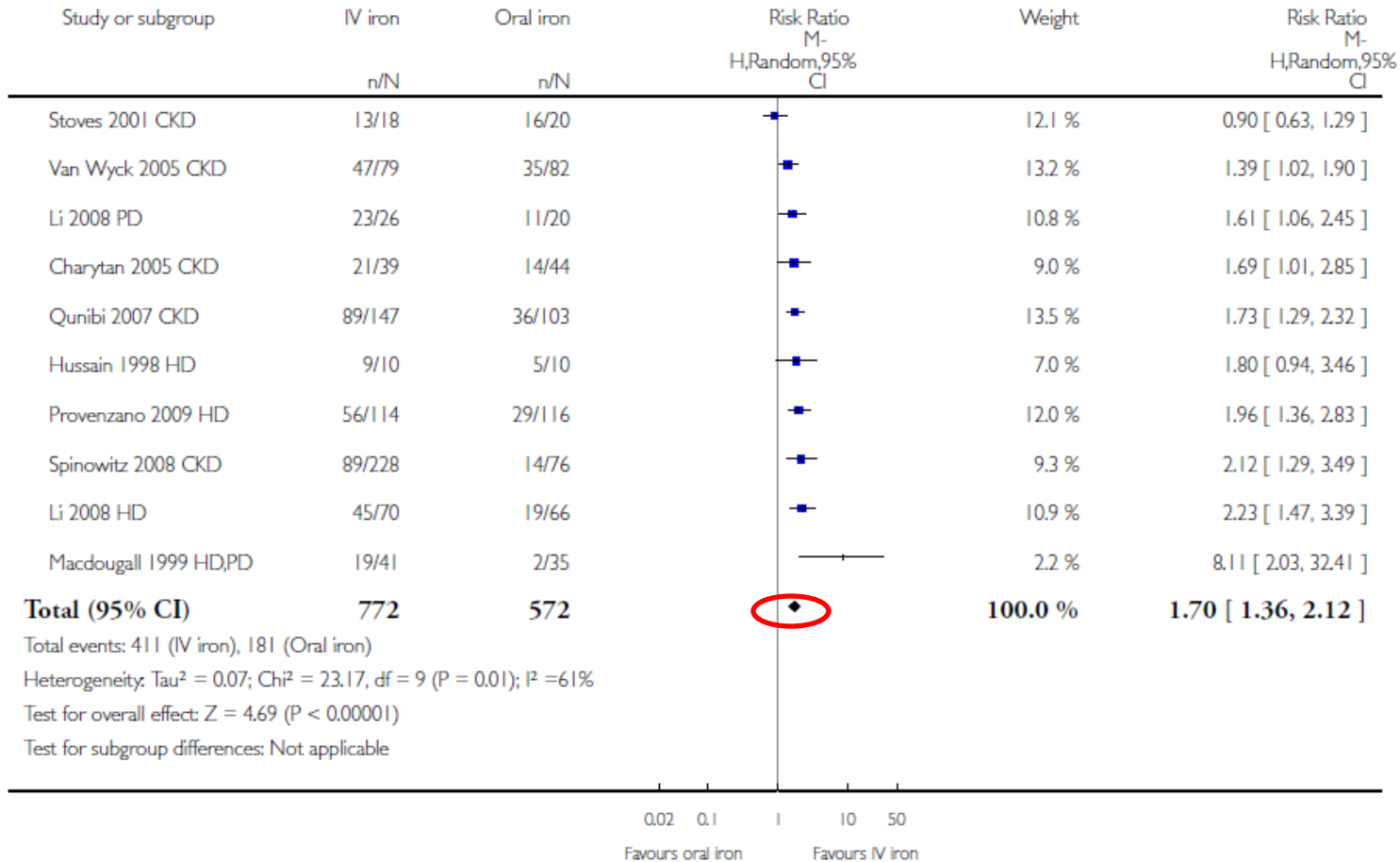
AĞIZDAN DEMİR TEDAVİSİ

- Erişkinlerde günde en azından 200 mg elementel demir
- 2-3 doza bölünmüş olarak
- +2 değerlikli demir daha kolay emilir, GIS yan etkileri daha fazladır
- +3 değerlikli demirin emilimi daha yavaş, GIS yan etkileri daha azdır
- Demir depoların dolması için 3 – 6 ay tedavi

DİYALİZ ÖNCESİ KBH

- Cochrane meta-analiz damardan Fe ağızdan Fe' e göre daha etkili
- **Hemoglobin:** 22 çalışma, 1862 hasta
- **Ferritin** 18 çalışma, 1457 hasta
- **ESA doz değişimi** 9 çalışma, 487 hasta

HGB > 1 GRAM ARTIŞ



FERRITIN

| Study or subgroup | IV iron | | Oral iron | | Mean Difference IV,Random,95% CI | Weight | Mean Difference IV,Random,95% CI |
|-------------------|---------|----------------|-----------|----------------|-------------------------------------|--------|-------------------------------------|
| | N | Mean(SD)[ug/L] | N | Mean(SD)[ug/L] | | | |
| Svara 1996 HD | 29 | 166 (123) | 28 | 109 (114) | + | 4.6 % | 57.00 [-4.54, 118.54] |
| Li 2008 HD | 70 | 495.7 (315.2) | 66 | 400.3 (264.1) | ++ | 4.2 % | 95.40 [-2.13, 192.93] |
| Michael 2007 HD | 33 | 80 (147) | 27 | -31 (130) | + | 4.5 % | 111.00 [40.86, 181.14] |
| Leehey 2005 CKD | 24 | 132 (162) | 24 | 19 (162) | ++ | 4.3 % | 113.00 [21.34, 204.66] |
| Warady 2002 HD | 17 | 259.1 (163.1) | 18 | 122 (118.8) | ++ | 4.2 % | 137.10 [42.11, 232.09] |

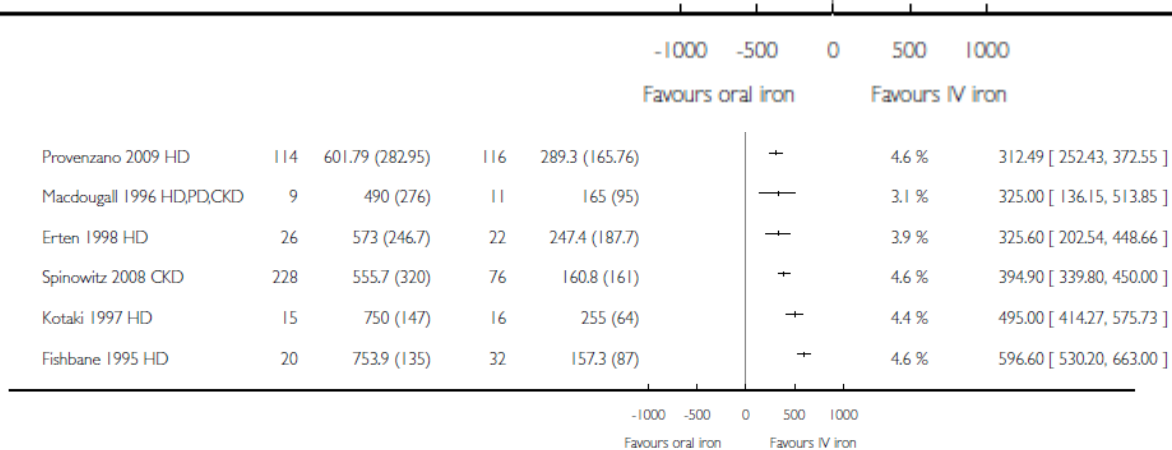
(... Continued)

| Study or subgroup | IV iron | | Oral iron | | Mean Difference IV,Random,95% CI | Weight | Mean Difference IV,Random,95% CI |
|-----------------------|------------|----------------|------------|----------------|-------------------------------------|----------------|-------------------------------------|
| | N | Mean(SD)[ug/L] | N | Mean(SD)[ug/L] | | | |
| Total (95% CI) | 956 | | 795 | | ◆ | 100.0 % | 243.25 [188.74, 297.75] |

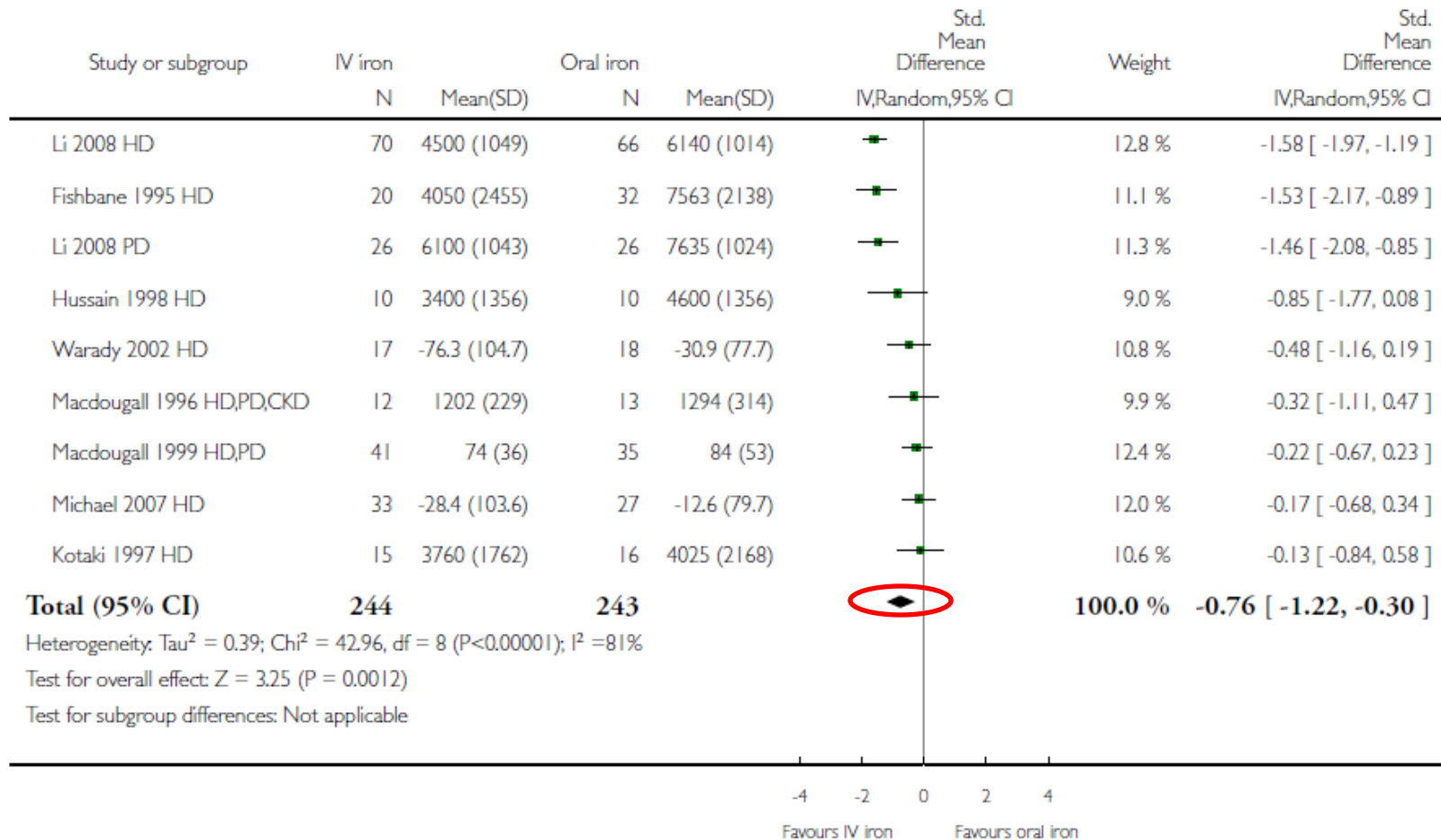
Heterogeneity: $\tau^2 = 15848.34$; $\chi^2 = 303.54$, $df = 23$ ($P < 0.00001$); $I^2 = 92\%$

Test for overall effect: $Z = 8.75$ ($P < 0.00001$)

Test for subgroup differences: Not applicable



ESA DOZ DEĞİŞİMİ



Diyaliz öncesi KBH

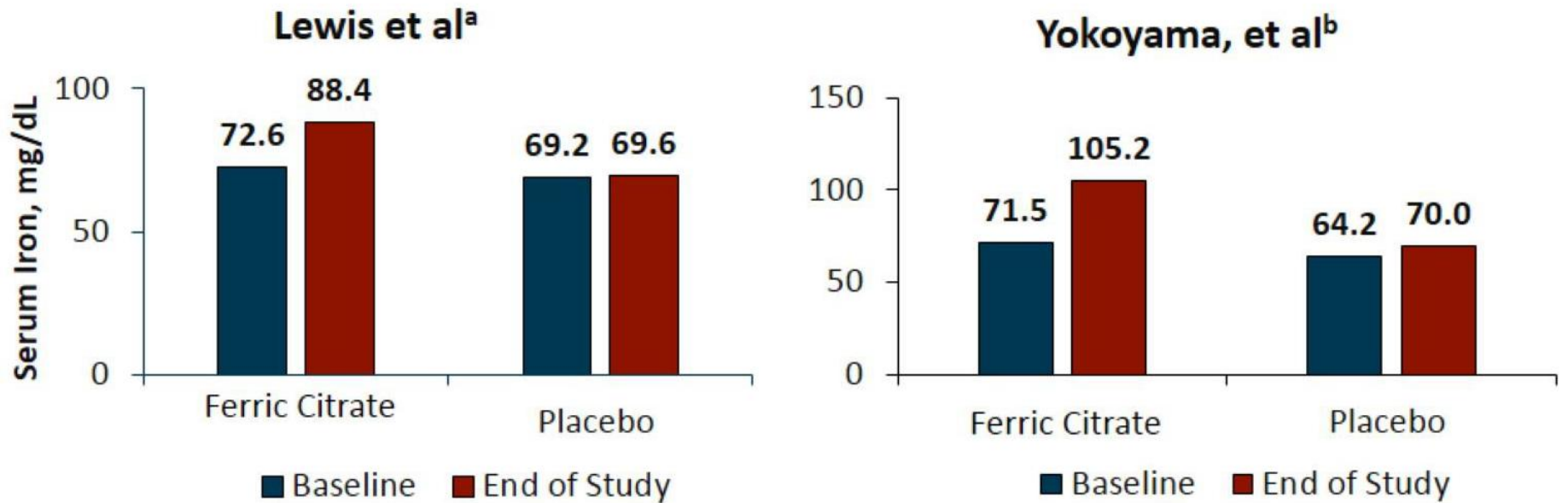
Demir verilif yolu

- Yapılan rdbdomize kontrollü çalıřmalarda damardan tedavi, ağızdan tedaviye üstün (Sükroz, Glukonat, Karboksi maltoz, Ferumoxytol)
- Ağızdan demire yanıtız olanlar, damardan tedaviye yanıt verebiliyor
- **Demir tedavisi ESA başlanmasını geciktirip, önleyebiliyor**
- **ESA alan demir eksiklikli KBH'lilere damardan demir önerilebilir**

DEMİR BAZLI FOSFOR BAĞLAYICILAR

- Sucroferric oxyhydrxyde (PA21)
- Ferrik sitrat

FERRİK SİTRAT



a. Lewis JB, et al. *J Am Soc Nephrol*. 2015;26:493-503^[14]; b. Yokoyama K, et al. *Clin J Am Soc Nephrol*. 2014;9:543-552.^[15]

LİPOZOMAL DEMİR (SİDERAL® FORTE)

- Ferric pyrophosphate
- Fosfolipid membran /askorbik asit
- Barsak mukozası ile doğrudan temas etmiyor
- Damardan Fe glukonat 1000 mg
- Ağızdan liposomal Fe (30 mg/gün)

LIPOZOMAL DEMİR

B 300

| Adverse event, <i>n</i> (%) | 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) |

T0

T1

T2

T3

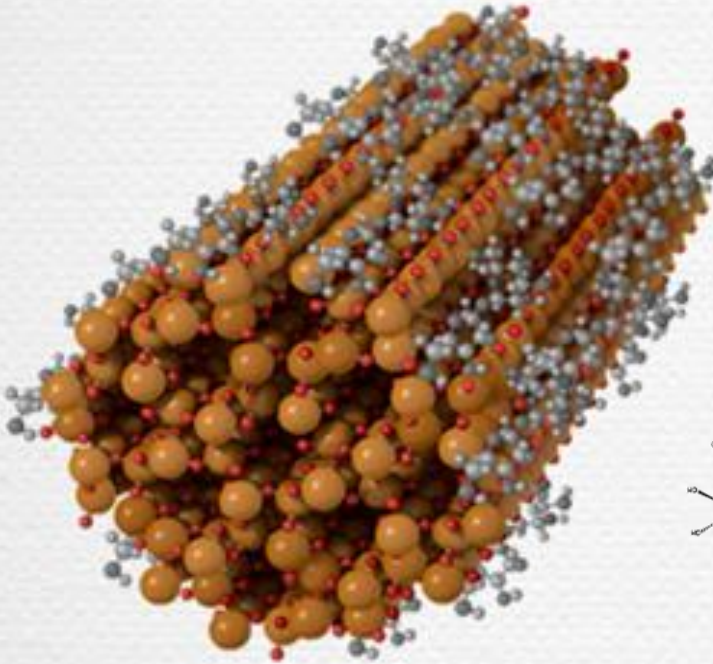
T4

DAMARDAN DEMİR PREPARATLARI

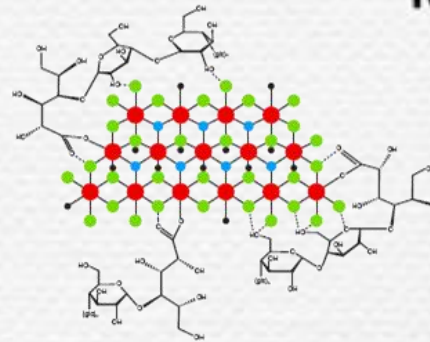
- Demir sitrat
- Demir dekstran
- Demir sükroz
- Demir glukonat
- Demir karboksimaltoz
- Demir isomaltozid 1000
- Ferumoxytol

DAMARDAN DEMİR PREPARATLARI

- IV demir kompleksleri, polinükleer demir (III)- hidroksit çekirdeğini çevreleyen bir karbonhidrat kılıftan oluşurlar



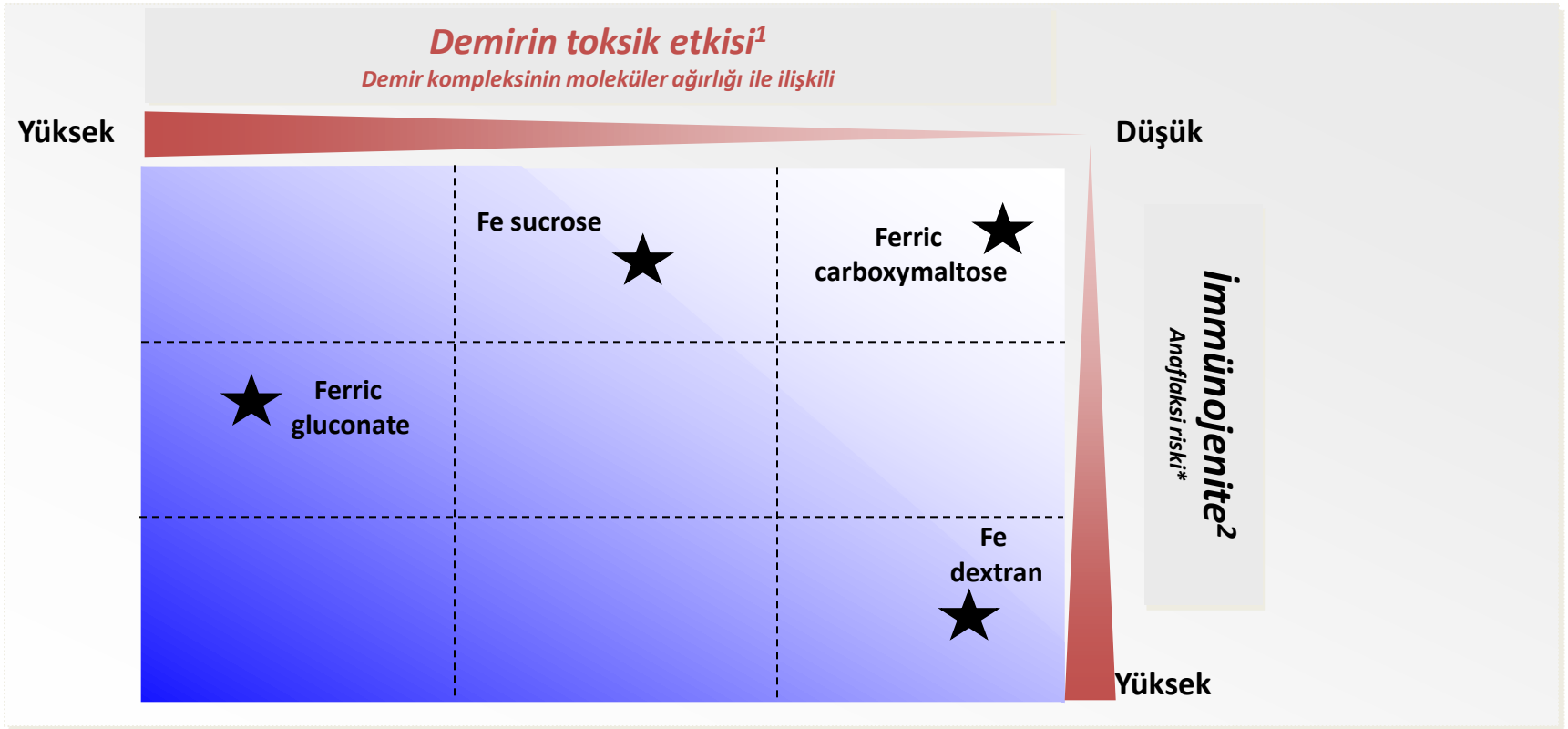
karbonhidrat
kılıf : sukroz



Ferric carboxymaltose

Fe³⁺
OH⁻
O²⁻
H₂O
Glucose
Hydrogen bond

DAMARDAN DEMİR MOLEKÜLLERİ

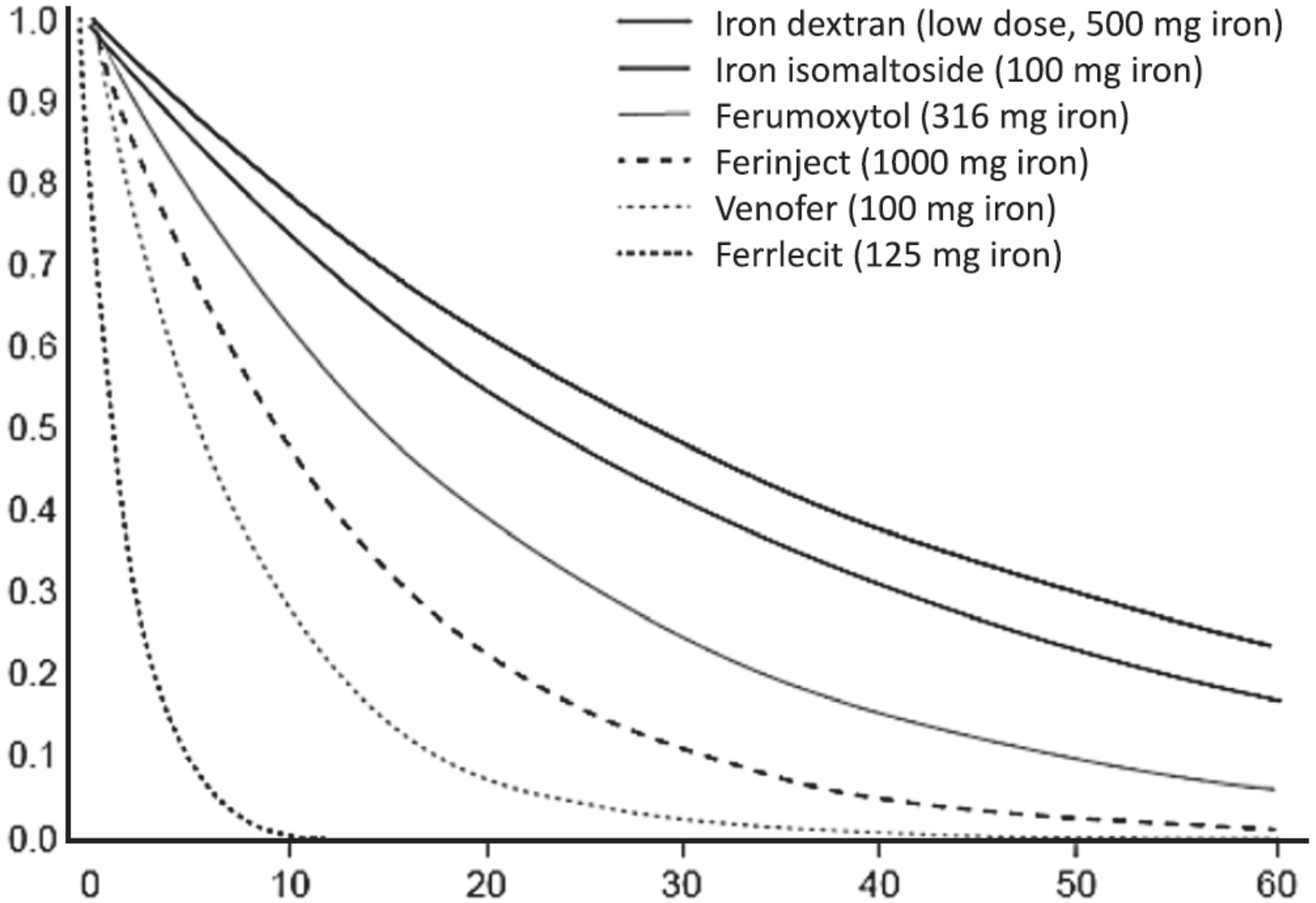


DAMARDAN DEMİR MOLEKÜLLERİ

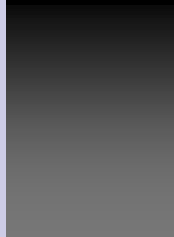

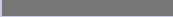





| Formül | Fe Karboksimaltoz | Fe dextran | Fe glukonat | Fe Sükroz |
|--------------------------------------|--------------------------|------------------------------|-----------------------|--------------------------------------|
| Kompleks tipi | Tip I Dayanıklı ve güçlü | Tip I Dayanıklı ve güçlü | Tip IV Labil ve zayıf | Tip III Yarı dayanıklı ve orta güçlü |
| Moleküler ağırlık (kDa) ² | ~150 | >100 | 38 | 43 |
| Kompleks stabilite | Yüksek | Yüksek | Düşük | Orta |
| pH | 5.0–7.0 | HMW: 4.5–7.0 LMW: 5.2–6.5 | 7.7–9.7 | 10.5–11.1 |
| Plazma yarı ömür (saat) | 7–12 | ~72 | 1 | 5–6 |
| Doğrudan Transferrine Fe verilmesi | 1–2 | 1–2 | 5–6 | 4–5 |

1. Crichton M *et al.* Fe therapy with special emphasis on intravenous administration. 4th edition. Bremen: UNI-Med; 2008:70–80
2. Geisser and Burckhardt, *Pharmaceutics* 2011, 3, 12-33
3. Munoz M *et al.* *World J Gastroenterol* 2009;15:4666–74

DAMARDAN DEMİR MOLEKÜLLERİ



DAMARDAN DEMİR MOLEKÜLLERİ

| | FKM | Fe dextran | Fe glukonat | Fe Sükroz |
|-----------------------|--|---|--|---|
| Max tek sefer Fe dozu |  15 mg/kg (1000 mg) |  20 mg/kg |  62.5 mg |  200 mg* |
| İnf. şekli | İnfüzyon | Total doz İnfüzyon | Bolus veya infüzyon | Bolus veya infüzyon* |
| Zaman | 15 dk  | 4–6 saat  | İnfüzyon=1 saat  Bolus=10 dk | İnfüzyon=30 dk  Bolus=10 dk |
| Doz aralığı | Haftada bir (max. İnfüzyon) | Haftada 2-3 | | Haftada 3 kez |

*500 mg verilebilir

FE KARBOKSİMALTOZ

- Iron
- Oxygen
- Ribbon-like carboxymaltose



Tek seferde yüksek doz(1000 mg*)

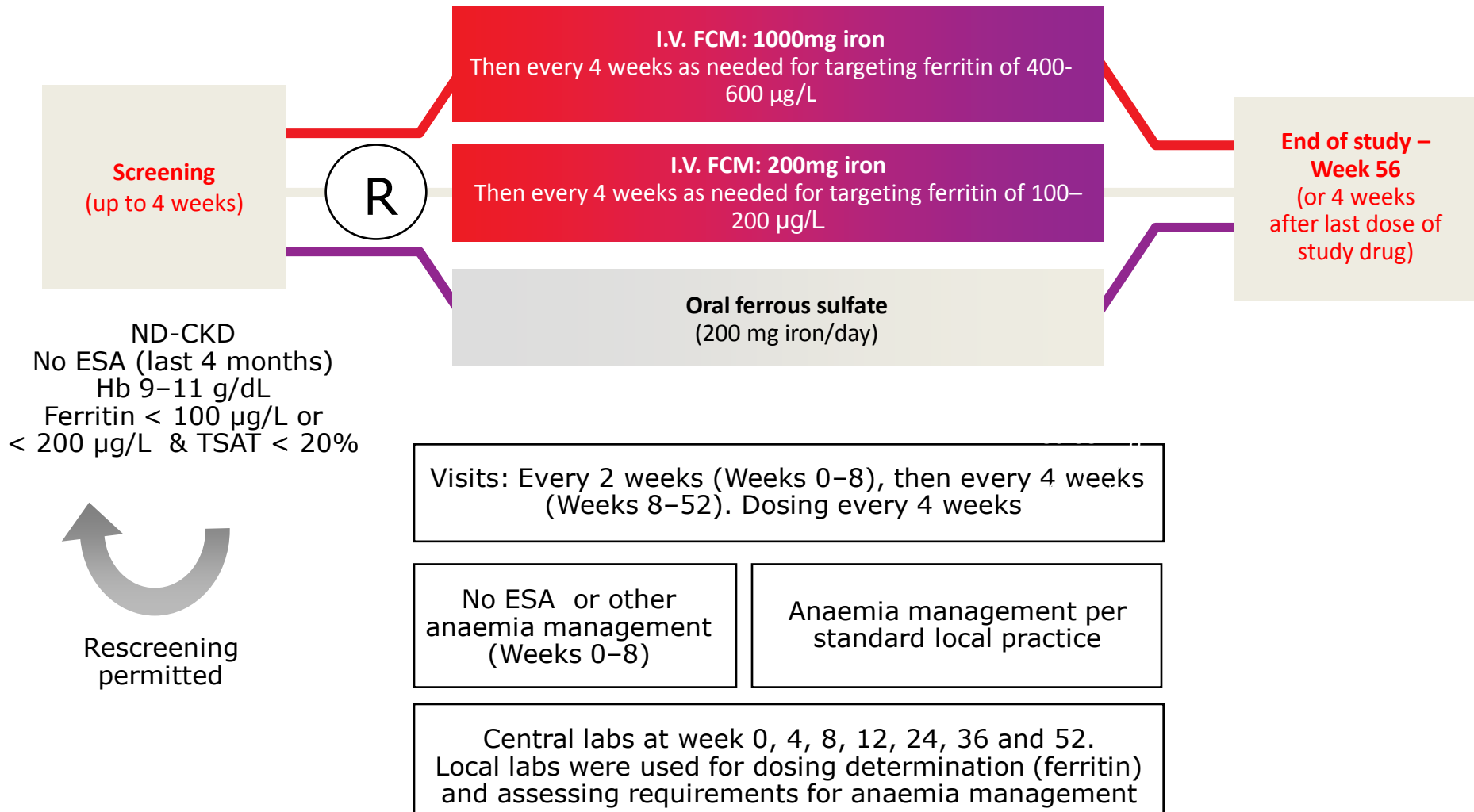
- Hızlı uygulama
 - 200 mg Fe bolüs
 - 1000 Fe 15 dakika infüzyon

düşük immüjenik yapı

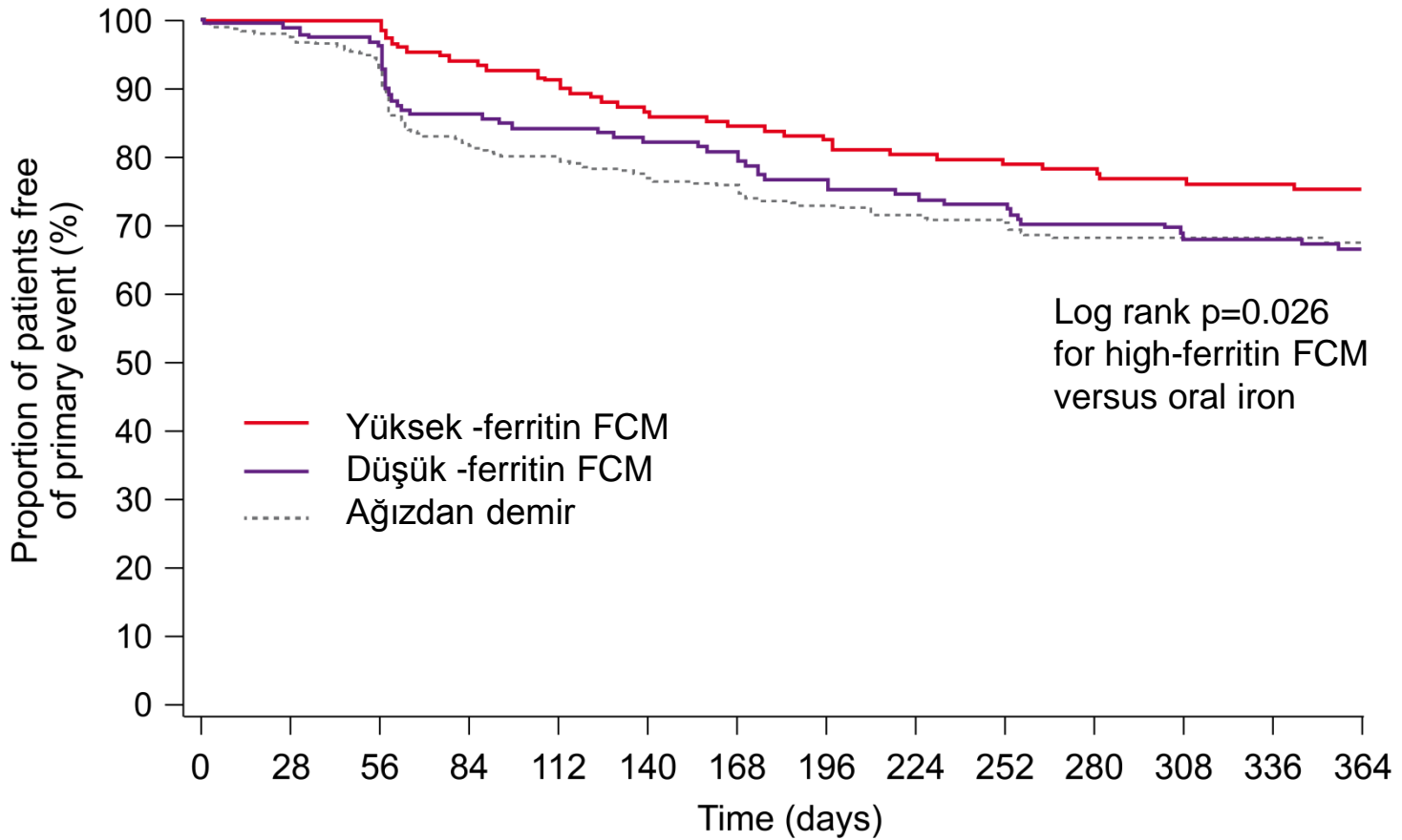
- dextran içermiyor
- Dextrana karşı gelişen antikorlarla çapraz reaksiyon yok
- Test dozuna gerek yok

*max 15 mg/kg

ÇALIŞMA PROTOKOLÜ

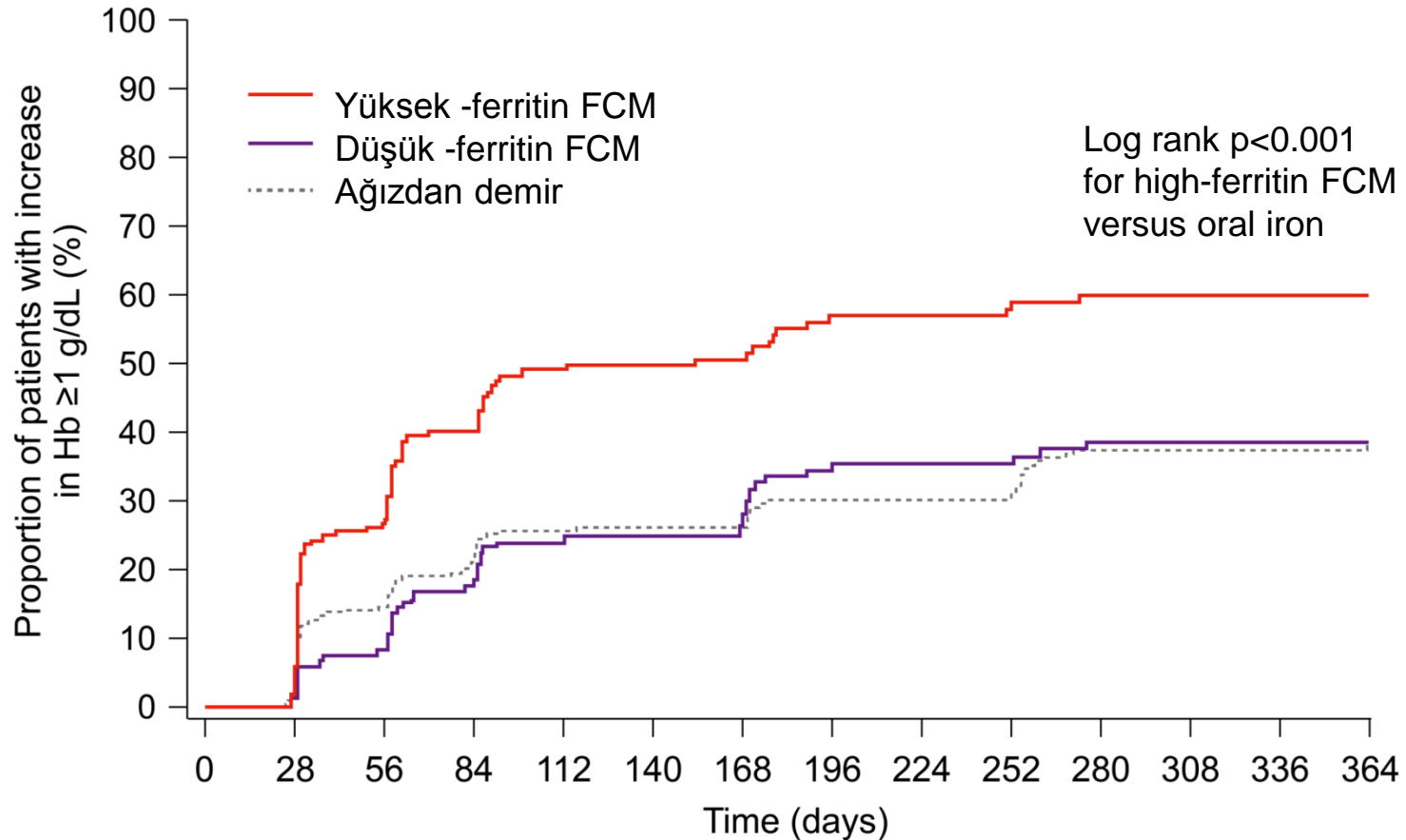


ALTERNATİF GİRİŞİM

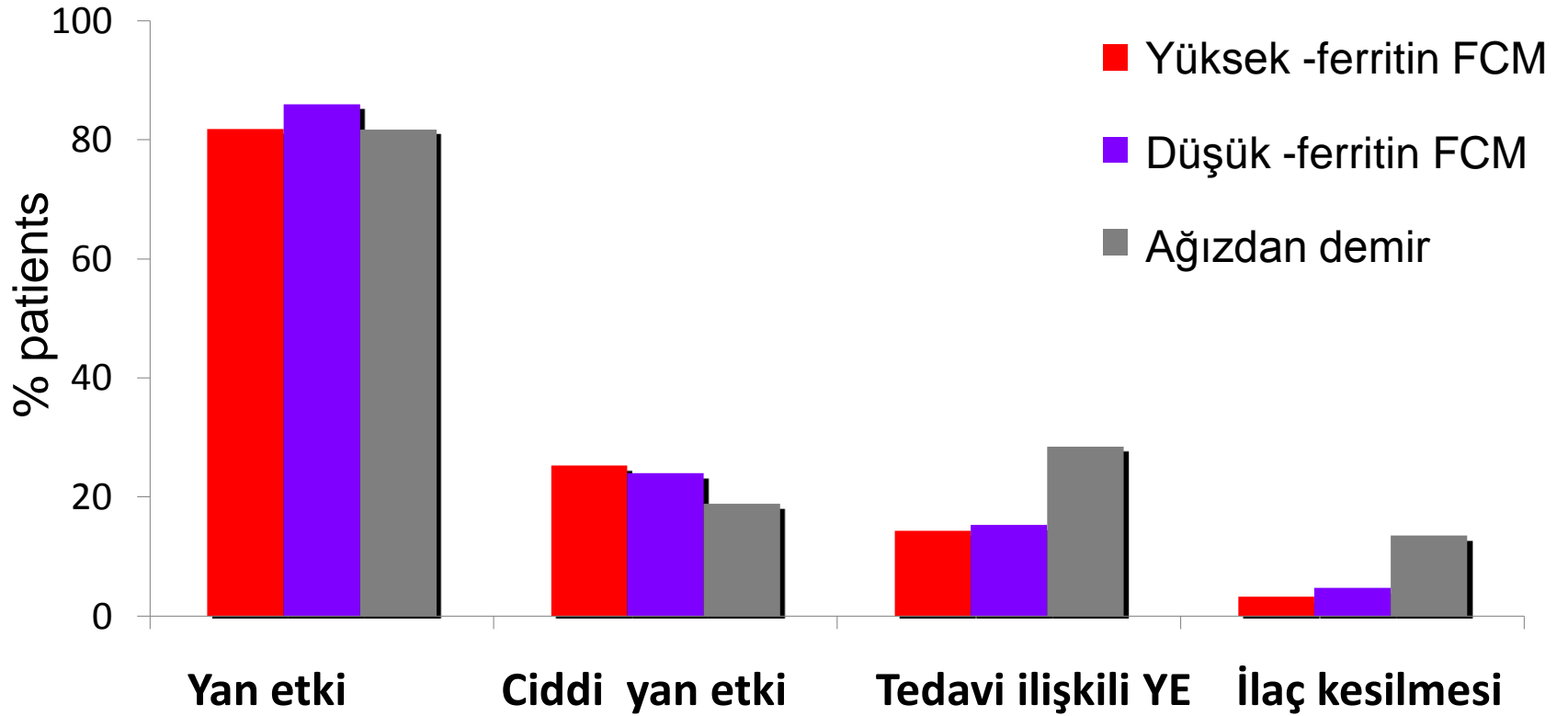


| No. at risk | 0 | 28 | 56 | 84 | 112 | 140 | 168 | 196 | 224 | 252 | 280 | 308 | 336 | 364 |
|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| High-ferritin FCM | 153 | 153 | 150 | 139 | 134 | 126 | 123 | 118 | 114 | 112 | 110 | 107 | 106 | 81 |
| Low-ferritin FCM | 152 | 150 | 145 | 129 | 124 | 121 | 117 | 109 | 106 | 103 | 96 | 93 | 93 | 75 |
| Oral iron | 308 | 299 | 278 | 241 | 229 | 219 | 212 | 203 | 198 | 194 | 185 | 185 | 184 | 151 |

HEMOGLOBİN ARTIŞI ≥ 1 g/dL

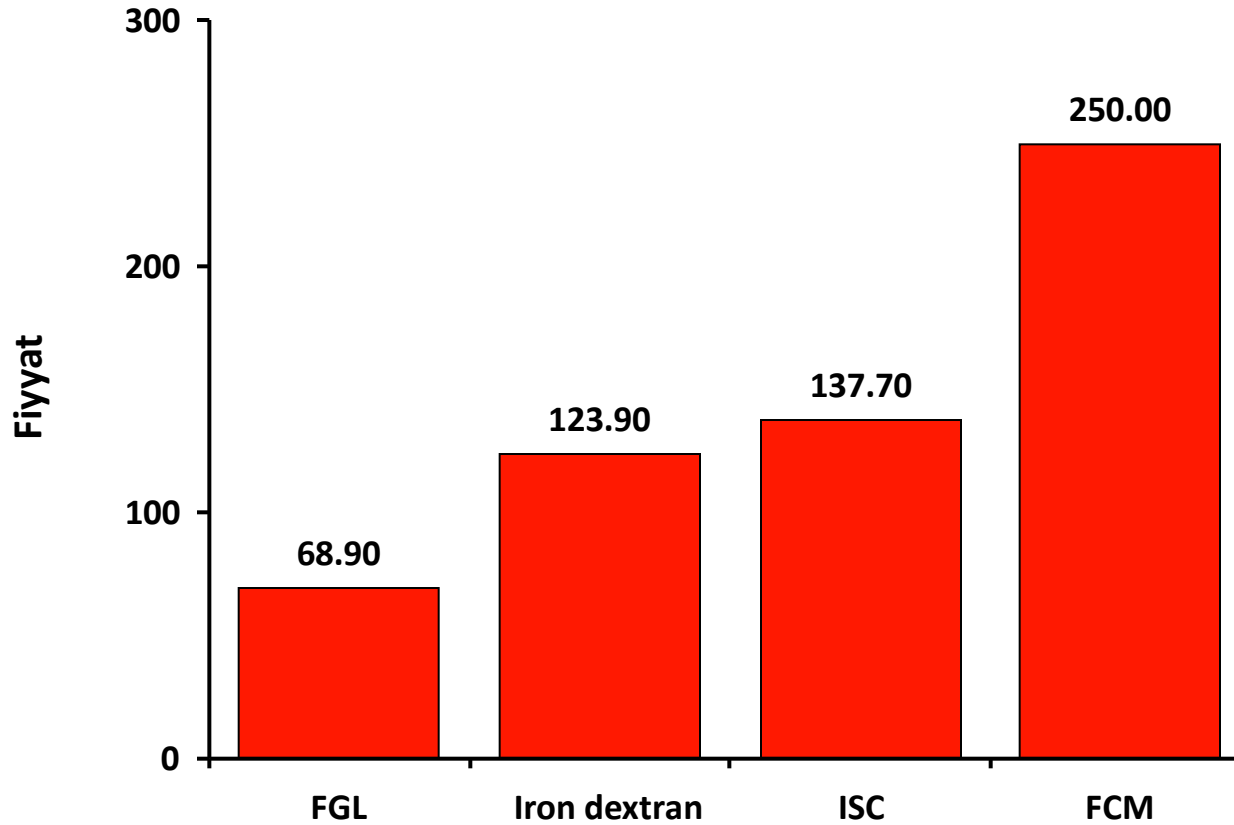


YAN ETKİ/CİDDİ YAN ETKİ



MALİYET

Fiyat 1000 mg I.V. Demir

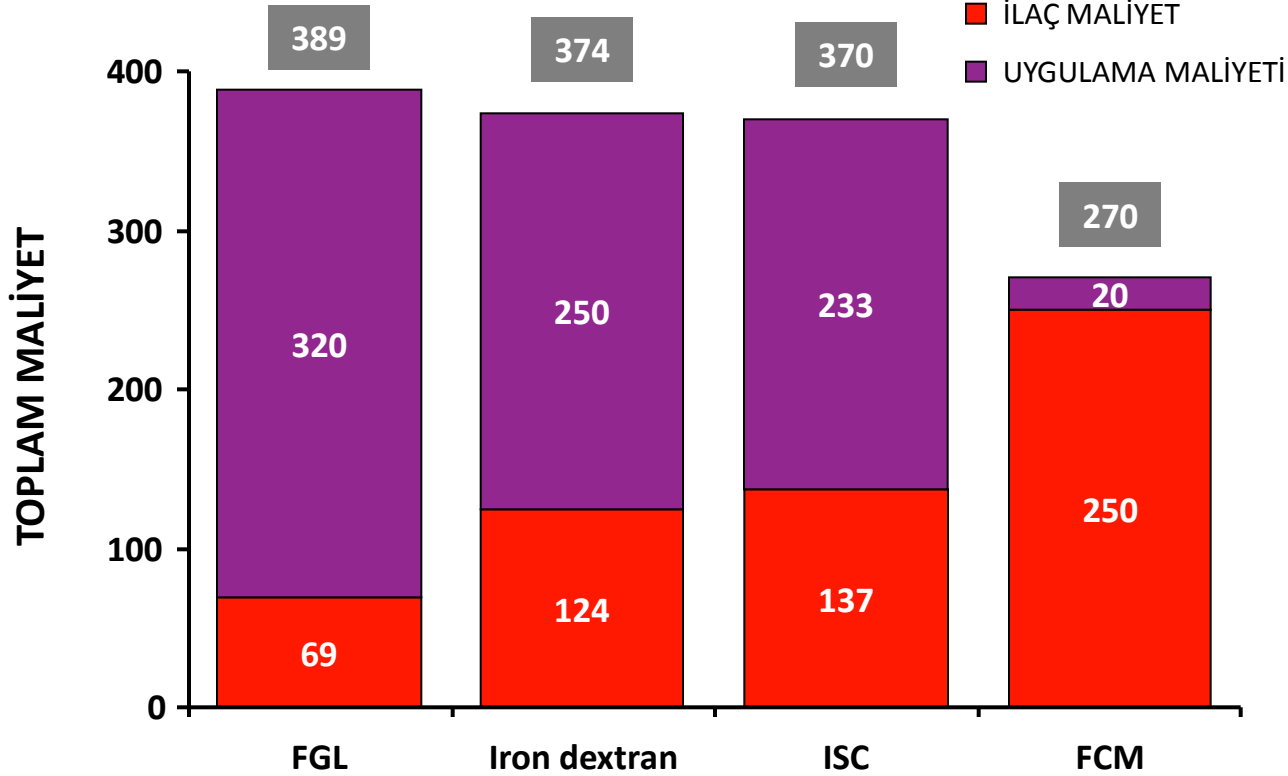


*Assumptions: All prices are ex-factory. As FGL and iron dextran are not available on the Swiss market, proposed prices assume a 10% discount for iron dextran and 50% discount for FGL or ISC. FCM's price is the proposed price in Europe

FGL, ferric gluconate; ISC, iron sucrose

MALİYET

Fiyat 1000 mg I.V. Demir



FGL, 16 x 62.2 mg iron in 10 minutes; Iron dextran, 1 x 1000 mg iron in 7 hours; ISC, 2 x 500 mg in 3.5 hours; FCM, 1 x 1000 mg iron in 15 minutes

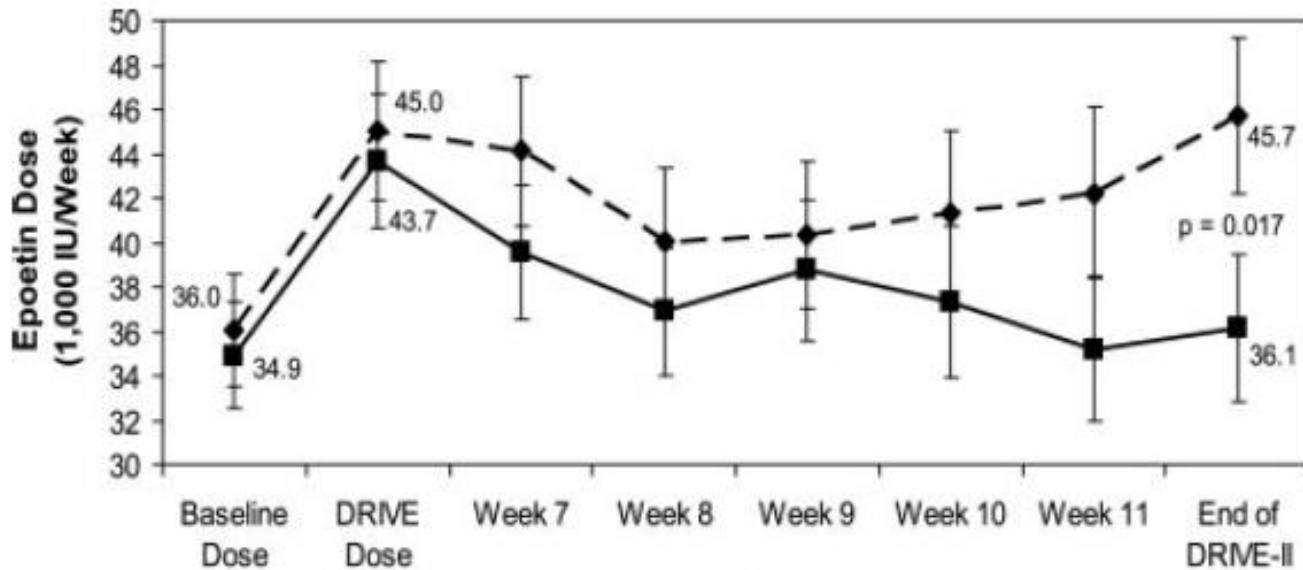
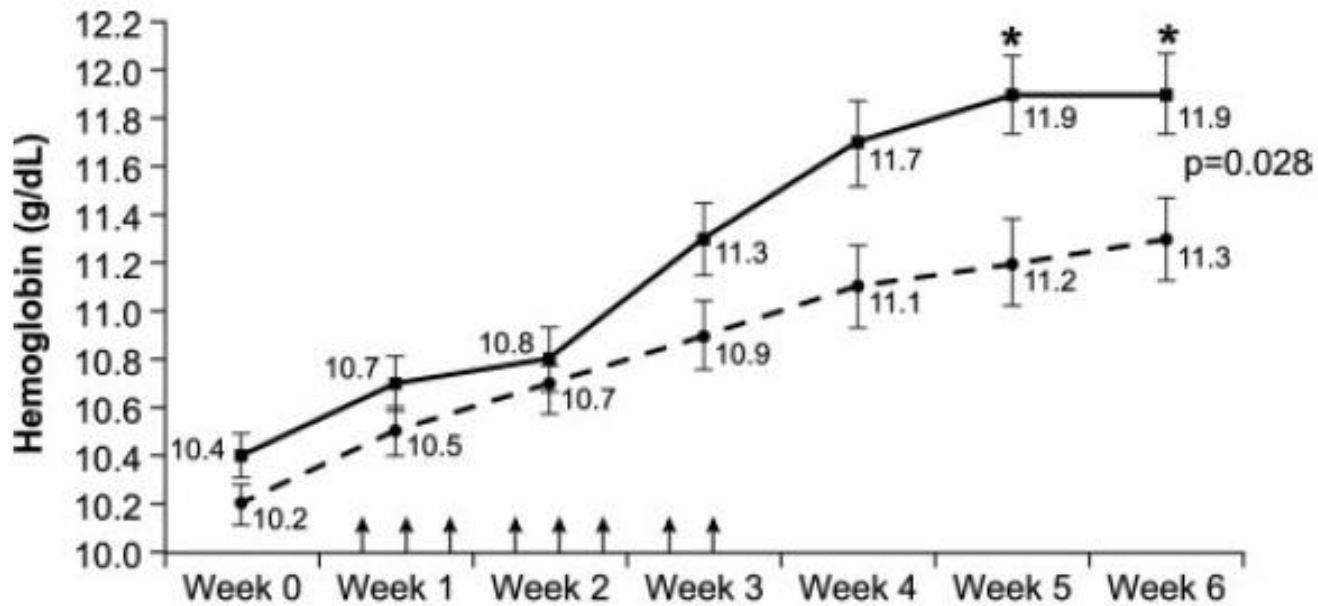
*Calculation of the administration costs for the individual products is based on the Swiss structure of rates for medical services (Tarmed)

DRIVE ve DRIVE II

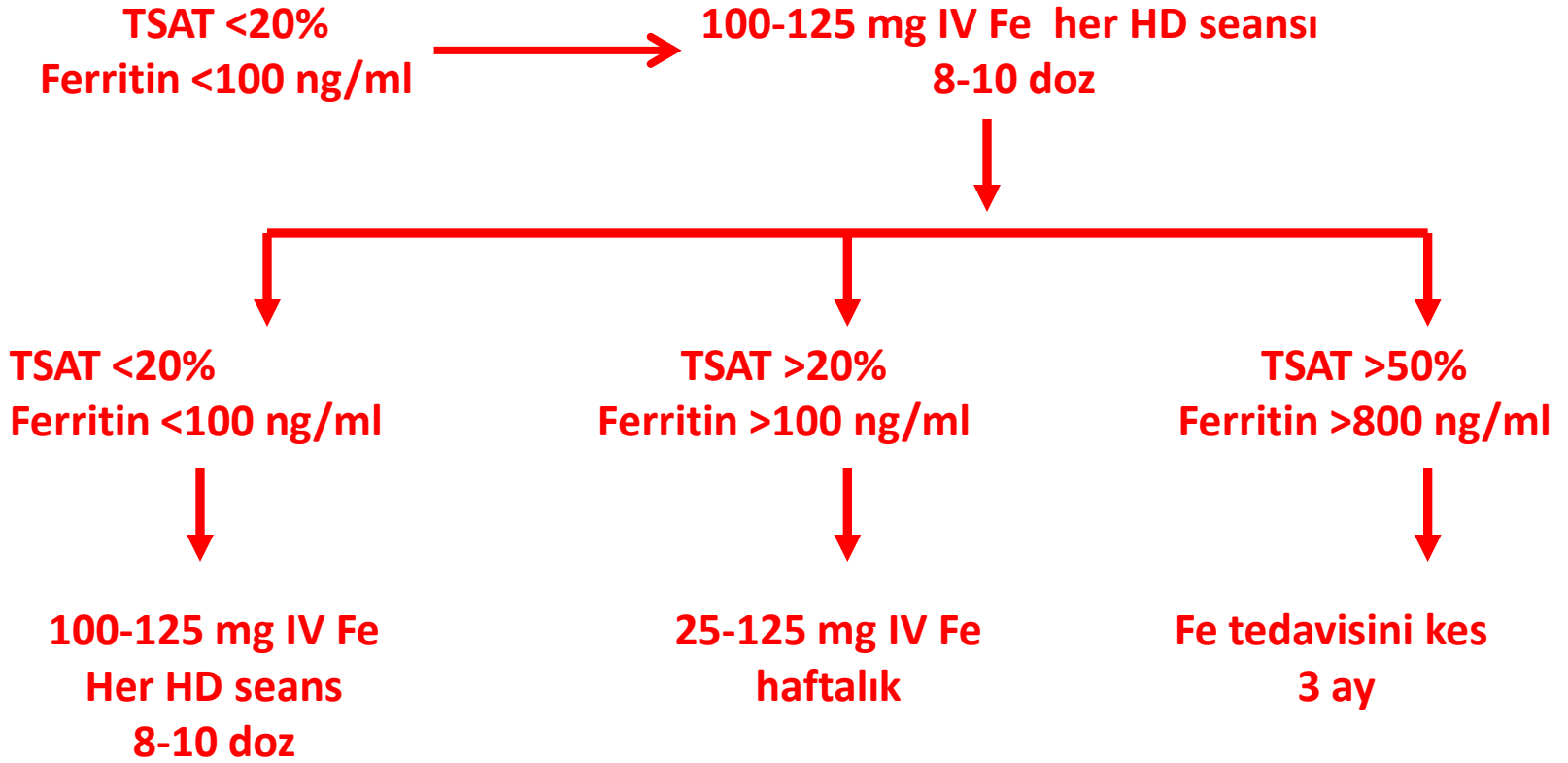
- 134 HD hastası
- Hb<11, TSAT<%25, Ferritin 500-1200,
- EPO >225 U/kg/hafta

8x125 mg İV Ferrik glukonat veya plasebo; 6 hafta izlem

Sonrasında serbest tedavi ile 6 haftalık izlem



DEMİR TEDAVİSİ



SORU

Hastanın demir parametreleri için kan almadan önce demir preparatları kesilmelidir?

100 mg Fe dextran 7 gün

500 mg Fe dextran 14 gün

100 mg Fe sukroz 24-48 saat

125 mg Fe glukonat 24-48 saat sonra bakılmalı

DAMARDAN DEMİR TEDAVİSİ

- Anaflaksi/anaflaktoid reaksiyon
- Enfeksiyon sıklığında artış
- Oksidatif stress
- Ateroskleroz
- Hemosiderozis

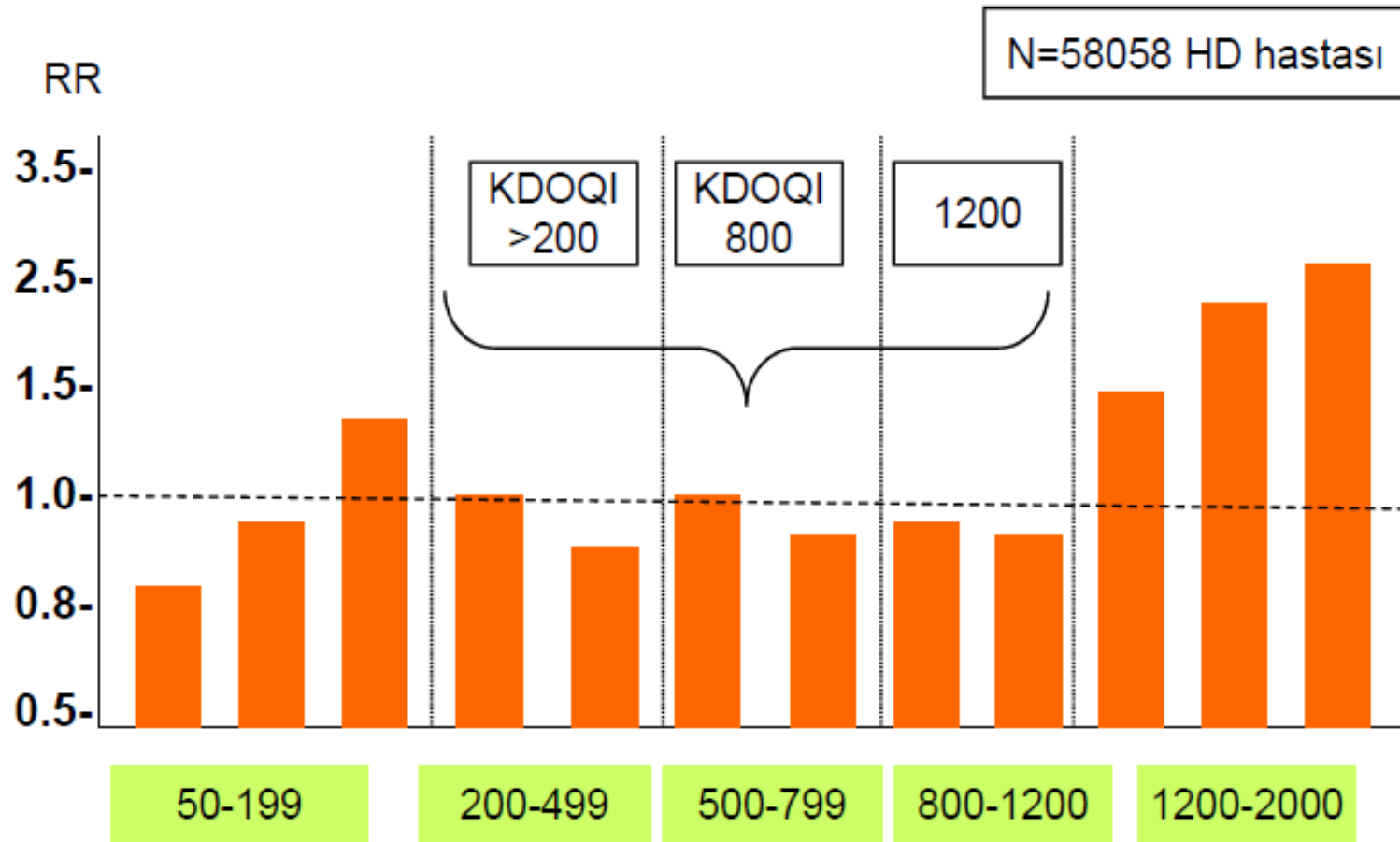
TEST DOZU

- GEREKLİ..... Demir dextran
- GEREKSİZ.....Dextran içermeyenler
- KDIGO tüm moleküllerde 60 dk izlem

FERRİTİN YÜKSEKLİĞİ

- Hemosiderozis
- İnflamasyon
- Enfeksiyon
- Karaciğer hastalığı
- Maligniteler

FERRİTİN/MORTALİTE



Ferritin; ng/ml

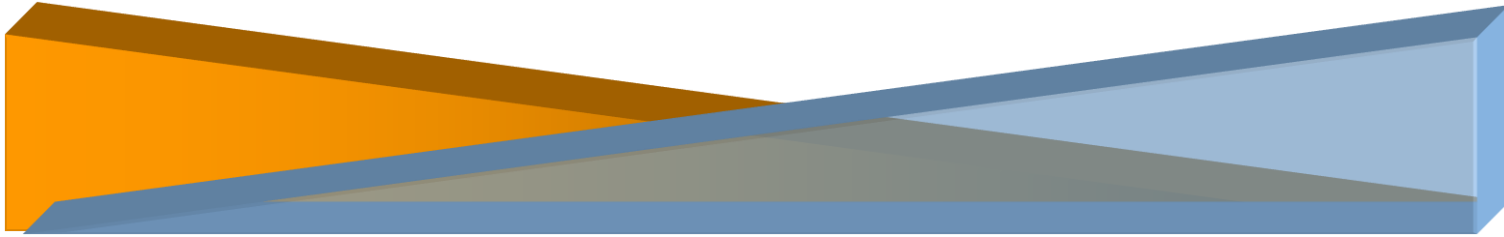
Kalantar-Zadeh K, J AM Soc Nephrol, 2005

Hepsidin

Fe

Hepsidin

Normal homeostazis



Herediter hemokomatozis
Fe- yüklenen kansızlık

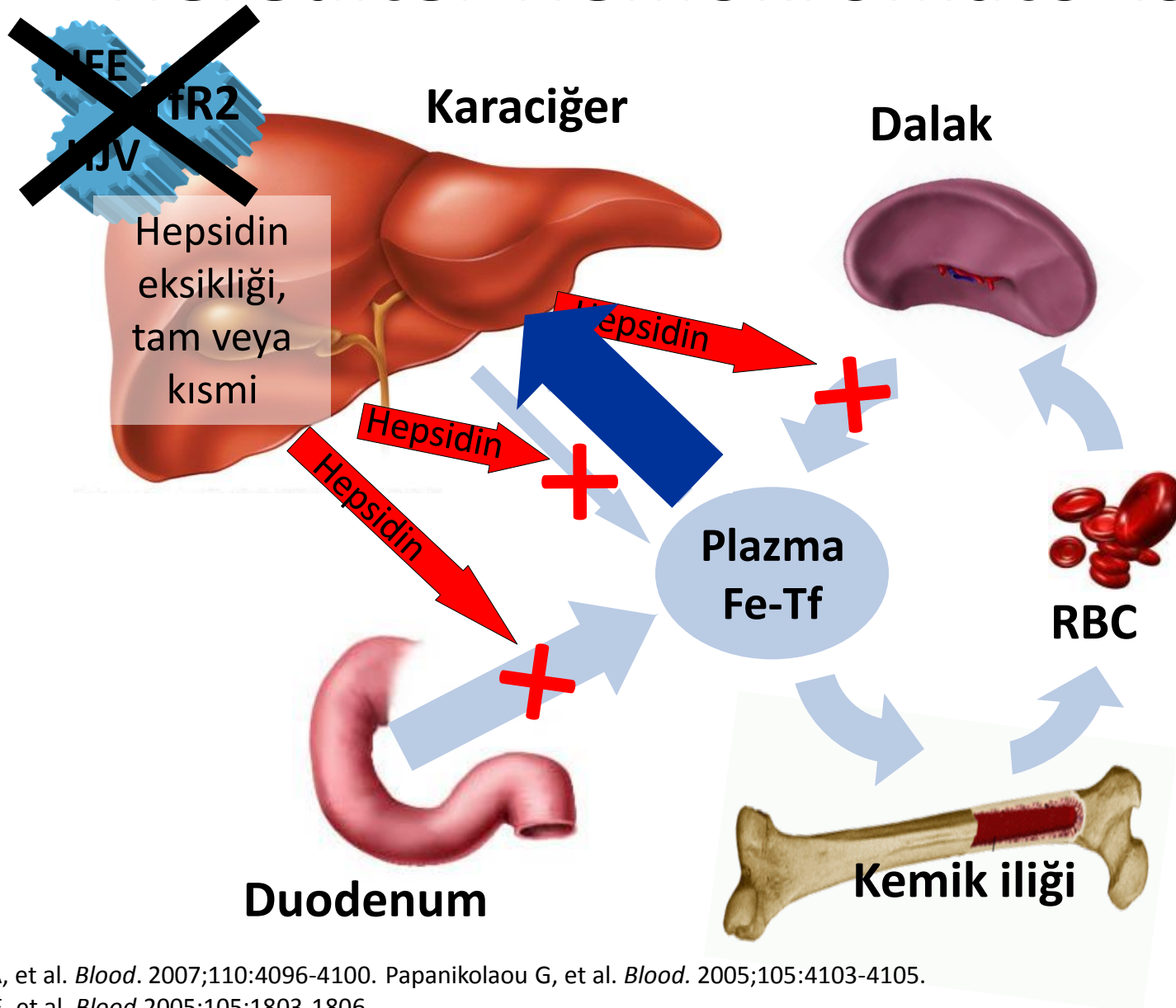
Kronik hastalık kansızlığı
Demir dirençli demir eksklığı
Hepsidin salgılayan tümör

Ganz T. *J Am Soc Nephrol*. 2007;18:394-400.

Ganz T, Nemeth E. *Am J Physiol Gastrointest Liver Physiol*. 2006;290:G199-G203.

Courtesy of Tomas Ganz, PhD, MD.

Hereditier Hemokromatozis



Piperno A, et al. *Blood*. 2007;110:4096-4100. Papanikolaou G, et al. *Blood*. 2005;105:4103-4105.

Nemeth E, et al. *Blood*. 2005;105:1803-1806.

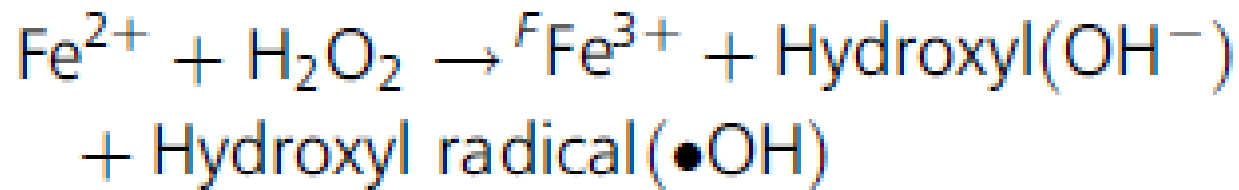
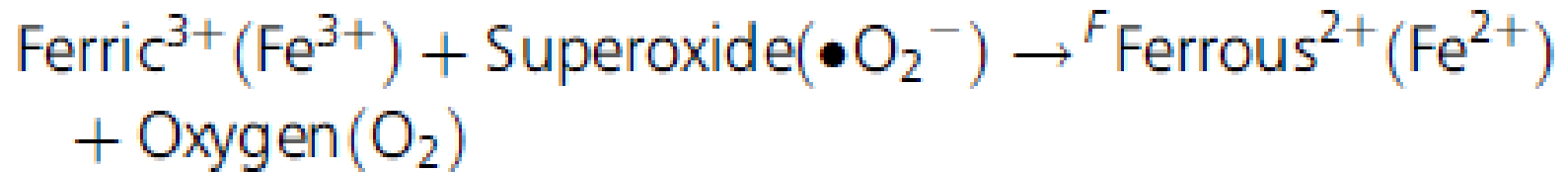
Courtesy of Tomas Ganz, PhD, MD, and Elizabeta Nemeth, MD.

KARACİĞERDE DEMİR BİRİKİMİ

- Karaciğer RES hücrelerinde depolanır.
- Karaciğer parankimal hücrelerde patolojik.
- Demir tedavisi alan hastaların karaciğerinde
 - Hafif-orta %84
 - Ağır %36.

OKSIDATIF STRESS

FENTON REAKSIYONU



“HYDROXYL” RADİKALLER

- Lipid peroksidasyonu
- DNA hasarlanması
- Protein denatürasyonu

DEMİR VE KARDİYOVASKÜLER ETKİ

- Damardan Fe endotel hasarı oluşturur
- Endotelial hücre kültüründe Fe ,
 - apoptozisin uyarılması,
 - proliferasyon baskılanması
 - monosit adezyonu.
- 100 mg Fe sükroz damar genişlemesini baskılıyor

ORIGINAL ARTICLE

Ferric Carboxymaltose in Patients with Heart Failure and Iron Deficiency

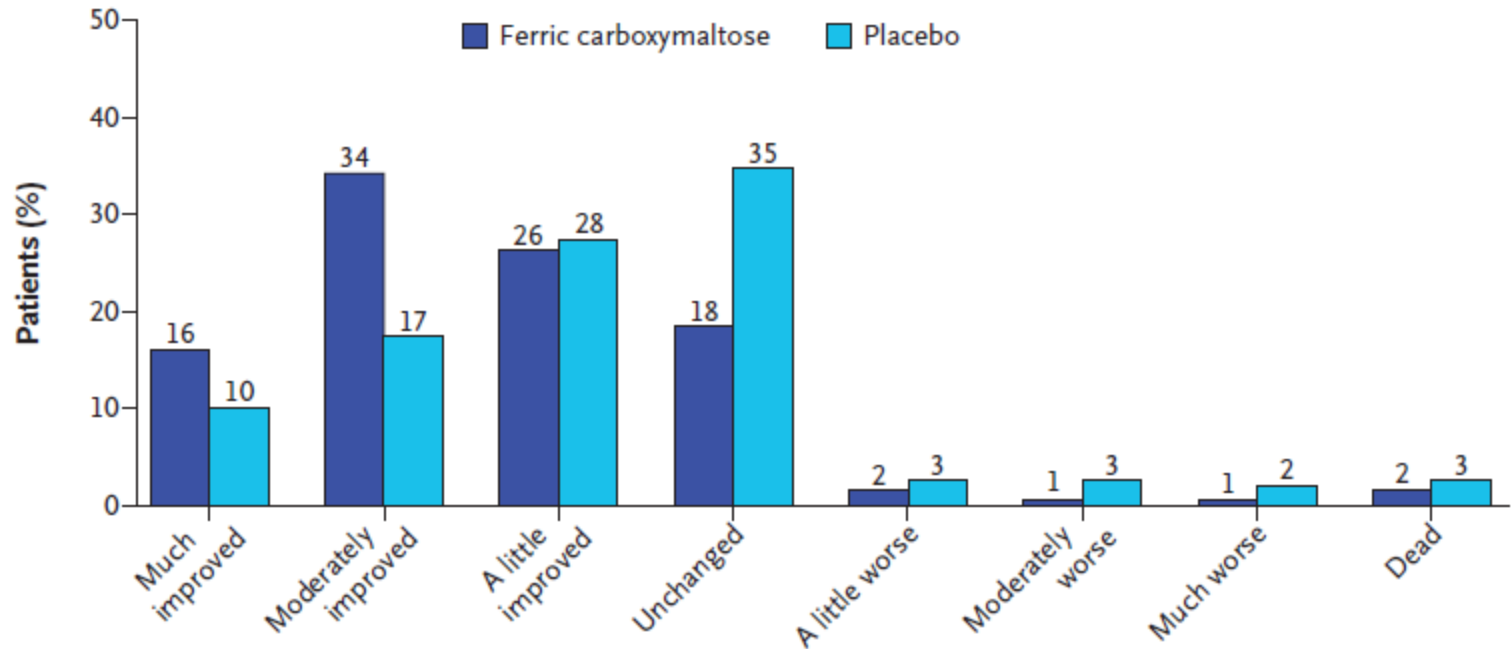
Stefan D. Anker, M.D., Ph.D., Josep Comin Colet, M.D.,
Gerasimos Filippatos, M.D., Ronnie Willenheimer, M.D.,
Kenneth Dickstein, M.D., Ph.D., Helmut Drexler, M.D.,*

Thomas F. Lüscher, M.D., Boris Bart, M.D., Waldemar Banasiak, M.D., Ph.D.,
Joanna Niegowska, M.D., Bridget-Anne Kirwan, Ph.D., Claudio Mori, M.D.,
Barbara von Eisenhart Rothe, M.D., Stuart J. Pocock, Ph.D.,
Philip A. Poole-Wilson, M.D.,* and Piotr Ponikowski, M.D., Ph.D.,
for the FAIR-HF Trial Investigators†

ABSTRACT

Ferric Carboxymaltose in Patients with Heart Failure and Iron Deficiency

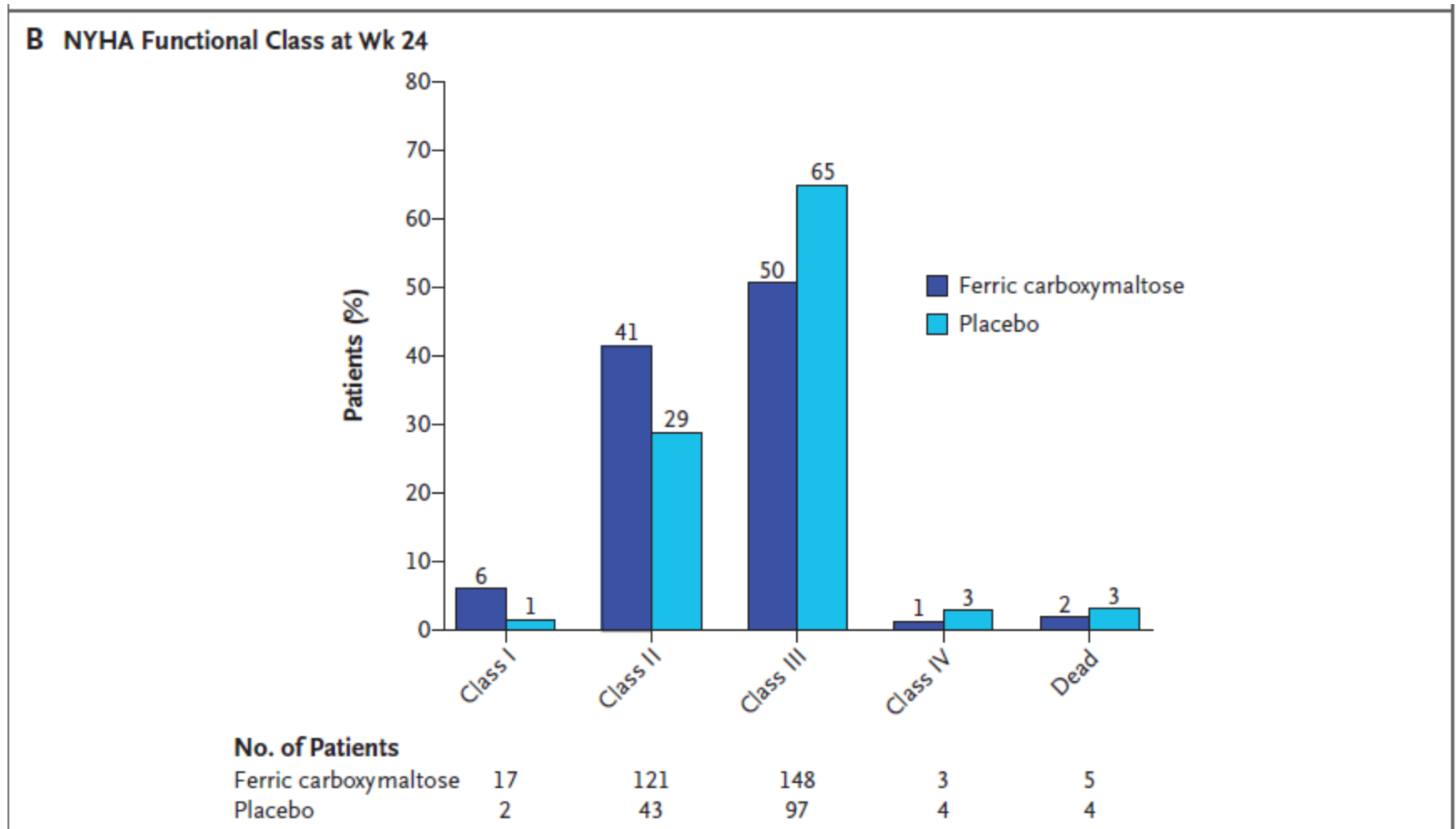
A Self-Reported Patient Global Assessment at Wk 24



No. of Patients

| | | | | | | | | |
|-----------------------|----|-----|----|----|---|---|---|---|
| Ferric carboxymaltose | 47 | 100 | 77 | 54 | 5 | 2 | 2 | 5 |
| Placebo | 15 | 26 | 41 | 52 | 4 | 4 | 3 | 4 |

Ferric Carboxymaltose in Patients with Heart Failure and Iron Deficiency



DEMİR VE ENFEKSİYON

- Demir tedavisi CD4+ T- hücre depleksyonu
- Demir tedavisi
 - fagositik aktiviteyi bozuyor
 - PNL öldürme kapasitesini azaltıyor

- BMC Nephrol 2010; 11:16
- Am J Nephrol 2012; 36: 50–57

Iron and Infection in Hemodialysis Patients

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Seminars in Dialysis—Vol 27, No 1 (January–February) 2014
pp. 26–36

FERRİTİN/ENFEKSİYON

TABLE 1. Association between serum ferritin and infection and infection-related mortality in hemodialysis patients

| Author/Year | Country/No. of centers | N ^a | Predictor(s) | Outcome(s) | Results ^b | Summary |
|--|------------------------|----------------|--|---|--|--|
| <i>Association between serum ferritin and infection or infection-related mortality</i> | | | | | | |
| Seifert 1987 (53) | Germany 2 centers | 184 | Mean SF during study period: 10–330, 331–1000 or 1001–2000 ng/ml | Bacterial infections (BIs)/ patient-year (PY) where BI includes septicemia and other BIs | 0.34 BIs/PY (SF 331–1000 ng/ml) vs. 0.18 BIs/PY (SF 10–330 ng/ml), <i>p</i> < 0.05. 0.59 BIs/PY (SF 1001–2000 ng/ml) vs. 0.18 BIs/PY (SF 10–330 ng/ml), <i>p</i> < 0.01. | Higher rates of BI were observed in the higher SF groups. |
| Boelaert 1987 (54) | Belgium 36 centers | 1421 | SF at time of questionnaire: <500 or >500 ng/ml | Proportion with <i>Yersinia</i> <i>enterocolitica</i> bacteremia (YEB) in the previous 5 years | 0.93% YEB (SF >500 ng/ml) vs. 0% YEB (SF <500 ng/ml), <i>p</i> < 0.05. | A higher proportion of previous YEB was observed in the higher SF group. |
| Tielemans 1989 (55) | Belgium 1 center | 61 | Mean SF during study period: ≤500 or >500 ng/ml | Bacterial infections (BIs)/ patient-year (PY) where BI includes septicemia and other BIs; time to first BI | 0.48 BIs/PY (SF >500 ng/ml) vs. 0.09 BIs/PY (SF ≤500 ng/ml), <i>p</i> < 0.001. Shorter time to first BI with higher ferritin, <i>p</i> < 0.005 (logrank). | A higher rate of BI and shorter time to BI were observed in the higher SF group. |
| Boelaert 1990 (56) | Belgium 1 center | 158 | SF classified every 3 months: <500, 500–1000, or >1000 ng/ml (<500 and 500–1000 ng/ml combined for analysis) | Bacteremic episodes (BEs)/ patient-year (PY) | 0.34 BEs/PY (SF >1000 ng/ml) vs. 0.12 BEs/PY (SF ≤1000 ng/ml), <i>p</i> < 0.005. | A higher rate of BEs was observed in the higher SF group. |
| Hoen 1995 (57) | France 13 centers | 607 | SF at first bacterial infection (BI) or end of study period if no BI: <500 or ≥500 ng/ml | Bacterial infection (BI) over 6-month period | OR for BI (SF ≥500 vs. <500 ng/ml): 1.79 (95% CI 1.06–3.00). | Higher SF was independently associated with higher odds of BI. |
| Teehan 2004 (58) | US 1 center | 87 | Iron deficiency (TSAT <20% and SF <100 ng/ml), functional iron deficiency (TSAT <20% and SF >100 ng/ml), iron replete (TSAT >20% and SF >100 ng/ml). Measured at baseline prior to initiation of IV iron. (Iron deficiency and functional iron deficiency combined for analysis.) | Proportion with bacterial infection (BI), which included bacteremia or bacterial pneumonia, and time to BI over 2 years | Higher proportion of BI in iron replete (56%) than functionally iron deficient (27%) or iron deficient (37%) groups. HR for BI (iron replete vs. non-iron replete): 3.1 (95% CI 1.4–6.8). | Iron repletion was independently associated with higher hazard of BI. |
| Teehan 2004 (28) | US 2 centers | 132 | Iron deficiency (TSAT <20% and SF <100 ng/ml), functional iron deficiency (TSAT <20% and SF ≥100 ng/ml), iron replete (TSAT ≥20% and SF ≥100 ng/ml). Based on mean values within 3 months of starting IV iron. (Iron deficiency and functional | Proportion with bacteremia and time to first bacteremic episode over 1 year | Proportion with bacteremia in iron replete (35%) vs. non-iron replete (18%), <i>p</i> 0.06. HR for bacteremia (iron replete vs. non-iron replete): 2.5 (95% CI 1.1–5.7). | Iron repletion was independently associated with higher hazard of bacteremia. |

FERRİTİN/ENFEKSİYON

- 13 çalışmanın 9'unda yüksek ferritin
 - Enfeksiyon görülme sıklığında artış
 - Enfeksiyon ilişkili mortalitede artış
 - 1.5-3.1 ortalama artış
- 4 çalışma hiçi bir ilişki yok
- ESA kullanımı
- Ferritin bakma zamanı, eşik değer

DEMİR KULLANIMI/ENFEKSİYON

- 24 çalışma
- 2 randomize kontrollü
 - DRIVE ve Besarab
 - Demir dozu ile enfeksiyon arasında ilişki yok
- 12 çalışma ilişki var
- 10 çalışma ilişki yok

EPIBACDIAL ÇALIŞMASI

Table 2. Characteristics of patients with ($n = 50$) and without ($n = 935$) bacteremic episode (BE)

| Characteristic | Patients with BE | Patients without BE | P Value ^a |
|---|------------------|---------------------|----------------------|
| Age, years (mean \pm SD) | 63.4 \pm 15.7 | 59.8 \pm 15.5 | 0.08 |
| Gender, male: n (%) | 26 (52.0) | 569 (60.9) | 0.21 |
| Comorbidity | | | |
| diabetes mellitus: n (%) | 9 (18.0) | 111 (11.9) | 0.20 |
| malignancy: n (%) | 9 (18.0) | 63 (6.7) | 0.003 |
| Time since start of dialysis, years (median and [range]) | 2.43 [0.2 to 24] | 3.62 [0.1 to 29] | 0.18 |
| Mode of dialysis | | | |
| hospital center: n (%) | 47 (94.0) | 789 (84.4) | 0.064 |
| History of transplantation: n (%) | 5 (10.0) | 148 (15.8) | 0.267 |
| Number of red cell packs transfused within the past 9 mo: (mean \pm SD) | 2.95 \pm 4.6 | 1.05 \pm 2.7 | <0.0001 |
| History of BE | | | |
| ≥ 1 within the past 18 mo: n (%) | 17 (34.0) | 82 (8.8) | <0.0001 |
| no. of previous BE (mean \pm SD) | 0.80 \pm 1.63 | 0.14 \pm 0.57 | <0.0001 |
| Current immunosuppressive therapy: n (%) | 6 (12.0) | 39 (4.2) | 0.009 |
| Current erythropoietin treatment | | | |
| no. of patients treated: n (%) | 30 (60.0) | 477 (51.0) | 0.22 |
| current dose, kU/wk: (mean \pm SD) | 4.64 \pm 4.99 | 2.85 \pm 3.57 | 0.02 |
| Iron Rx within past 6 mo: n (%) | 27 (54.0) | 502 (53.7) | 0.96 |
| Nasal swab positive for <i>S. aureus</i> : n (%) | 15 (31.3) | 265 (29.4) | 0.79 |
| Surgical procedure within 1 mo: n (%) | 2 (4.0) | 43 (4.6) | 0.84 |
| Vascular access | | | |
| A/V fistula | 25 (50.0) | 778 (83.2) | |
| A/V graft and shunt | 7 (14.0) | 117 (12.5) | <0.0001 |
| dialysis catheter | 18 (36.0) | 40 (4.3) | |

^a P value of χ^2 , or Mann-Whitney U test, as appropriate. Abbreviations as in Table 1.

EPIBACDIAL ÇALIŞMASI

| Risk Factor | Relative Risk (95% confidence interval) |
|--|--|
| Vascular access | |
| fistula | 1 |
| graft and shunt | 1.29 (0.50 to 3.34) |
| catheter | 7.64 (3.73 to 15.67) |
| History of bacteremia | |
| no previous episode | 1 |
| 1 previous episode | 1.19 (0.44 to 3.23) |
| ≥2 previous episodes | 7.33 (3.27 to 16.43) |
| Current immunosuppressive treatment | |
| no | 1 |
| yes | 3.01 (1.20 to 7.56) |
| Corpuscular hemoglobin (per 1 g/dl increment) | 0.75 (0.60 to 0.93) |

Aktif sistemik enfeksiyon varlığında
damardan Demir tedavisinden kaçının
(Not Graded)



SONUÇ

- Demir eksikliği sık görülen bir sorun
- Tedavi kan verilmesi, ESA kullanımını azaltıyor
- Damardan yol daha çok tercih ediliyor
- Damardan demir tamamen masum değil