



Aktuelles von der Anämie- und Eisenfront

Gunnar Heine

Pathophysiologie

Therapien von

gestern?

EKs und EPO

Therapien von

heute?

Eisen

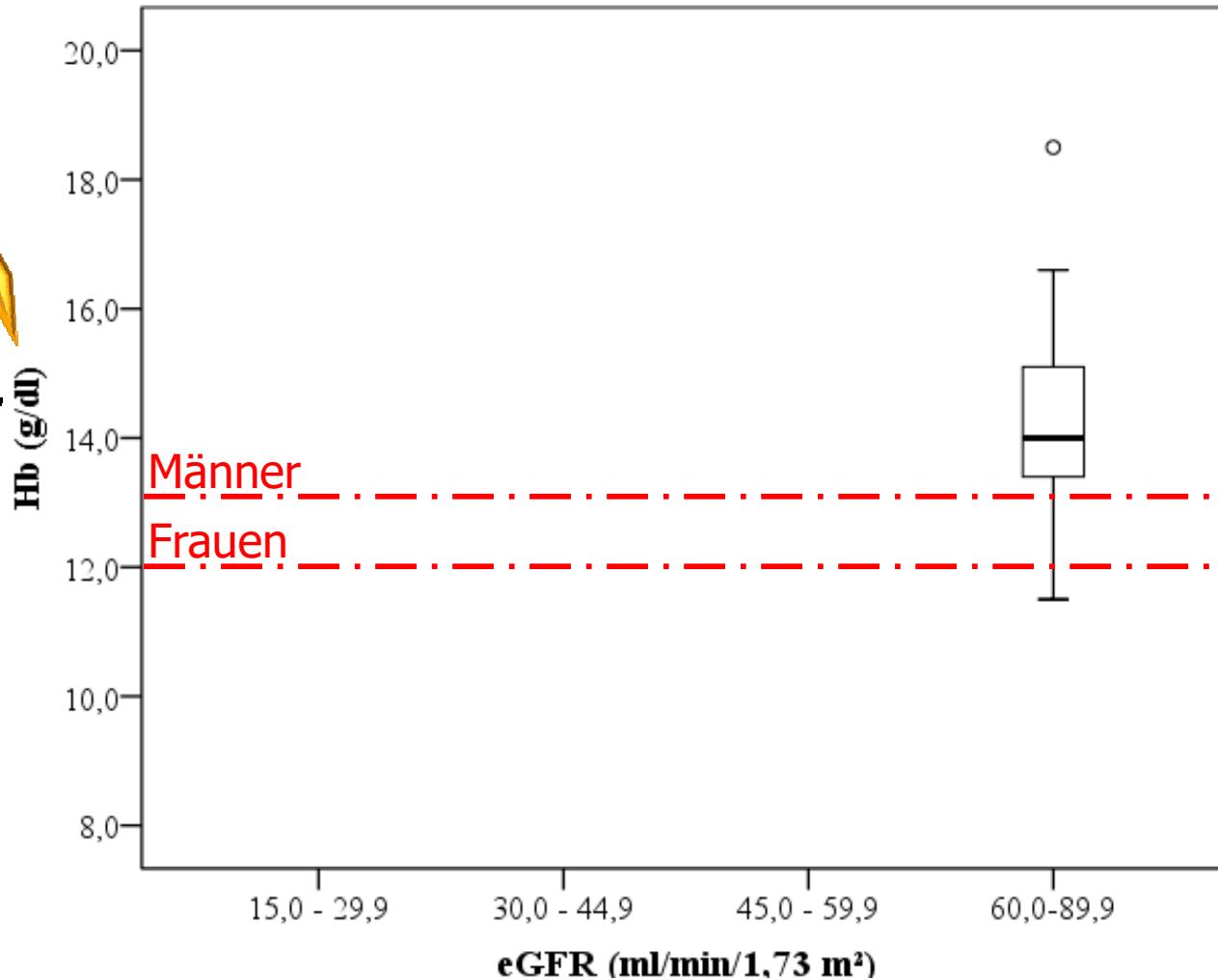
Therapien von

morgen?

HIF Stabilizers

Anämie bei CKD

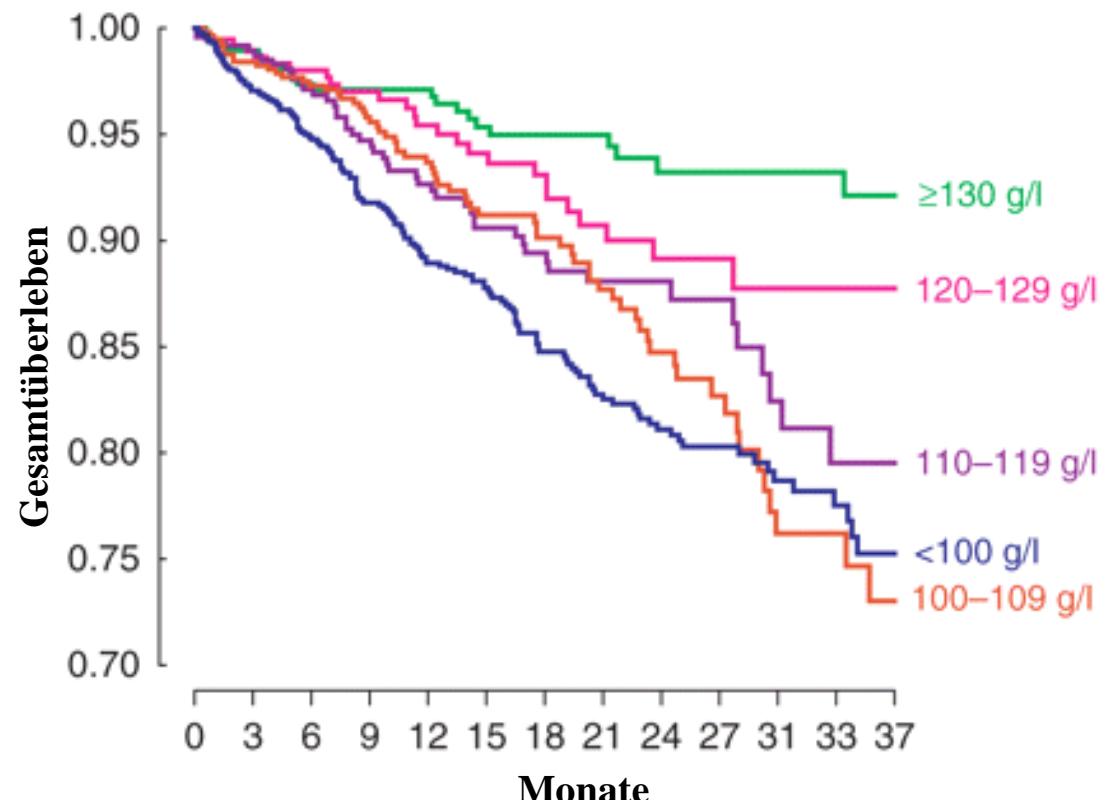
Prävalenz



Anämie bei CKD

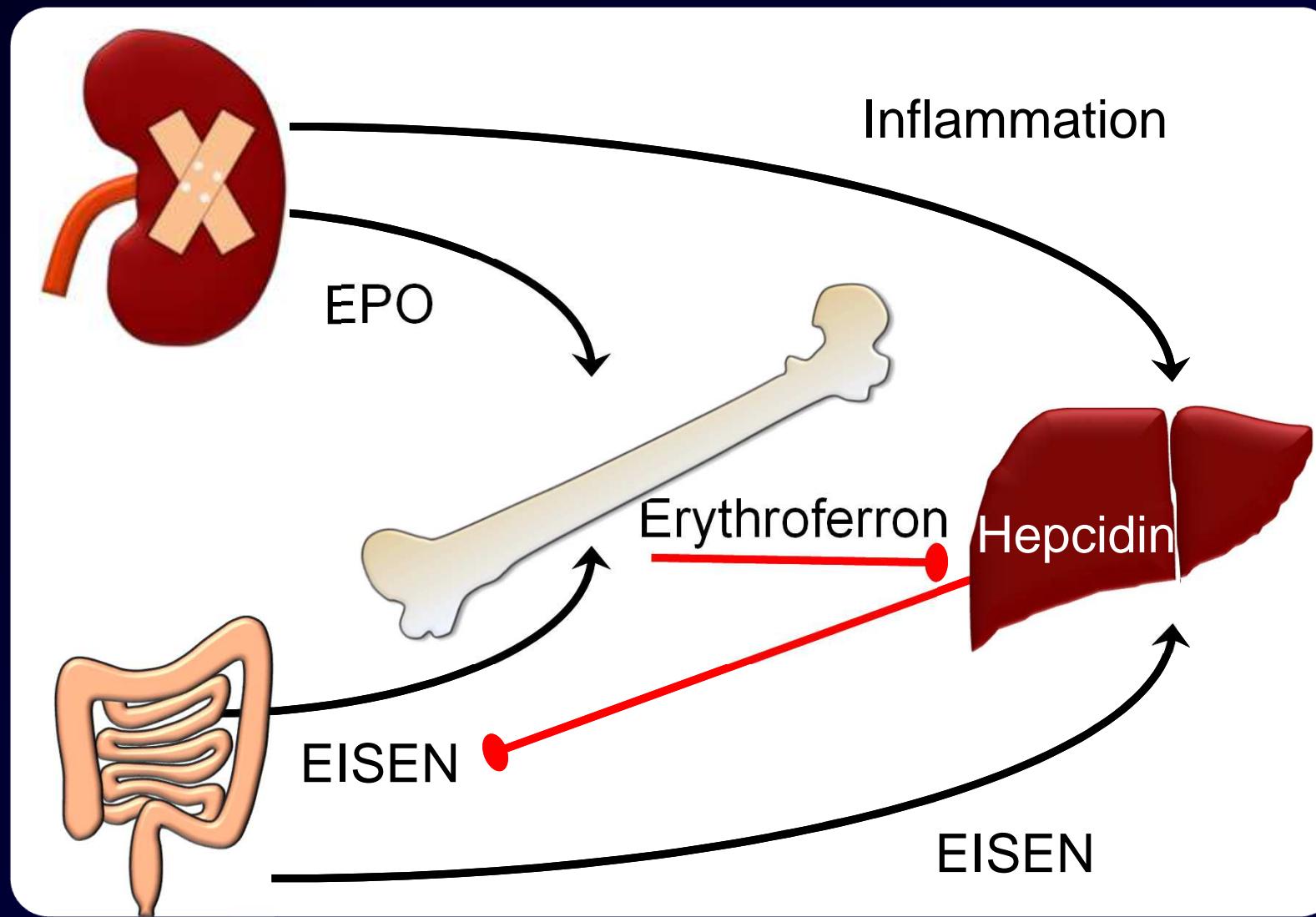
A Levin *et al* Nephrol Dial Transplant 2006

3028 Pat. CKD 3-5; 1998–2002 nephrol. Erstvorstellung
Endpunkt: Überleben bis zum 31.12.2003



Anämie bei CKD

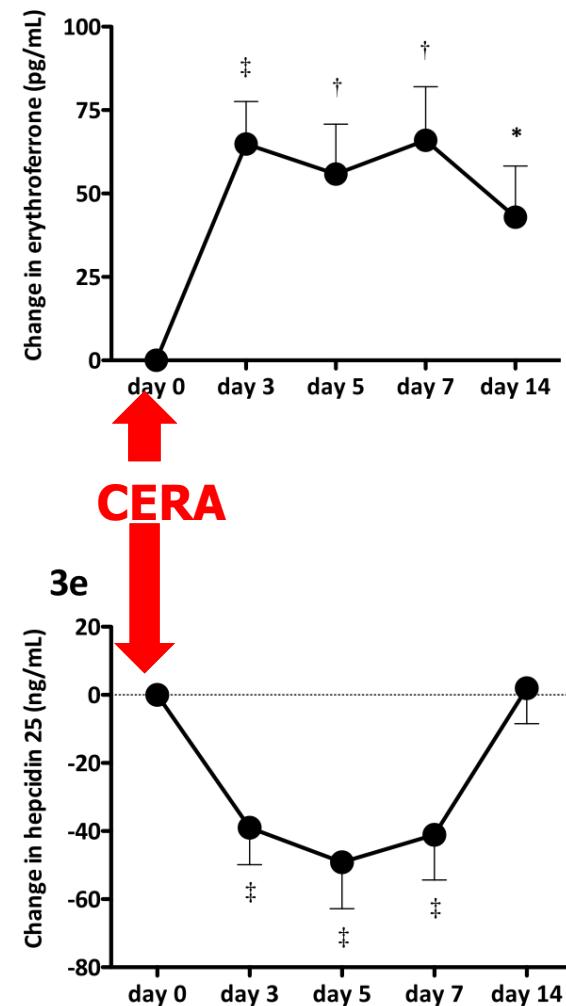
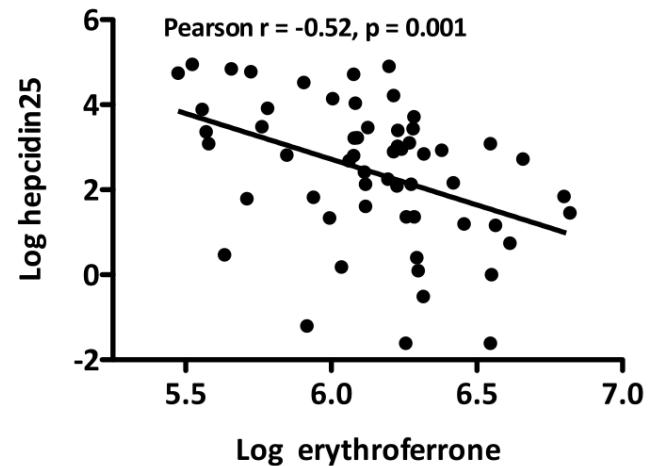
Pathophysiologie





Anämie bei CKD

H Honda et al PLOS ONE 2016





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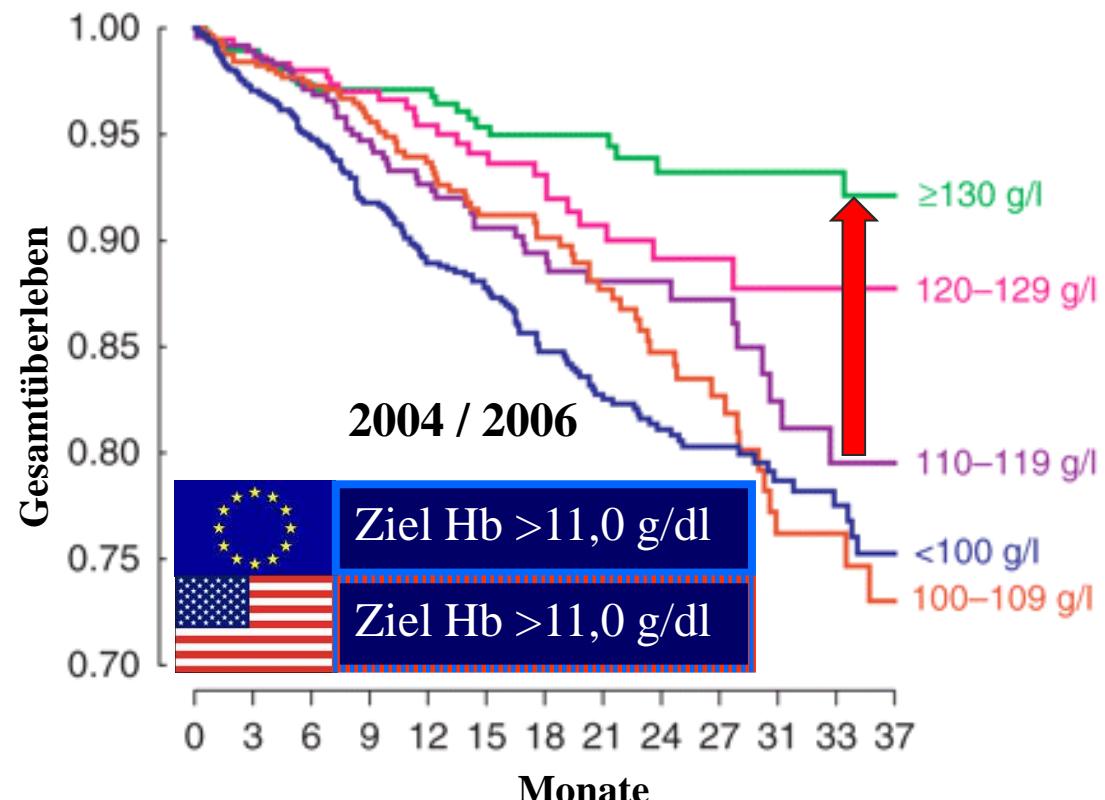
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Anämie bei CKD

MA Pfeffer et al New Engl J Med 2009



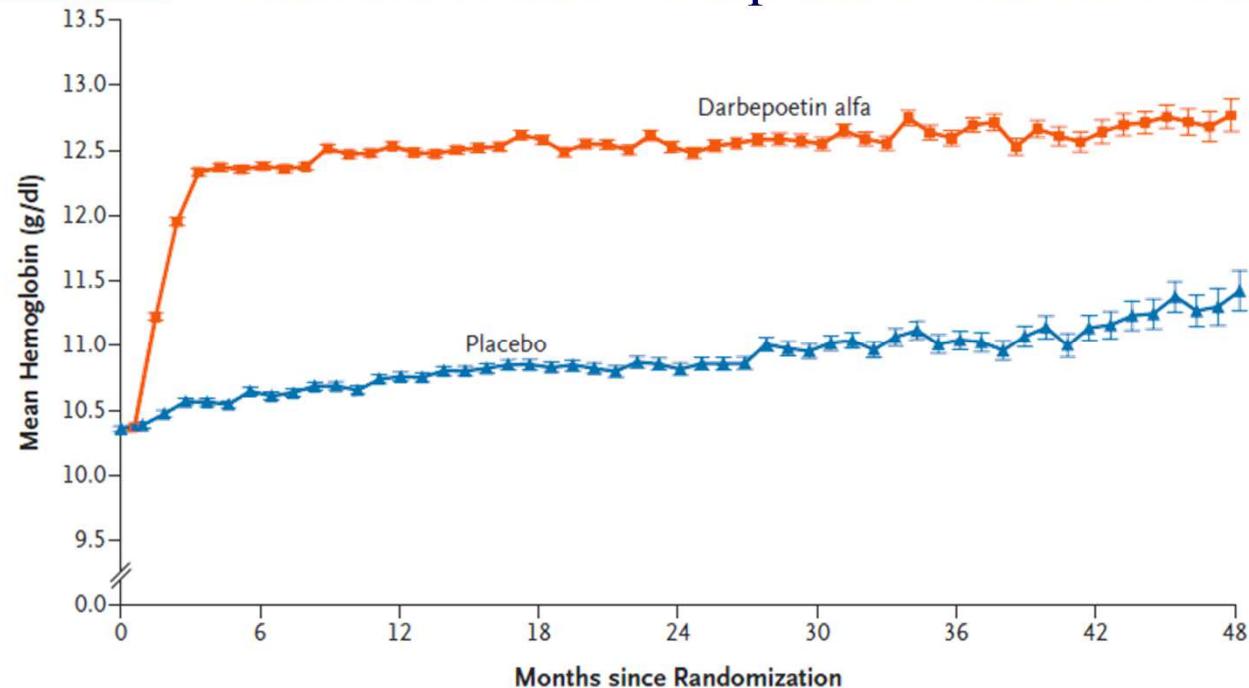
Diabetes Mellitus 2; GFR 20-60 ml/min/1,73 m²



Hb: 13,0 g/dl vs 9,0 g/dl

Primärer CV Endpunkt: CV Ereignis / Tod

Primärer renaler Endpunkt: ESRD / Tod



Anämie bei CKD

MA Pfeffer et al New Engl J Med 2009



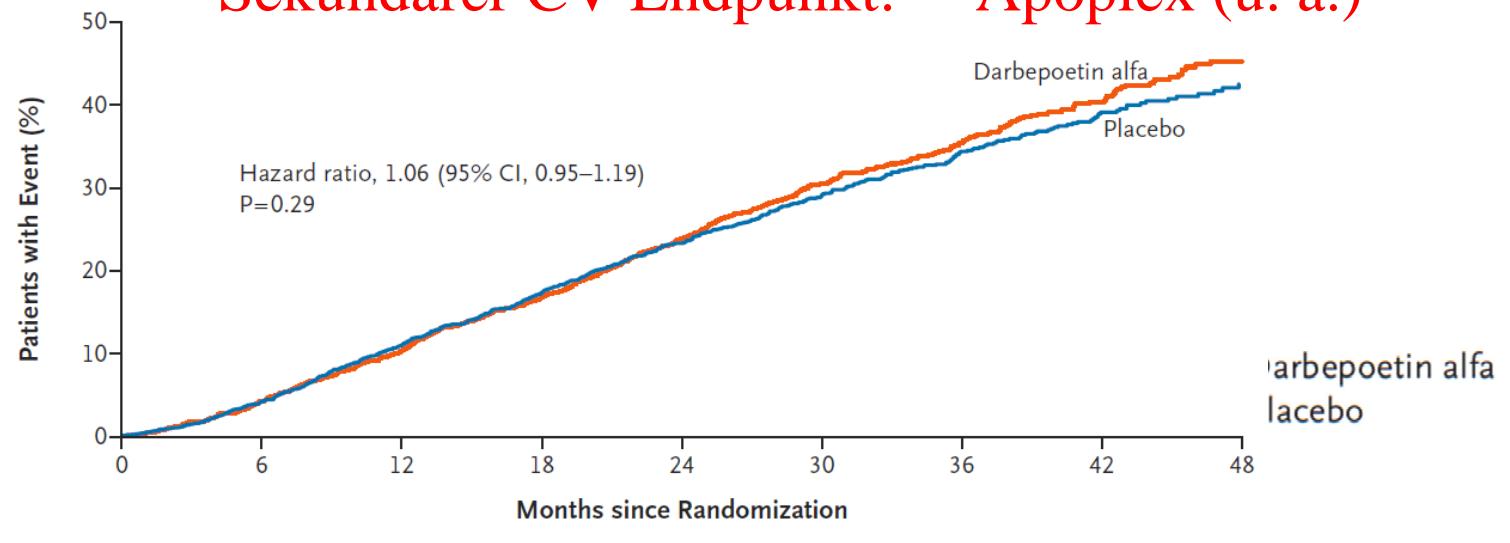
Diabetes Mellitus 2; GFR 20-60 ml/min/1,73 m²



Primärer CV Endpunkt: CV Ereignis / Tod

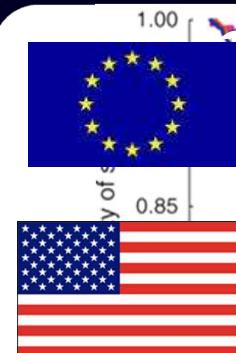
Primärer renaler Endpunkt: ESRD / Tod

Sekundärer CV Endpunkt: Apoplex (u. a.)



Anämie bei CKD

MA Pfeffer et al New Engl J Med 2009



Diabetes Mellitus 2; GFR 20-60 ml/min/1,73 m²
Haemoglobin
Kein Benefit durch
Hb: 13,0 g/dl vs 9,0 g/dl höheren Hb?

Primärer CV Endpunkt: CV Ereignis / Tod
Residuale Confounding?

Primärer renaler Endpunkt: ESRD / Tod
Reverse Causality?

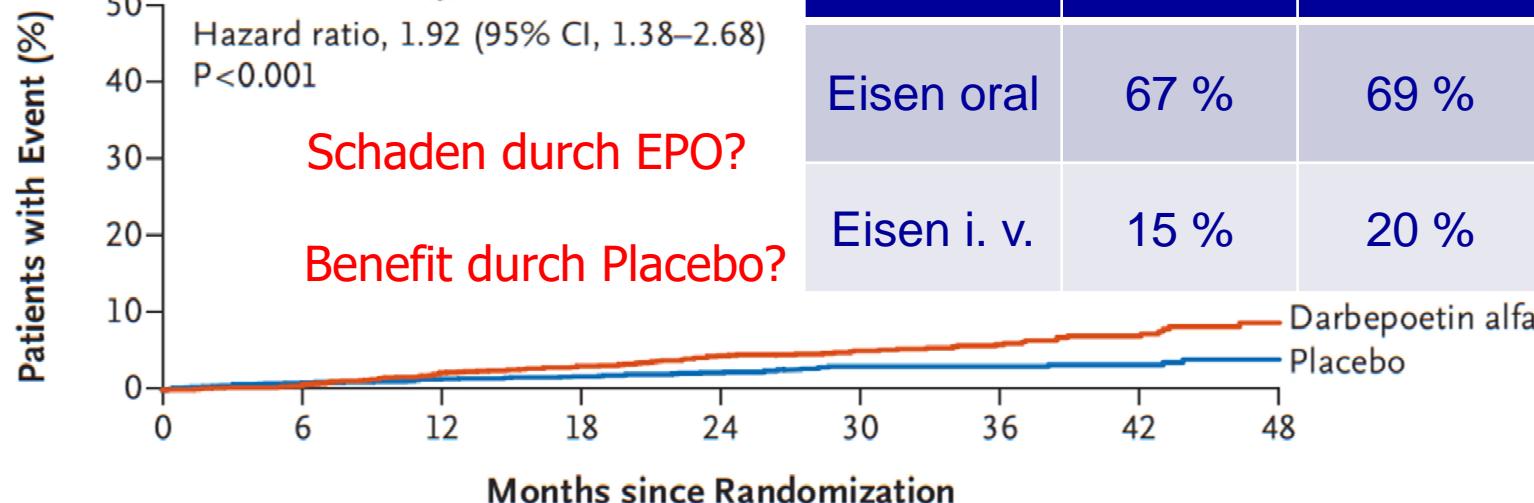
Sekundärer CV Endp

Hazard ratio, 1.92 (95% CI, 1.38–2.68)
 $P < 0.001$

Schaden durch EPO?

Benefit durch Placebo?

TREAT	ESA	Placebo
Eisen oral	67 %	69 %
Eisen i. v.	15 %	20 %





Anämie bei CKD

Intervention (ESA)



U.S. Food and Drug Administration

Protecting and Promoting Your Health

THERAPIEBEGINN

CKD-ND

Hb <10 g/dl UND

Ziel: Ø Transfusion

STOP: Hb >10 g/dl



U.S. Food and Drug Administration

Protecting and Promoting Your Health

THERAPIEBEGINN

CKD-D

Hb <10 g/dl

STOP: Hb >11 g/dl



CKD-ND

THERAPIEBEGINN

Hb <10 g/dl UND

Abwägung Symptome /
Transfusionsbedarf

STOP: Hb >11,5 g/dl



CKD-D

THERAPIEBEGINN

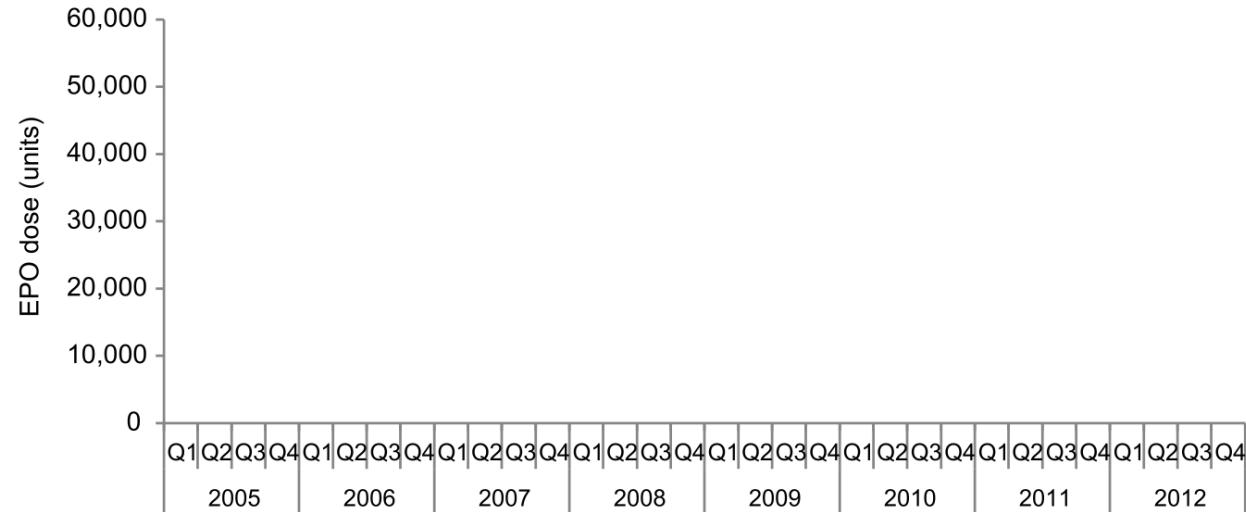
Hb <10 g/dl

STOP: Hb >11,5 g/dl



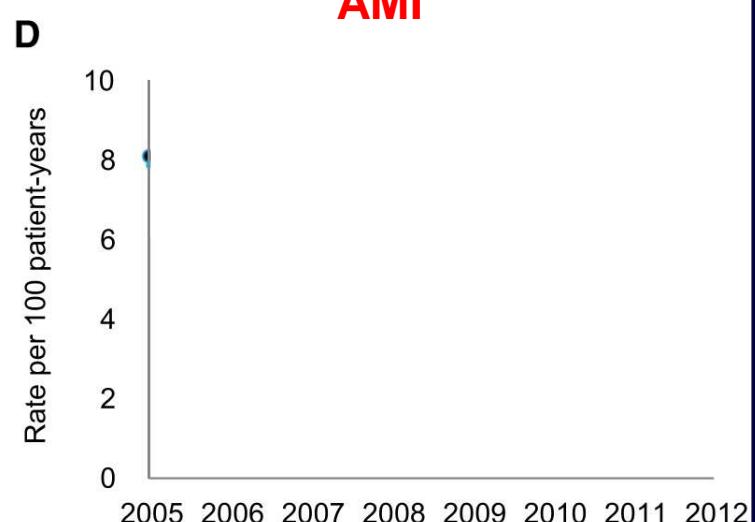
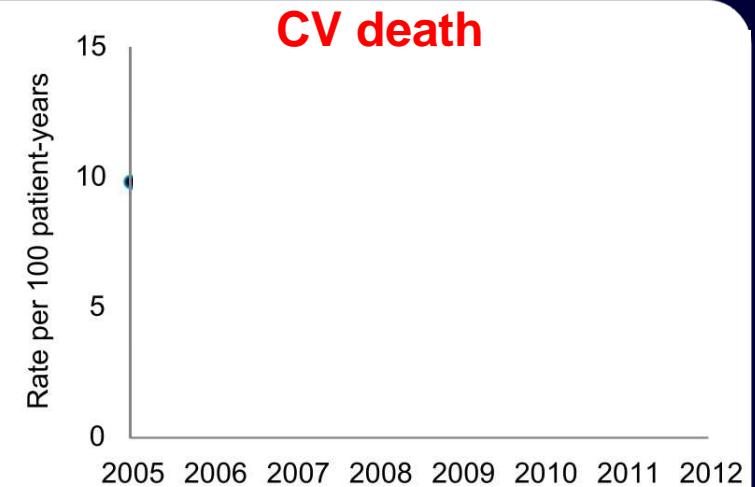
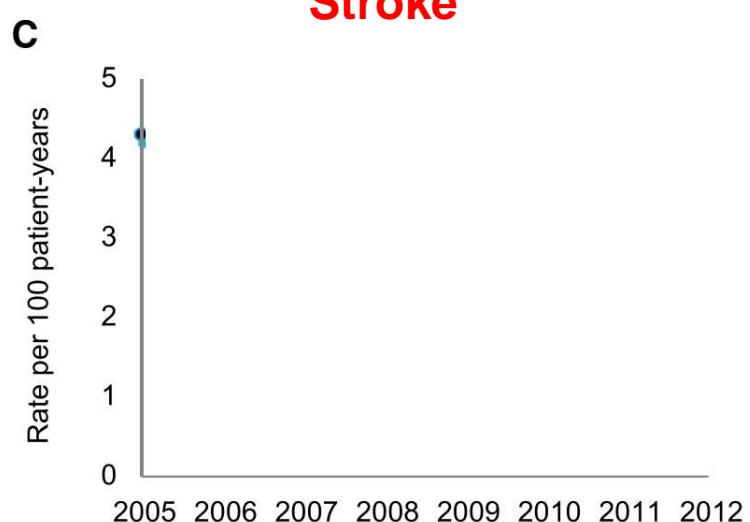
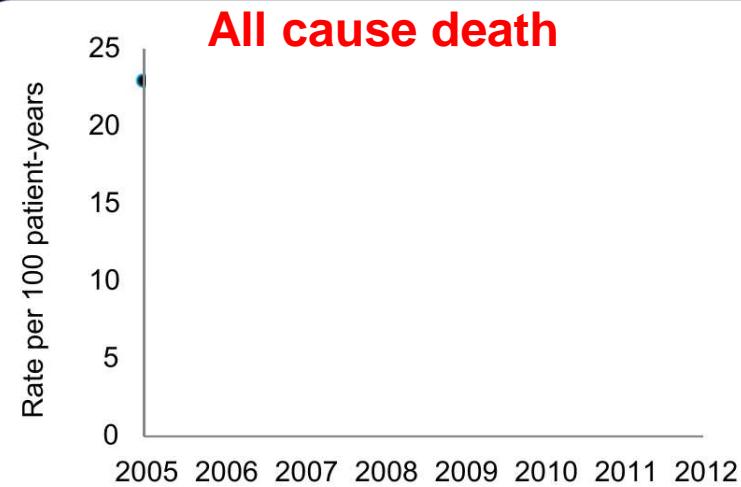
Anämiebehandlung bei CKD 5

G Chertow *et al.* J Am Soc Nephrol 2016



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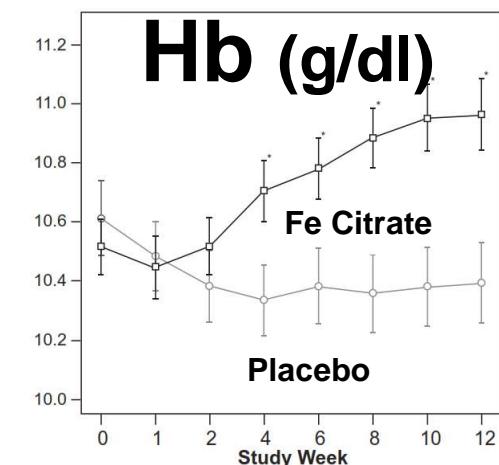
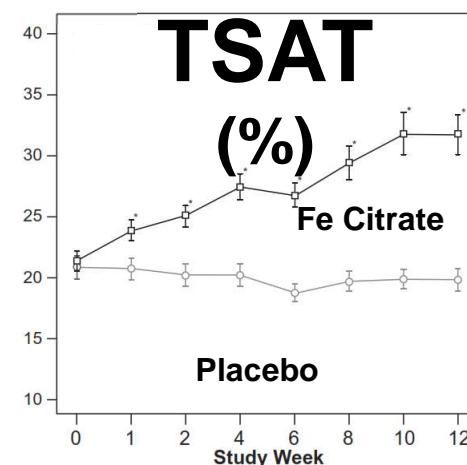
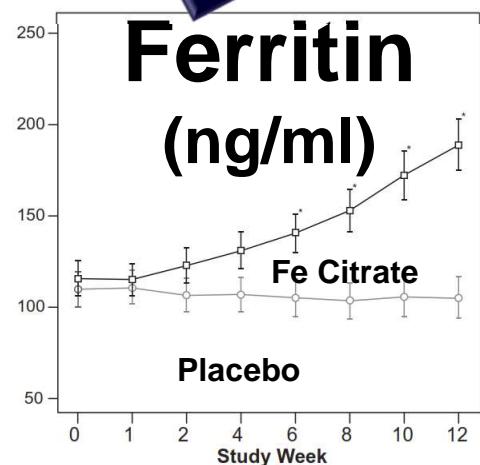
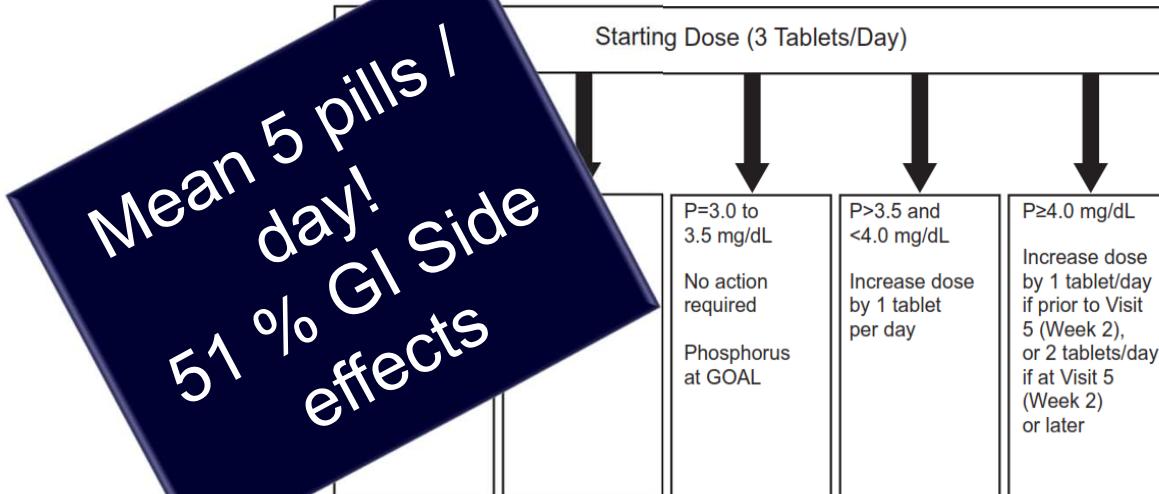
HIF Stabilizers



Effects of ferric citrate on Anemia

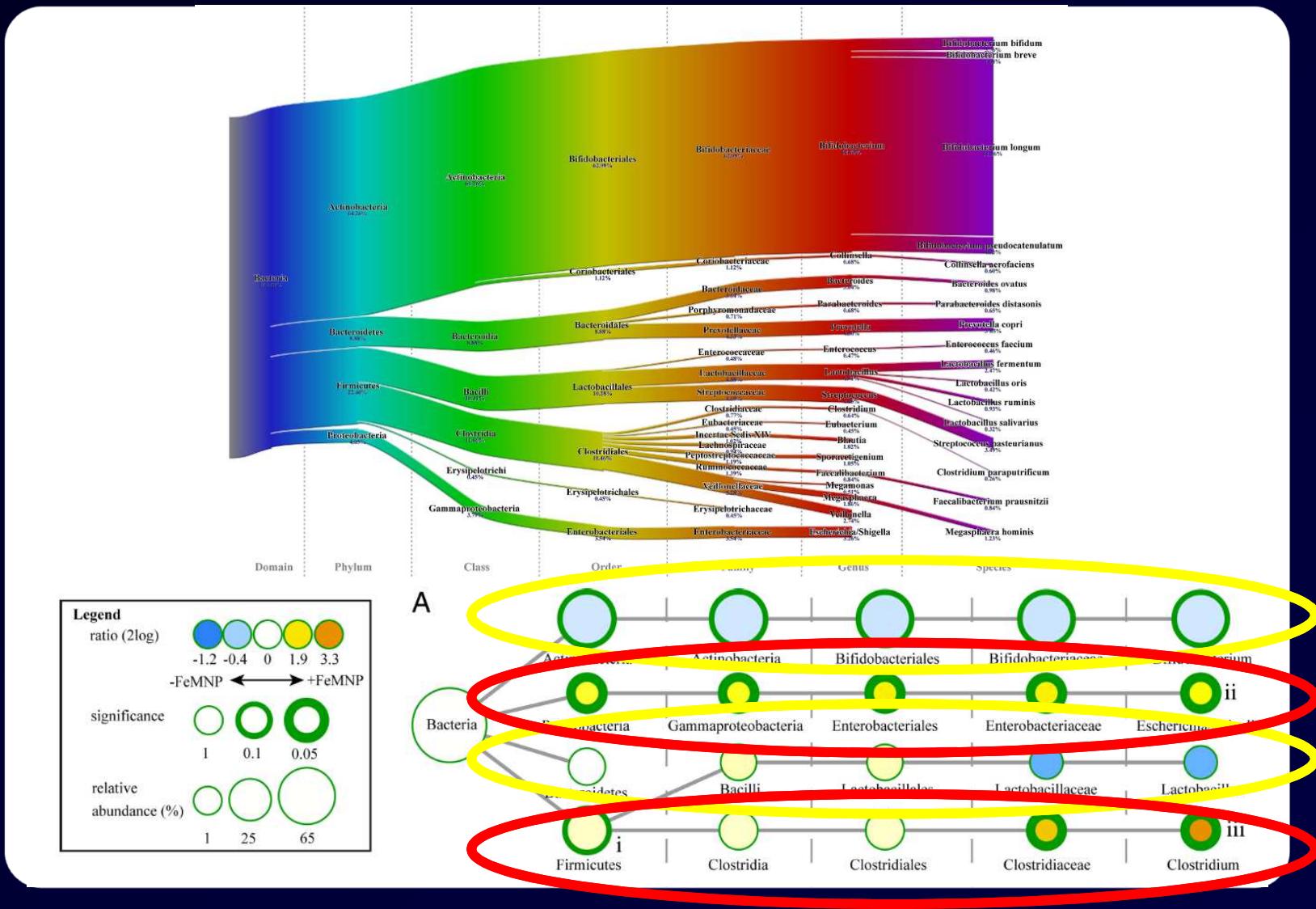
G Block et al. Am J Kid Dis 2015

Mean 5 pills /
day!
51 % GI Side
effects



Iron fortification will affect gut microbiome

T Jaeggi et al. Gut 2016



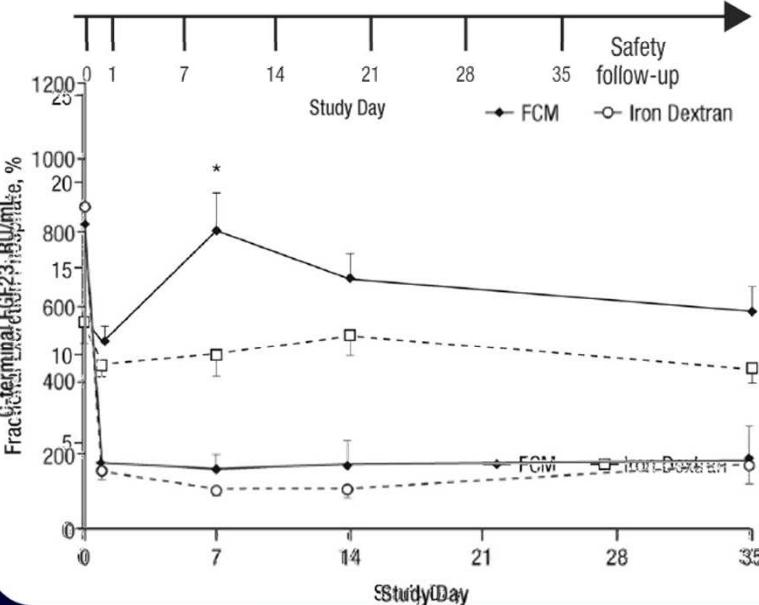
Effects of *i. v.* iron compounds on FGF-23

M Wolf et al. J Bone Miner Res 2013

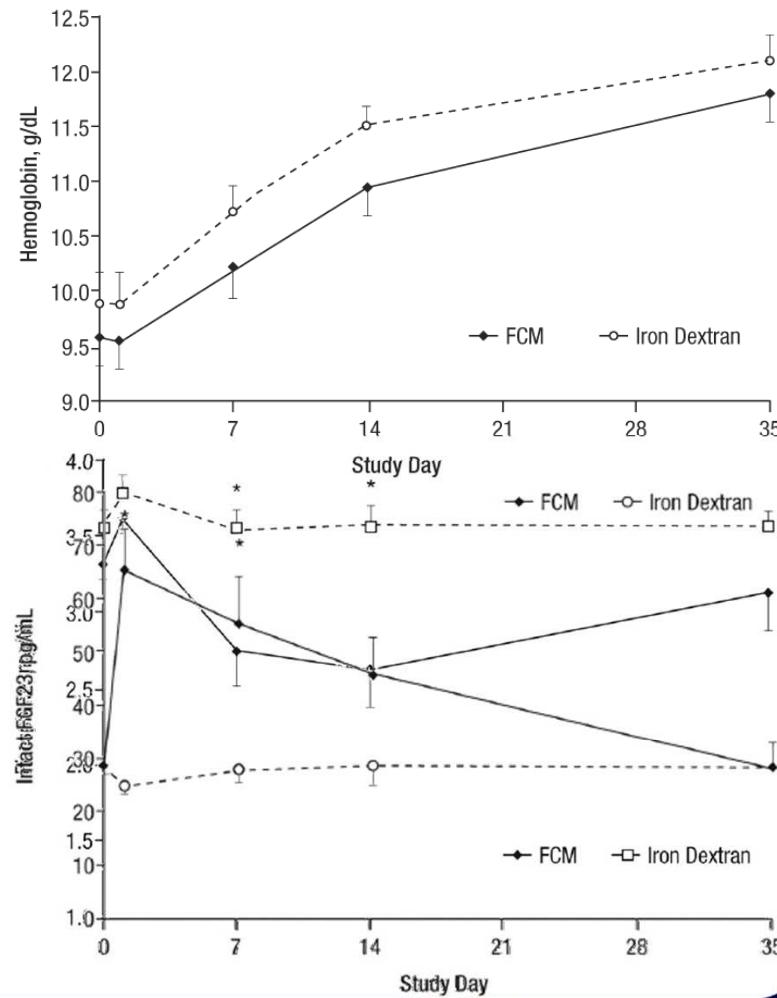
Heavy uterine bleeding
Hgb < 12 g/dL
&
Ferritin \leq 100ng/mL
Or
Ferritin \leq 300ng/mL
with TSAT \leq 30%

N = 69

Ferric carboxymaltose, 15 mg/kg up to 1000mg x 1 on study day 0
Randomization
Iron dextran, 15 mg/kg up to 1000mg x 1 on study day 0



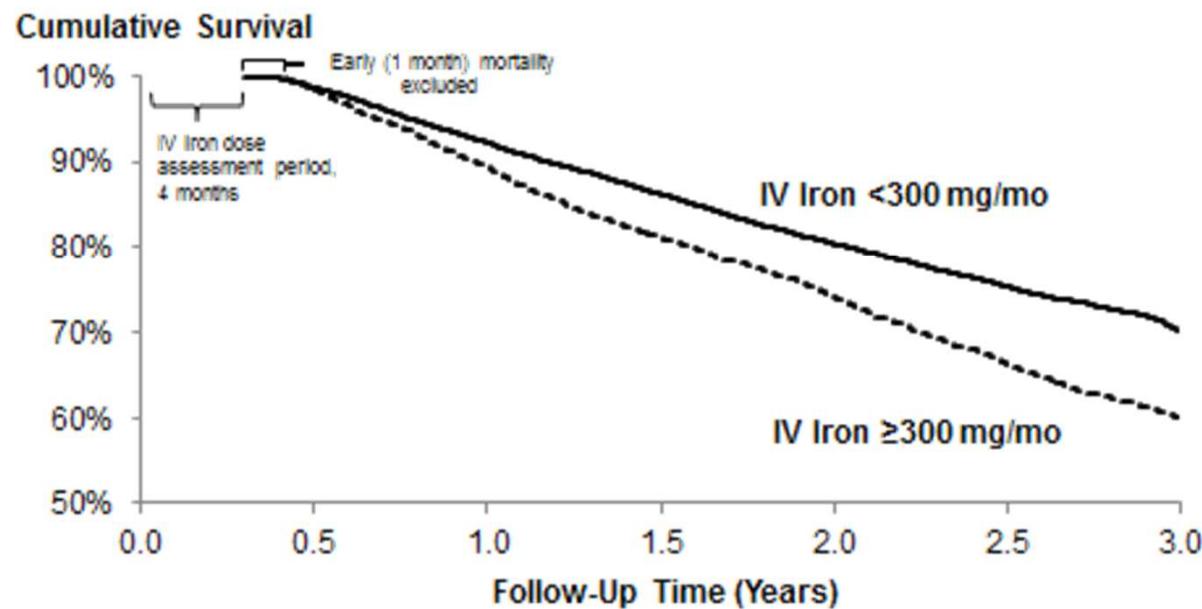
A



Anämiebehandlung bei CKD 5

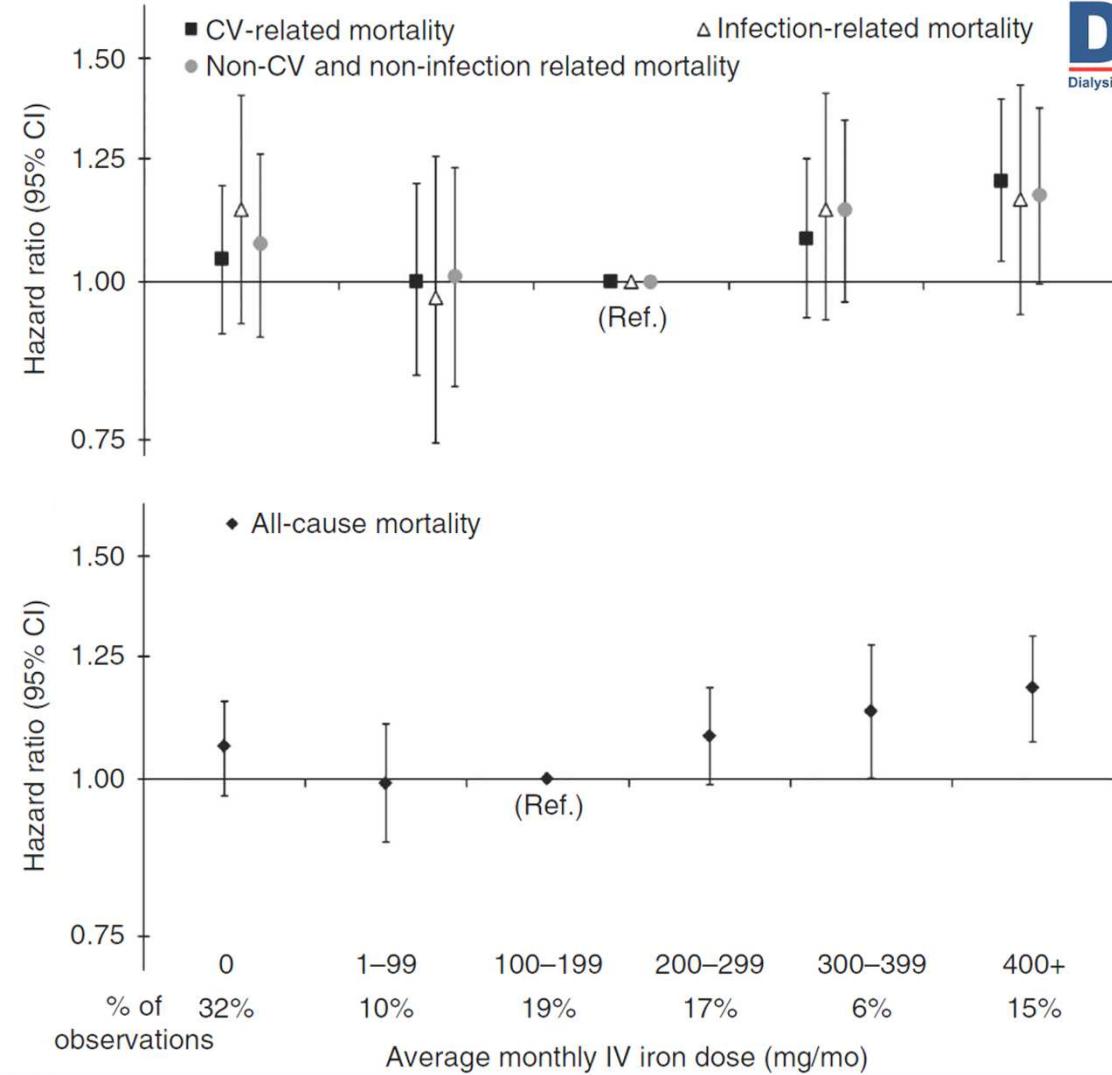
G. Bailie et al. Kidney Int 2014

- 32435 CKD 5 patients from four continents
- Four months baseline data
- Mean iv Iron dose (IV iron mg / mo)
- Median FU 1.7 years



Anämiebehandlung bei CKD 5

G. Bailie et al. Kidney Int 2014





Anämiebehandlung – Eisentherapie

KDIGO Controversies Conference

PIVOTAL
Proactive IV iron therapy in hemodialysis patients

Network of Sites



www.kidneyresearchuk.org

Registered Charity No: 252892 Registered Scottish Charity No: SC039245



Founded 1959
Kidney Research Consortium:
Renal Anemia CSG

King's College Hospital **NHS**

NHS Foundation Trust

England

Queen Elizabeth Hospital, Birmingham; Heartlands Hospital, Birmingham; Royal Free, London, King's College Hospital, London; Guy's & St Thomas', London; St Helier, Surrey; St George's, London; Royal Liverpool Hospital, University Hospital Aintree; Sheffield Teaching Hospital; Lister Hospital, Stevenage; Salford Royal Hospital, Manchester; Manchester Royal Hospital; Queen Alexandra Hospital, Portsmouth; Kent & Canterbury Hospital, Leicester General Hospital, Hull Royal Infirmary; Freeman Hospital, Newcastle; Churchill Hospital, Oxford; University Hospital of North Staffordshire, Stoke-on-Trent; Southmead Hospital, Bristol; Royal Cornwall Hospital, Nottingham City Hospital; Norfolk & Norwich Hospital; New Cross Hospital, Wolverhampton; Royal London Hospital; Wirral University Teaching Hospital; Royal Shrewsbury Hospital, Royal Devon & Exeter Hospital, Royal Preston Hospital, St James' Hospital, Leeds; Hammersmith Hospital, London

Wales

Morrison Hospital, Swansea; University Hospital, Cardiff

Scotland

Western Infirmary, Glasgow; Victoria Hospital, Kirkcaldy; Ninewells Hospital, Dundee; Dumfries (PI tbc), Edinburgh (PI tbc)

N. Ireland

Belfast City Hospital

Kidney Research UK
Funding research to save lives



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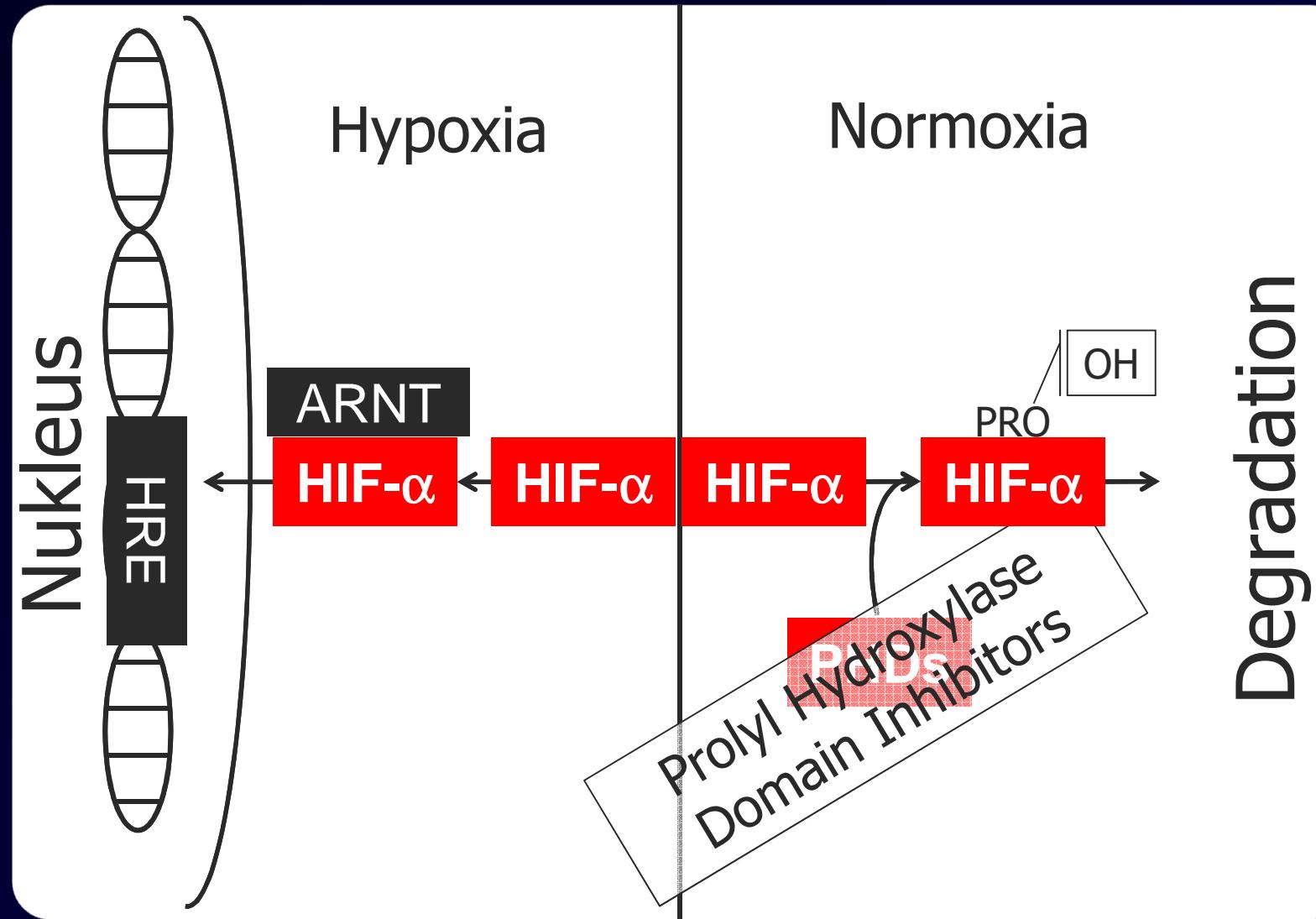
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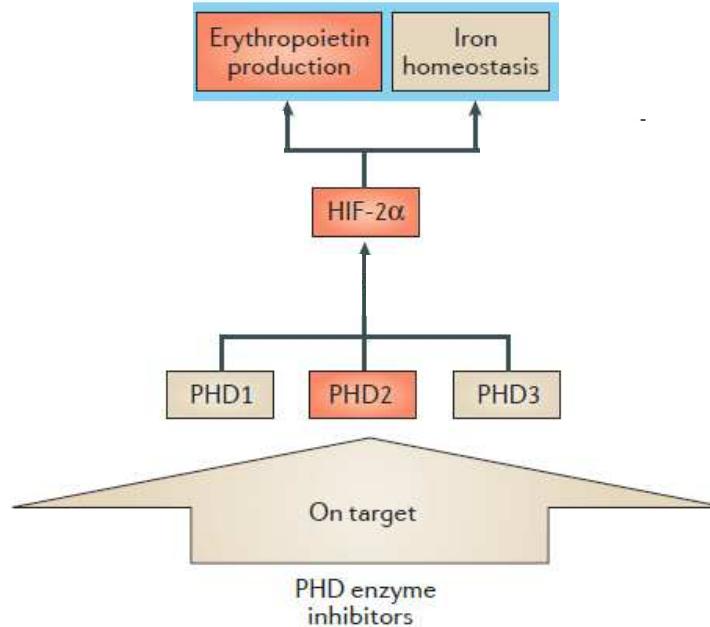
Anämiebehandlung – PHDs

C Forristal Stem Cells Translational Medicine 2014



Anämiebehandlung – PHDIs

PH Maxwell and KU Eckardt Nat Rev Nephrol 2016



Anämiebehandlung - GSK 1278863

L Holdstock et al J Am Soc Nephrol 2016

Non-dialysis study (CKD G 3 – G 5)

No EPO in preceding weeks

Stable Hb 8.5 –11.0 g/dl

Ferritin \geq 40 ng/ml

Active Treatment 4 weeks
Follow-up 2 weeks

Placebo

GSK 1278863

0,5 mg

GSK 1278863

2 mg

GSK 1278863

5 mg

No Treatment

Hb (g/dL)

9.0 10.0 11.0 12.0

BL

W 1

W 2

W 3

W 4

No Treatment

9.0 10.0 11.0 12.0



Anämiebehandlung - GSK 1278863

L Holdstock et al J Am Soc Nephrol 2016

Non-dialysis study (CKD G 3 – G 5)

No EPO in preceding weeks

Stable Hb 8.5 –11.0 g/dl

Ferritin \geq 40 ng/ml

Active
Treatment
4 weeks

EPO (U/I)
(BL / peak)

Δ Hepcidin
(μ g/l)

Placebo

GSK 1278863

0,5 mg

GSK 1278863

2 mg

GSK 1278863

5 mg

12.4 / 16.6

13.8 / 15.6

9.9 / 22.4

11.2 / 34.4

-7.3

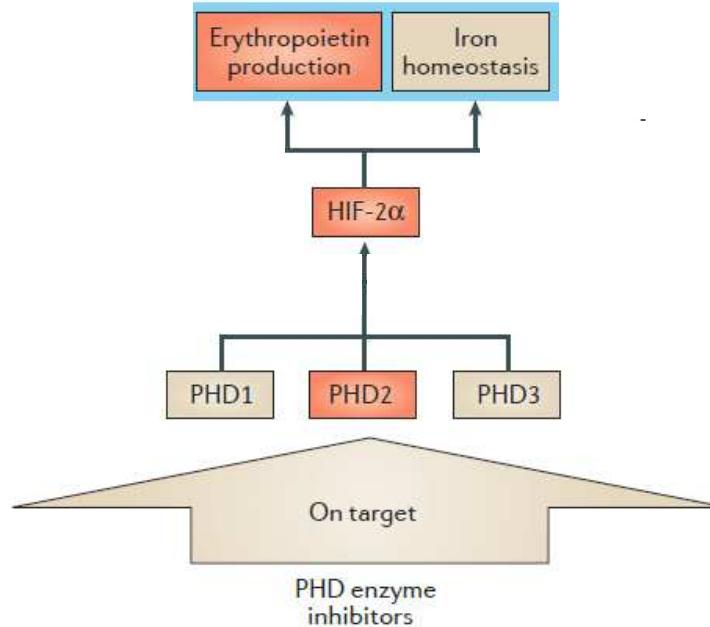
-16.2

-82.1

-143.6

Anämiebehandlung – PHDIs

PH Maxwell and KU Eckardt Nat Rev Nephrol 2016





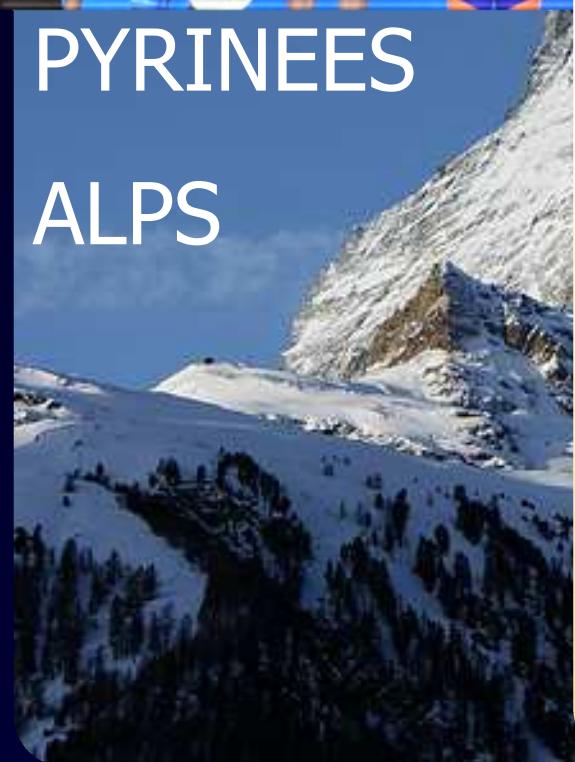
Anämiebehandlung – PHDI

III Studien



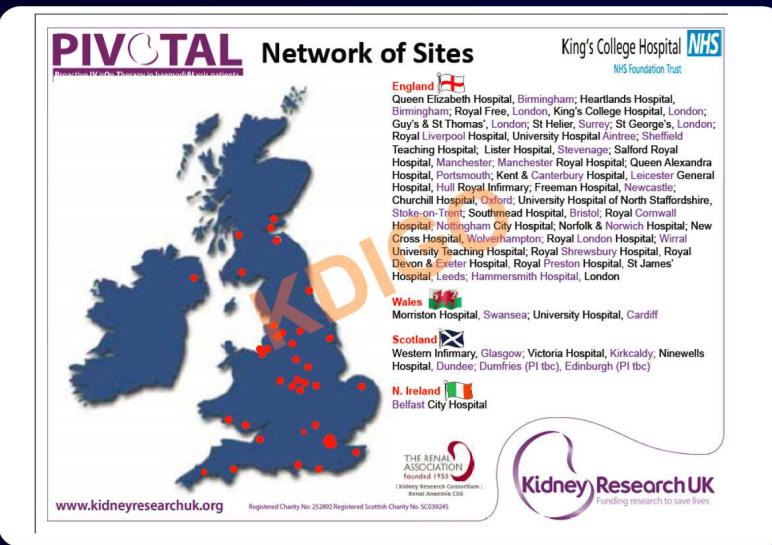
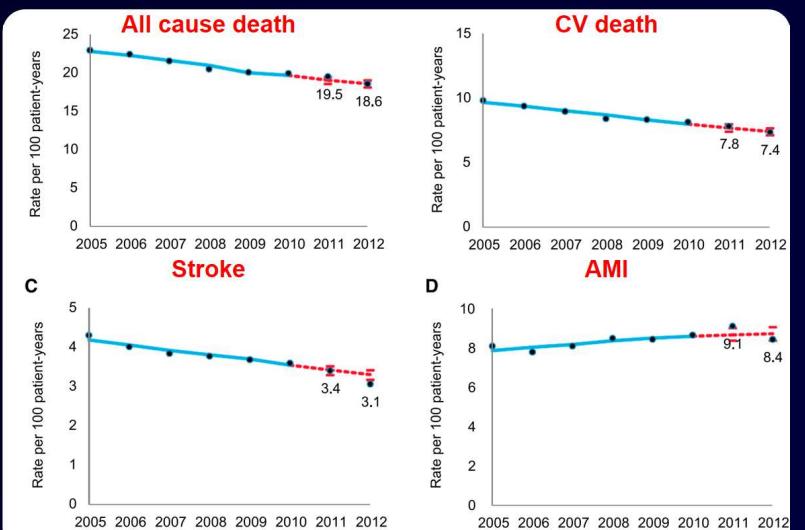
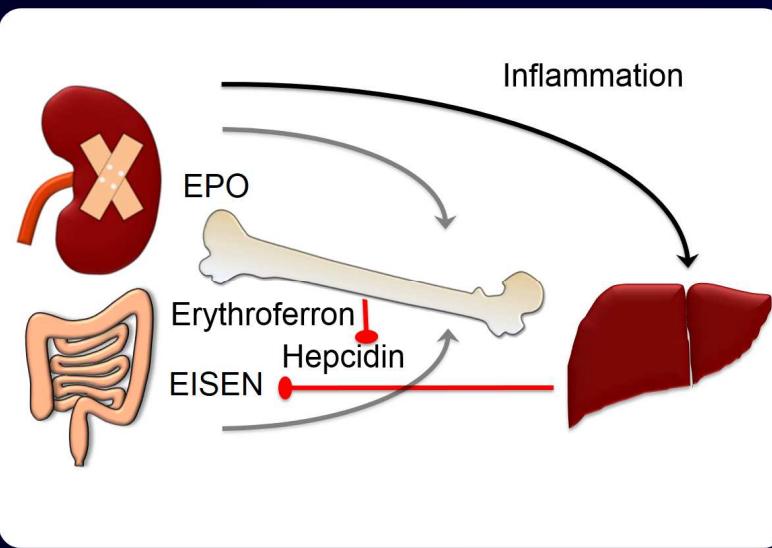
PYRINEES

ALPS



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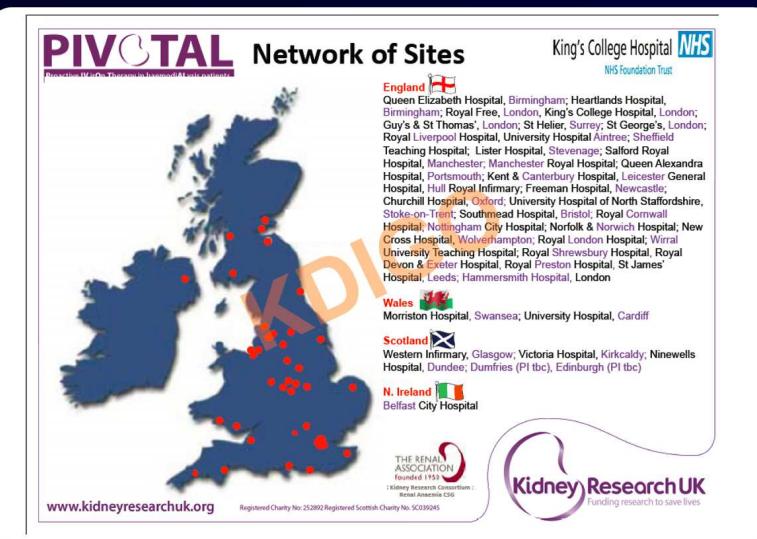
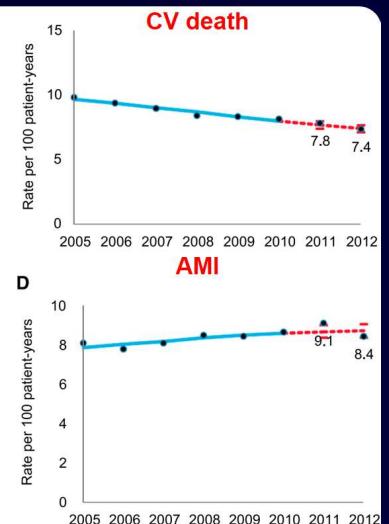
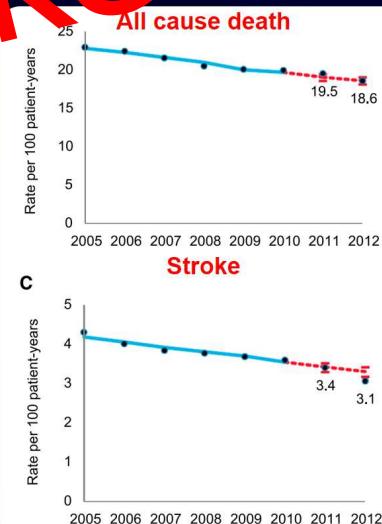
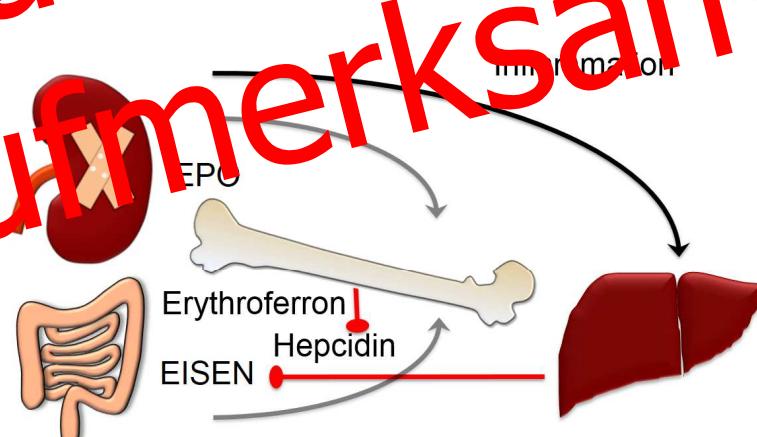
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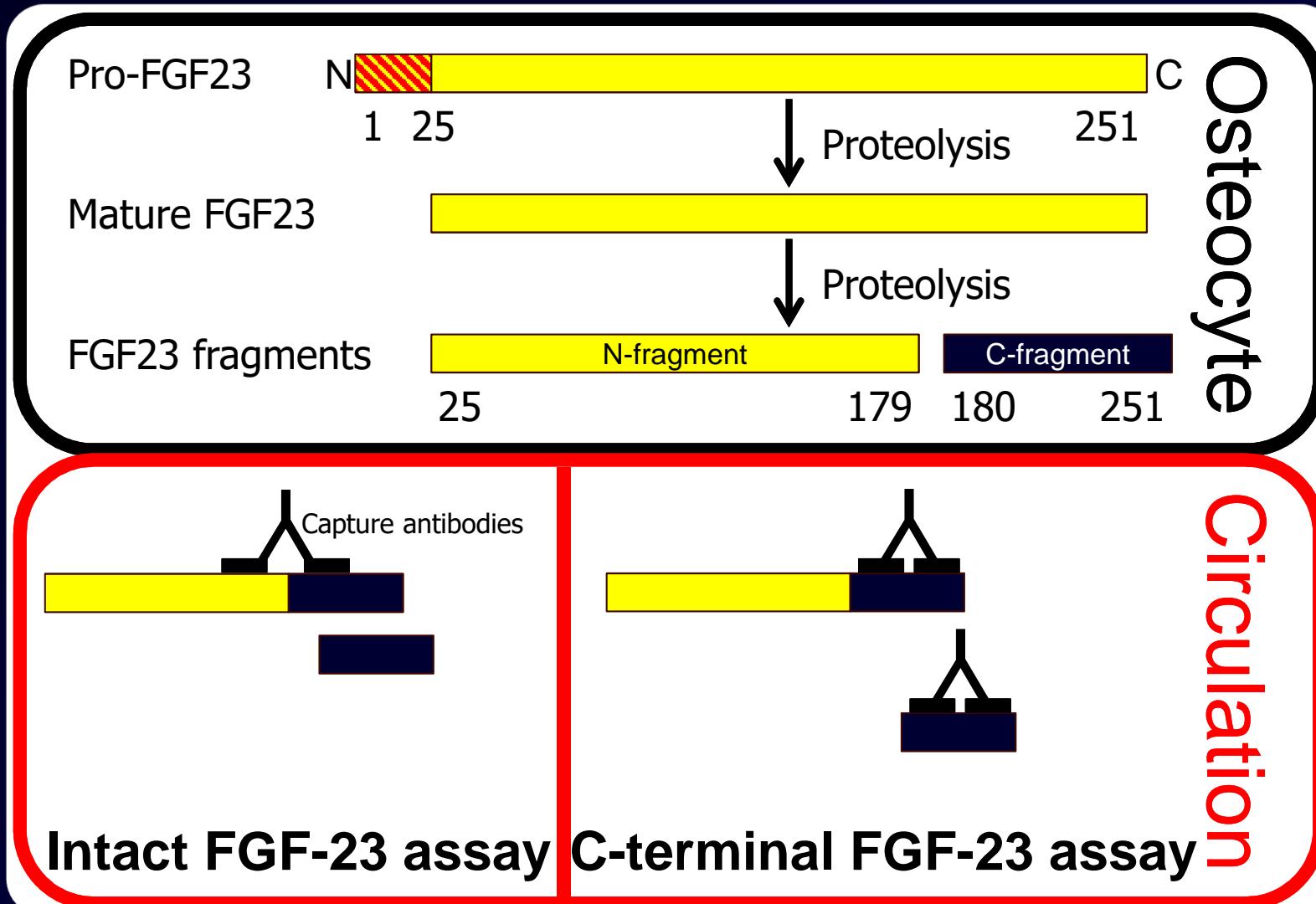
Danke für Ihre
Aufmerksamkeit





FGF-23 production and cleavage

M. Wolf / K. White Curr Opin Nephrol Hypertens 2014



FGF-23 production and cleavage

M. Wolf / K. White Curr Opin Nephrol Hypertens 2014

