PATIENT BLOOD MANAGEMENT IN RENAL NEPHROLOGY

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Outline

- Chronic kidney disease and anaemia
- How to evaluate iron deficiency anaemia
- How to replace iron - practical tips
- How to initiate and maintain erythropoiesis stimulating agent ESA - what target of Hb to aim, and why
Main reference

- KDIGO clinical practice guideline for anemia in chronic kidney disease (2012)

- NICE guideline recommendation on diagnosis and management of iron deficiency in CKD (2016)

- Recent publication after 2016 guidelines
Case 1

- A 75-year-old smoker
- Hypertension for 2 years and told to have chronic kidney disease
- Knee pain due to OA; self medication with COX-II inhibitor nimesulide for 4 weeks
- ESR 25 mm/hour, Hb 11.3 g/dL, serum Cr 180 µmol/L
Case 1

- No improvement after stopping COX-II inhibitor (after 6 months) with persistent abnormality
- Hb 11.9 g/dL, serum Cr 170 µmol/L, urine protein 0.3 g/day
- CKD-EPI equation estimated GFR 37 ml/min/1.73 m²
# Staging of CKD

<table>
<thead>
<tr>
<th>GFR category (mL/min/1.73 m²)</th>
<th>1 if CKD</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4+</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 Normal or high ≥90</td>
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<td>G2 Mildly decreased 60–89</td>
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<tr>
<td>G3a Mildly to moderately decreased 45–59</td>
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<tr>
<td><strong>G3b Moderately to severely decreased 30–44</strong></td>
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<tr>
<td>G4 Severely decreased 15–29</td>
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<td>G5 Kidney failure &lt;15</td>
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<table>
<thead>
<tr>
<th>Persistent albuminuria categories</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description and range</td>
<td></td>
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<tr>
<td>Normal to mildly increased</td>
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<tr>
<td>Moderately increased</td>
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<tr>
<td>Severely increased</td>
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<tr>
<td>&lt;30 mg/g &lt;3 mg/mmol</td>
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<tr>
<td>30–300 mg/g 3–30 mg/mmol</td>
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<tr>
<td>&gt;300 mg/g &gt;30 mg/mmol</td>
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</table>

Case 1

- Stage G3bA3 chronic kidney disease with serum Cr 170 μmol/L and Hb 11.9 g/dL, normochromic normocytic

- Is he suffering from anaemia of chronic kidney disease?
Renal anaemia

- Not all anaemic patients with CKD are “renal anaemia”

- When to think of (and exclude) other causes of anaemia?

- Is there really a disease called “renal anaemia” or anaemia of CKD?
Rule of thumb

If eGFR > 60 ml/min/1.73 m², anaemia is more likely to be related to other causes (and triggering other investigation)

Pathophysiology of Anaemia

- Decreased RBC production
- Increased RBC destruction
- Blood Loss
Which types of Anaemia

- Decreased RBC production
  - Anaemia of chronic illness or anaemia of CKD
  - Increased RBC destruction
  - Blood Loss
Anaemia of CKD - Why?

Decreased \textit{erythropoietin} EPO production (inappropriately low EPO despite anaemia)
Anaemia - more than EPO deficiency

**ESA resistance** - relative decrease in bone marrow response to erythropoiesis stimulating agent (ESA)
- Uraemic inhibitors (for example, parathyroid hormone, inflammatory cytokines)
- Functional or absolute iron deficiency

**Others**
- Blood loss (either occult or overt)
- Reduced half-life of circulating blood cells
Molecular mechanism of ESA resistance

**Hepcidin**

- Inhibits iron absorption from small intestine and release from macrophages (iron store)
- Production increased by inflammation
- Higher level due to kidney failure itself (even without inflammation)
Hepcidin in CKD

- Oral iron less likely to be taken up by bone marrow macrophage
- Blunted bone marrow response to erythropoietin
Diagnosis of Iron Deficiency

In practice, we are asking:

**Does the patient respond to iron therapy with an increase in haemoglobin level?**
Iron Deficiency: TSAT

- Transferrin saturation
- Serum iron level as a percentage of total iron-binding capacity (TIBC)
- If $\text{TSAT} < 20\%$ is used as threshold for diagnosing iron deficiency, sensitivity (63%) and specificity (80%) is suboptimal
Iron Deficiency: Ferritin level

- **A low ferritin level**: reliable marker of “absolute” iron deficiency
- **A high ferritin level**: can be indicative of inflammation (acute-phase reactant)
- **A normal ferritin level**: cannot reliably exclude iron deficiency in the presence of inflammation
Case 1

- TSAT 22%
- Ferritin 270 pmol/L

Would you give him iron supplement, and what form?
2012 Cochrane review

- Compare oral versus iv iron in CKD patients
- Haemoglobin, ferritin, TSAT increased significantly more with iv than oral iron therapy
- Adverse effects reported in only 50% of included studies

KDIGO clinical practice guideline

Kidney Disease: Improving Global Outcomes (KDIGO)

For adult CKD patients with anaemia not on iron or ESA therapy we suggest a trial of iv iron if

- an increase in Hb concentration without starting ESA is desired and

- TSAT ≤ 30% and ferritin ≤ 1125 pmol/L
Meta-analysis

Intravenous iron associated with an increase in risk of infection (RR 1.33; 95% CI 1.10 - 1.64) compared with oral or no iron supplementation

Avoid administering iv iron to patients with active systemic infections (Not Graded)
Higher-dose intravenous iron is not associated with higher risk of mortality, infection, cardiovascular events, or hospitalizations in adult patients on dialysis.

### Oral versus iv iron in CKD patients

<table>
<thead>
<tr>
<th></th>
<th>Oral Iron</th>
<th>Intravenous Iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioavailability</td>
<td>X</td>
<td>√</td>
</tr>
<tr>
<td>Cost</td>
<td>√</td>
<td>X</td>
</tr>
<tr>
<td>Ease of administration</td>
<td>√</td>
<td>X</td>
</tr>
<tr>
<td>Adherence</td>
<td>X</td>
<td>√</td>
</tr>
<tr>
<td>Vein preservation</td>
<td>√</td>
<td>X</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal side effect</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Concern with hepcidin</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Infection concern</td>
<td></td>
<td>?</td>
</tr>
<tr>
<td>Iron overload</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

Practical tips for iv Iron

- The first dose should be administered in a clinical facility

- The iv doses of iron sucrose (Venofer) should not exceed 200 mg/dialysis - risk for iron not binding immediately to transferrin and resulting in a reaction to labile iron

Newer iron formulations

Iron isomaltoside (Monofer) - a matrix structure that results in tight iron binding and slow release of labile free iron

Ferric carboxymaltose (Ferinject) - another iron complex with a ferric hydroxide core stabilized by a carbohydrate shell, allowing for controlled delivery of iron to target tissues

- Advantage of larger dose administration in a single infusion (20 mg/kg over 15 minutes)
Practical tips for iv Iron

- No need to observe for 30 minutes after completing infusion (not associated with a severe delayed reaction, as is observed with subcutaneous antigen vaccination)

- No evidence for pretreatment with corticosteroids or antihistamines

New Perspective on iv Iron

- Proactive IV Iron Therapy in Haemodialysis Patients (PIVOTAL) Study: 2141 patients on haemodialysis, randomization to high-dose and low-dose group iv iron

- **High-dose** iron sucrose: proactive (400 mg monthly, unless the ferritin concentration >1573 pmol/L or TSAT ≥40%)

- **Low-dose** iron sucrose, reactive (0 to 400 mg monthly, with a ferritin concentration of <449 pmol/L or TSAT <20% being a trigger for iron administration)

• High-dose iv iron noninferior to low-dose intravenous iron regimen administered reactively

• Not associated with higher risks of (composite primary end-point) death, major adverse cardiovascular events, or infection
Benefits of high-dose iv iron

- less likely to receive blood transfusions than those in the low-dose group (hazard ratio, 0.79; 95% CI, 0.65 to 0.95)

- lower doses of erythropoiesis-stimulating agent (median difference, −7539 IU; 95% confidence interval [CI], −9485 to −5582)

Case 1

- Patient received regular monitoring and management of CKD
- Regular treatment with oral iron supplement
- Reached stage 4 chronic kidney disease with serum Cr 470 µmol/L and Hb 9.9 g/dL, normochromic normocytic anaemia
- TSAT 32%, serum ferritin 800 pmol/L

- He asked you about the use of ESA. What would you do?
Erythropoiesis stimulating agent (ESA)

- A drug that has revolutionised the care of anaemic patients with CKD

- Almost completely eradicated severe anaemia of end-stage renal disease (ESRD)

Winearls CG, Oliver DO, Pippard MJ, Reid C, Downing MR, Cotes PM. Effect of human erythropoietin derived from recombinant DNA on the anaemia of patients maintained by chronic haemodialysis. Lancet. 1986;2:1175-1178
Erythropoiesis stimulating agent (ESA)

First generation ESA
- Epoetin alfa
  - Eprex
- Epoetin beta
  - Recormon

Second generation ESA
- Darbepoetin alfa
  - Aranesp
  - NESP
- Methoxy-polyethylene glycol-ePOETIN beta
  - Mircera
Erythropoiesis stimulating agent (ESA)

First generation ESA
- Epoetin alfa
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Second generation ESA
- Darbepoetin alfa
- Aranesp
- NESP
- Methoxy-polyethylene glycol-epoetin beta
- Mircera
Major Benefit of ESA

- Reduced need or avoidance of blood transfusion
- Concern with blood transfusion
  - Large Hb level fluctuation
  - Limited availability
  - Alloantigenic antibodies and subsequent likelihood of kidney transplant (rejection)
Second Generation of ESA

- Longer duration of action
- No difference between iv and sc routes of administration based on the pharmacokinetic properties

<table>
<thead>
<tr>
<th>Drug</th>
<th>Half-life (intravenous)</th>
<th>Half-life (subcutaneous)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epoetin alfa, Eprex</td>
<td>6.8 hours</td>
<td>19.4 hours</td>
</tr>
<tr>
<td>Darbepoetin alfa, NESP</td>
<td>25.3 hours</td>
<td>48.8 hours</td>
</tr>
<tr>
<td>Methoxy polyethylene glycol-epoetin beta, Mircera</td>
<td>130 hours</td>
<td>133 hours</td>
</tr>
</tbody>
</table>

Practical Tips of ESA Use

Monitor (and control) blood pressure at the initial stage of starting ESA

- Adverse event of hypertension much more evident at the beginning of ESA use, when anemia used to be corrected too fast, starting from very low Hb levels, without leaving the cardiovascular system enough time to adapt to new condition
Hypertension from ESA Use

Avoid aiming for excessively high Hb level

- Targeting higher Hb levels with ESA therapy worsens hypertension
- Meta-analysis: cumulative risk of hypertension has decreased over time

Hb level: Do not Go too High

Meta-analysis of 9 randomized trials (5143 patients):
Raising Hb to higher targets

- Increase risk for **poorly controlled blood pressure** (risk ratio 1.27)
- Increase risk of **arteriovenous access thrombosis** (risk ratio 1.34)

High Hb Linked to worsening Hypertension

ESA - Correct Anaemia but not Aiming High

Normalization of Hemoglobin Level in Patients with Chronic Kidney Disease and Anemia
Tilman B. Drechsle, M.D., Francesco Locatelli, M.D., Naomi Glyne, M.D., Kai-Uwe Eckardt, M.D., Iain C. Macdougall, M.D., Dimitrios Tsakiris, M.D., Hans-Ulrich Burger, Ph.D., and Armin Scherhag, M.D., for the CREATE Investigators

Correction of Anemia with Epoetin Alfa in Chronic Kidney Disease
Ajay K. Singh, M.B., B.S., Lynda Szczech, M.D., Kezhen L. Tang, Ph.D., Huiman Barnhart, Ph.D., Shelly Sapp, M.S., Marsha Wolfson, M.D., and Donal Reddan, M.B., B.S., for the CHOIR Investigators
Correction of Hemoglobin and Outcomes in Renal Insufficiency (CHOIR) trial

**US Study:** open-label trial of 1432 patients with chronic kidney disease not on dialysis

target Hb level of 13.5 g/dL (vs 11.3):

increased risk of composite events (death, myocardial infarction, hospitalization for congestive heart failure, or stroke)

Cardiovascular Risk Reduction by Early Anemia Treatment with Epoetin Beta (CREATE) Trial

CREATE Study: conducted in Europe, Asia and Mexico, enrolled 603 patients with stage 3-4 CKD

Group 1: target Hb 13.0 to 15.0 g/dL
Group 2: target Hb 10.5 to 11.5 g/dL

Complete correction of anemia did not reduce the likelihood of a first cardiovascular event.

KDIGO clinical practice guideline

Kidney Disease: Improving Global Outcomes (KDIGO)

3.4.1

For CKD ND patients with Hb ≥ 10.0 g/dL, we suggest that ESA therapy not be initiated

For CKD 5D patients, we suggest that ESA therapy be used to avoid having Hb level fall below 9.0 g/dL by starting ESA when Hb is between 9.0 - 10.0 g/dL.
We suggest that ESA not be used to maintain Hb concentration above 11.5 g/dL in adult patients with CKD.
How to Interpret the Guideline?

What are our main concern with treating chronic kidney disease patients with ESA?

- Is ESA treatment *per se* of concern?
- Is the target Hb level of concern?
ESA and FDA alert: Less is More

ESA should be given in the lowest possible dose required to gradually increase hemoglobin "to the lowest level sufficient to avoid the need for blood transfusions"

## Transfusion target

<table>
<thead>
<tr>
<th></th>
<th>Target control (Hb level, g/dL)</th>
<th>Reference, year</th>
<th>Clinical outcomes for lower Hb target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip Surgery</td>
<td>8.0 vs 10.0</td>
<td>Carson JL, 2011</td>
<td>No change in OS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No change in walking ability at 60 days</td>
</tr>
<tr>
<td>Upper gastrointestinal Bleeding</td>
<td>7.0 vs 9.0</td>
<td>Villanueva C, 2013</td>
<td>Increase in OS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Decrease in rebleeding</td>
</tr>
<tr>
<td>Septic shock</td>
<td>7.0 vs 9.0</td>
<td>Holst LB, 2014</td>
<td>No change in OS</td>
</tr>
<tr>
<td>Cardiac surgery</td>
<td>7.5 vs 9.0</td>
<td>Murphy GJ, 2015</td>
<td>NO change in OS</td>
</tr>
</tbody>
</table>

OS = overall survival
If there is “FDA” for transfusion ...

Transfusion should be given only to maintain Hb at ≥7 to 8 g/dL rather than 10 g/dL for most medical and surgical patients who are hemodynamically stable, as well as ambulatory patients.
Case 1

- Patient is now 78-year-old
- Not a candidate for renal transplant
-_opts for conservative management

- Should we give him ESA?
Experience of ESA in Palliative Care

- Retrospective observational study
- Adults patients with stage 4-5 CKD on palliative care
- 39 cases on ESA, 39 (matched) controls on supportive treatment
- Follow up for 12 months
- All patients received subcutaneous ESA

<table>
<thead>
<tr>
<th></th>
<th>ESA treatment group ( (n = 39) )</th>
<th>Control group ( (n = 39) )</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>79 ± 8</td>
<td>75 ± 11</td>
<td>0.07</td>
</tr>
<tr>
<td>Women</td>
<td>22 (56.4%)</td>
<td>16 (41.0%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>54.9 ± 10.5</td>
<td>62.3 ± 9.9</td>
<td>0.003</td>
</tr>
<tr>
<td>Thalassaemia trait</td>
<td>3 (7.7%)</td>
<td>0 (0%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Serum creatinine (µmol/L)</td>
<td>443 ± 148</td>
<td>456 ± 135</td>
<td>0.69</td>
</tr>
<tr>
<td>Estimated GFR (ml/min/1.73 m²)</td>
<td>11.5 ± 6.7</td>
<td>11.7 ± 4.5</td>
<td>0.91</td>
</tr>
<tr>
<td>Baseline haemoglobin (g/dL)</td>
<td>10.2 ± 1.5</td>
<td>10.1 ± 1.4</td>
<td>0.76</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>37.1 ± 9.3</td>
<td>37.5 ± 8.8</td>
<td>0.83</td>
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<tr>
<td>Phosphorus level (mmol/L)</td>
<td>1.37 ± 0.24</td>
<td>1.39 ± 0.24</td>
<td>0.83</td>
</tr>
<tr>
<td></td>
<td>ESA treatment group (n = 39)</td>
<td>Control group (n = 39)</td>
<td>P value</td>
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<tr>
<td>--------------------------</td>
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<tr>
<td>Transferrin saturation (%)</td>
<td>29 ± 13</td>
<td>26 ± 11</td>
<td>0.17</td>
</tr>
<tr>
<td>Serum ferritin (pmol/L in median and interquartile range)</td>
<td>594 (317 - 942)</td>
<td>506 (317 - 1023)</td>
<td>0.66</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>19 (48.7%)</td>
<td>26 (66.7%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Treatment with oral iron</td>
<td>16 (41.0%)</td>
<td>9 (23.1%)</td>
<td>0.072</td>
</tr>
<tr>
<td></td>
<td>ESA treatment group (n = 39)</td>
<td>Control group (n = 39)</td>
<td>P value</td>
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<td>--------------------------</td>
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</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>12 (30.8%)</td>
<td>10 (25.6%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>6 (15.4%)</td>
<td>15 (38.4%)</td>
<td>0.04</td>
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<tr>
<td>Active malignancy</td>
<td>2 (5.1%)</td>
<td>1 (2.6%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Past history of malignancy and in remission</td>
<td>4 (10.3%)</td>
<td>2 (5.1%)</td>
<td>0.68</td>
</tr>
<tr>
<td>Charlson Comorbidity Index (median and interquartile range)</td>
<td>4 (3 - 6)</td>
<td>3 (0 - 5)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Benefits of ESA over 12 months

Overall, 129 transfusion events per 100 person-years

- Blood transfusions: 12 patients in ESA group and 27 control patients

- ESA group: 34 units of red cell transfusion
- Control group: 128 units of red cell transfusion

Benefits of ESA over 12 months

Overall, length of hospital stay was 2.1 days per patient-month

Incidence rates of hospitalization from any cause:
- ESA group: 0.17 per patient month
- Control group: 0.41 per patient month

Median length of stay LOS:
- ESA group: 3 days (IQR 0 - 13)
- Control group: 31 days (IQR 7 - 50)

<table>
<thead>
<tr>
<th></th>
<th>ESA group (n = 39)</th>
<th>Control group (n = 39)</th>
<th>Incidence rate ratio IRR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Red cell transfusion</strong></td>
<td></td>
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<tr>
<td>Incidence rate of blood</td>
<td>0.07</td>
<td>0.27</td>
<td>3.63 (2.49 - 5.31)</td>
<td>&lt; 0.000001</td>
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<tr>
<td>transfusion requirements*</td>
<td></td>
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<tr>
<td><strong>Hospitalization</strong></td>
<td></td>
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</tr>
<tr>
<td>Incidence rate of hospital admission for transfusion*</td>
<td>0.04</td>
<td>0.17</td>
<td>3.69 (2.28 - 5.96)</td>
<td>&lt; 0.00001</td>
</tr>
<tr>
<td>Incidence rate of all-cause hospitalization*</td>
<td>0.17</td>
<td>0.41</td>
<td>2.34 (1.80 - 3.03)</td>
<td>&lt; 0.000001</td>
</tr>
</tbody>
</table>
ESA in Patients receiving Palliative Care

- Avoiding blood transfusions and reducing hospitalization

- Shorter length of hospitalization beneficial not only in reducing healthcare cost but, more importantly, considered a meaningful gain by patients who opt for conservative management
Patients receiving Palliative Care

- ‘Time lost’ to hospital admission implies less time spent with the family before the end of life

- Treatment option of ESA should be incorporated in the serious illness conversations for renal failure patients who opt for palliative care
Good News for HA patients

New Special Drug Formulary indication since this month

- CKD stage 5 patients decided not for dialysis and under renal or renal palliative care service with Hb <9 g/dL and had symptoms of fatigue; target Hb not to exceed 11 g/dL [Specialists: Pall Care/Renal]
Something new in ESA - biosimilar

Patent on Epoetin alfa, a form of rHuEPO (developed by Amgen and introduced in 1989) expired in 2013
Darbepoetin’s EU patent expired in 2016

Is biosimilar an option?

ESA biosimilar

- FDA issued approval for epoetin hospira on May 15, 2018, under the generic name epoetin alfa-epbx and the brand name Retacrit

- Supported by four human studies
<table>
<thead>
<tr>
<th>Study Number</th>
<th>Description</th>
<th>N</th>
<th>Predefined End Points</th>
<th>Results</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPOE-12-02</td>
<td>Single-center, open-label, randomized PK/PD study of epoetin hospira versus Epogen/Procrit after single 100 U/kg SC dose in healthy subjects</td>
<td>81</td>
<td>Epoetin AUC and $C_{\text{max}}$; reticulocyte AUEC and $E_{\text{max}}$</td>
<td>PK and PD similarity with 90% CI for ratios of geographic means within 80%-125% as prespecified by FDA</td>
<td></td>
</tr>
<tr>
<td>EPOE-14-01</td>
<td>Single-center, open-label, parallel group PK/PD study of epoetin hospira versus Epogen/Procrit after 100 U/kg SC tiw for 4 wk in healthy subjects</td>
<td>129</td>
<td>Hb AUC at 28 d; epoetin AUC and $C_{\text{max}}$ after final dose</td>
<td>PK and PD similarity with 90% CI for ratios of geographic means within 80%-125% as prespecified by FDA</td>
<td></td>
</tr>
<tr>
<td>EPOE-10-13</td>
<td>Randomized, double-blind, parallel group study of SC epoetin hospira versus Epogen/Procrit in patients receiving HD previously receiving iv Epogen/Procrit</td>
<td>246</td>
<td>Mean weekly epoetin dose and mean weekly Hb during last 4 wk of treatment</td>
<td>No clinically meaningful differences</td>
<td>No significant differences</td>
</tr>
<tr>
<td>EPOE-10-01</td>
<td>Randomized, double-blind, parallel group study of iv epoetin hospira versus Epogen/Procrit in patients receiving HD previously receiving iv Epogen/Procrit</td>
<td>612</td>
<td>Mean weekly epoetin dose and mean weekly Hb during last 4 wk of treatment</td>
<td>No clinically meaningful differences</td>
<td>No significant differences</td>
</tr>
</tbody>
</table>
Landmark trial of ESA biosimilar

- 612 patients with ESRD on hemodialysis and stable anemia maintained with iv epoetin alfa
- randomly assigned to treatment with either intravenous epoetin alfa-epbx or epoetin alfa
- End point at 24 weeks: no difference in mean weekly hemoglobin levels, mean weekly epoetin dose, or incidence of adverse events between two groups

Clinically equivalent (efficacy and safety) and at a lower cost

- large sample size
- double-blind design
- use of the intention-to-treat population as the primary analysis population

Conclusion
Anaemia of chronic kidney disease

- Something we know
- Many more thing we don’t know
- Many many many many things we think we know, but don’t know
Something we know

Causes of anaemia in CKD

- Chronic kidney disease
  - ↓ Erythropoietin generation
  - ↑ Hepcidin production
  - Inflammation, infection

- Anaemia
  - Iron deficiency
  - Deficient iron intake, blood loss

- Deficiency of folic acid and vitamin B12, erythrocyte fragility
Something we don’t know

Diagnosis of iron deficiency in CKD

- TSAT < 20% -- sensitivity ~ 60% and specificity ~ 80%
- What about TSAT 30% from PIVOTAL Study?
- Ferritin < 450 pmol/L - sensitivity ~80% but low specificity
- We need combined TSAT and ferritin level, at least
Something we don’t know

How to supplement iron

- **Oral iron** - not too many patients will take it and concern with bioavailability, hepcidin

- **Intravenous iron** - less concern of oxidative stress, infection with newer study, and improved dosing convenience for nurses
Something we think we know (and agree)

Target Hb level for CKD patients

- 10 g/dL for nondialysis CKD
- \( \leq 11.5 \) g/dL for dialysis patients -- this target should not be moved by a quest for a “higher QOL”
Something we think we know (and agree)

Erythropoiesis stimulating agents (ESA)

- Second generation is easier for patient with less frequent dosing, and subcutaneous use
- Equally important for palliative care patients, not just those on dialysis
- Consider to start if Hb is 9.0 - 10.0 g/dL for dialysis patients
- Do not start if Hb $\geq$ 10.0 g/dL for nondialysis CKD patient
Half of everything we teach you is wrong ... unfortunately, we don't know which half