# ANEMIA OF CKD: Hemoglobin Control – Landmark Trials Summary

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| | Trials<br>Mean follow-up, n | Intervention | Population<br>CKD stage, age, etc. | Key Baseline Indices<br>(e.g. Iron Studies) | Results | Comments |
|---|---|---|---|---|---|---|
| Iron Trials | **Charytan *et al.*** [1]<br>43 days; n=96; RCT, OL | **Oral vs IV iron** for ND-CKD<br>FeSO4 325mg po TID x 29 days vs Iron sucrose 200mg IV weekly x 5 doses; assessments made up to 14 days after last dose | ND-CKD; Age mean ~61; mostly ♀, (71% oral, 60% IV); multi-racial<br>Included: CrCl(C-G)≤40ml/min, Hgb<105g/L, TSAT<25%, ferritin<300ug/L \| Excluded: iron tx or blood transfusion w/in last month, apparent GI bleed, Alb<30g/L | Hgb (g/L): 97 oral vs 98 IV<br>Ferritin (ng/mL): 103 oral vs 125 IV<br>TSAT (%): 15.6 oral vs 16.6 IV | • △Hgb (g/L): +7 oral vs +10 IV; NS<br>• △Ferritin (ng/mL): -5.1 oral vs 288 IV; p<0.0001<br>• Change in TSAT (%): day 36=2.1 oral vs 5.1 IV \| day 43=0.5 oral vs 4.5 IV; sig increase for IV, but not oral<br>• # of pts achieved Hgb >110g/L: 31.3% vs 54.2% IV (p=0.028)<br>• AE: similar between groups, most common is GI in oral group, & taste-disturbances more common in IV group | **Iron therapy:**<br>• Should be guided by iron status tests, Hgb levels, ESA dose, & pt status CSN 2008 Guidelines<br>**Iron Therapy in *Non*-hemodialysis CKD pts (ND-CKD)**<br>• Route of admin has been shown to have no difference in reaching Hgb targets Charytan, & IV is superior to oral Van Wyck; but in light of lack of conclusive superiority evidence & due to ↑ access risk problems & ↑cost, recommend **oral iron first** CSN 2008 Guideline<br>• QOL has not been shown to differ between patients treated with oral or IV iron Van Wyck<br>• Studies show that ↑Hgb may occur following iron tx with **ferritin ~100ug/L** Charytan & Van Wyck<br>• IV iron produces greater results regardless of ESA use Van Wyck<br>**Iron Therapy in Hemodialysis CKD pts (HD-CKD)**<br>• Patients with higher ferritin (~400 vs 200 mcg/L) require lower doses of ESAs DeVita, thus it is recommended to treat when **ferritin ≤500 mcg/L** with iron therapy KDIGO 2012 Guidelines<br>• Weigh benefits vs risks of initiating iron tx in pts with ferritin >800ug/L & TSAT <25% DRIVE<br>• Pts with higher TSAT% (30-50 vs 20-30) maintain Hgb with lower doses of ESAs Besarab, therefore recommend to treat when **TSAT ≤30%** with iron therapy KDIGO 2012Guidelines<br>• Studies looking at oral iron vs placebo have shown that oral iron is no better than placebo (in Hgb improvements Mcdougall or ESA dose minimization)<br>• **IV iron** has been shown to be superior to oral iron with respect to ↑Hgb Fishbane & Besarab & ↓ESA dose Fishbane<br>• Proactive IV iron sucrose doses (400mg) given monthly when ferritin ≤700 & TSAT <40% shown to decrease CV events & ESA doses. PIVOTAL |
| | **Van Wyck *et al.*** [2]<br>~56 days; n=161; RCT, OL, ITT | **Oral vs IV iron** for ND-CKD pts<br>FeSO4 325mg po TID for 56 days vs Iron sucrose 1g IV x2 doses over 14 days | Stage 3-5 ND-CKD; Age mean ~63; mean eGFR ml/min/1.73m2: 28.5 oral vs 30.4 IV; 98 pts *NOT* on ESAs<br>Included: Hgb≤110g/L, TSAT≤25%, ferritin≤300ug/L; if on Epo, no △ for 8 wks prior or during study | Hgb (g/L): 101 oral vs 102 IV<br>Ferritin (ug/L): 104 oral vs 93 IV<br>TSAT (%): 17 oral vs 16 IV | • % of pts w/Hgb ↑ of ≥10g/L: 28% po vs 44.3% IV; p=0.0344<br>• % of IV pts with outcome: 53.1 ESA-use oral vs 38.3 no ESA; NS<br>• % of oral pts with outcome: 32.2 ESA-use oral vs 25.5 no ESA; NS {Primary outcome was a Hgb increase > or =1 g/dL}<br>• △eGFR (ml/min/1.73m2): -4.4 oral vs -1.45 IV; p=0.01<br>• △QOL: no statistically significant differences | |
| | **DeVita *et al.*** [3]<br>~5mos; n=36; RCT | **IV iron to high>400 vs low>200 ferritin** for HD-CKD pts on ESAs<br>Each subject below target received an IV iron dextran load, Hct was maintained between 32.5-36% by adjusting Epo dose | HD-CKD; Age mean ~66.5;<br>Included: Hct≤33, Ferritin 70-400 | Hct (%): 30.5 High vs 29.5 Low<br>**Ferritin (ug/L): 203.7 High vs 166.4 Low** | • Hct (%): 34.0 High vs 36.1 Low {NS diff.}<br>• **Mean Ferritin (ug/L): 387 high-ferritin vs 261 low-ferritin**<br>• **End Ferritin (ug/L): 298.6 high-ferritin vs 469.4 low-ferritin**<br>• △Epo dose (u/kg/wk): -154 high-ferritin vs -31 low-ferritin; p<0.001 | |
| | **Besarab *et al.*** [4]<br>~6mos; n=42; RCT, OL, ITT, single-centre | **IV iron to high30-50 vs low20-30 TSAT** for HD-CKD pts on ESAs<br>{16-20wk run-in period with IV iron dextran & erythropoietin to get to study levels of TSAT=20-30% & Hgb=95-120}<br>25-150mg IV iron dextran control VS load of 100mg x6 doses for 2wk then 25-150mg/wk study | HD-CKD; Age mean ~60.8;<br>25 males, 17 females | Hgb (g/L): 105 control vs 106 study<br>Ferritin (ug/L): 287 control vs 285 study<br>**TSAT (%): 23.9 control vs 24.6 study**<br>Epo dose (units 3X/wk): 3782 control vs 3625 study | • Hgb (g/L): 103 control vs 104 study<br>• Ferritin (ug/L): 298 control vs 731 study<br>• **TSAT (%): 27.6 control vs 32.6 study**<br>• Epo dose @6mos: 40% lower dose for study group vs control group (significant) | |
| | **Macdougall *et al.*** [5]<br>~4mos; n=25; RCT | **Oral vs IV iron vs No iron** for HD-CKD pts on ESAs<br>Oral ferrous sulfate 200mg TID vs iron dextran 250mg q2wks vs no iron | HD-CKD; Age mean ~58<br>oral, 47 IV, & 54 no iron | Hgb(g/L): 72 oral vs 73 IV vs 73 no iron<br>Ferritin (ug/L): 309 oral vs 345 IV vs 458 no iron | • Hgb (g/L): 102 oral vs 119 IV vs 99 no iron; p<0.05<br>• ESA dose (unit/dose): 1294 oral vs 1202 IV vs 1475 no iron; NS | |
| | **Fishbane *et al.*** [6]<br>~4mos; n=52 | **Oral vs IV iron** for HD-CKD pts on ESAs<br>Oral iron vs Iron dextran 100mg IV x2 wkly | HD-CKD; Age mean ~49.5<br>Included: TSAT>15%, ferritin<100ng/mL | Hgb (g/L): 106 oral vs 108 IV<br>ESA dose (units/treatment): 6750 oral vs 7100 IV | • Hgb (g/L): 106 oral vs 115 IV; p<0.05<br>• Hct (%): 31.8 oral vs 34.4 IV; p<0.05<br>• ESA dose (units/treatment): 7563 oral vs 4050 IV; p<0.05<br>• Serum ferritin (ng/mL): 157.3 oral vs 753.9 IV; p<0.05 | |
| | **DRIVE I** [7]<br>~6wks; n=129 **modified ITT**; RCT, OL, multi-centre | **IV iron vs No iron** in HD-CKD pts with high ferritin, low TSAT<br>Ferrous gluconate 125mg IV with 8 consecutive HD sessions vs no iron; epo doses ↑ 25% in both groups at trial onset (no other △ permitted) | HD-CKD; Age mean ~59-60; ~1:1male:female; multi-racial<br>Included: Hgb≤110g/L, TSAT≤25%, ferritin=500-1200ug/L (stratified before rand'n to < or > 800ug/L) | Hgb (g/L): 104 IV vs 102 no iron<br>Ferritin (ug/L): 759 IV vs 765 no iron<br>TSAT (%): 18 IV vs 19 no iron | • △Hgb (g/dL): 1.6 IV vs 1.1 no iron; p=0.028<br>• % of responders ≥20g/L ↑ (%): 49.6 IV vs 29.2 no iron; p=0.041<br>• △ferritin (ug/L): 173 IV vs -174 no iron; p<0.001<br>• baseline ferritin was not predictive of iron response<br>• safety was no different if < or > 800 baseline ferritin (not powered to show safety)<br>• △TSAT (%): 7.5 IV vs 1.8 no iron; p<0.001 | |
| | **DRIVE II** [8]<br>~6wks; n=129 | Observational study of duration of effect from IV iron under usual clinical mgt | Extension<br>(i.e. used same **DRIVE** pts) | Epo dose in **DRIVE** (units/wk): 45,000 IV vs 43,700 no iron | • △Epo dose (units/wk) from dose given in DRIVE: -7527 IV (p=0.003) vs 649 no iron (p=0.809)<br>• % of pts with Hgb>110(g/L): 83.9 IV vs 67.9 no iron; p<0.05 | |
| | **PIVOTAL** [20]<br>2.1 years; n=2141; ITT, RCT, OL, multi-centre (UK) | IV iron sucrose monthly: High-dose (400mg unless ferritin >700ug/L or TSAT ≥40%) vs low-dose (0-400mg when ferritin <200ug/L or TSAT <20%).<br>Median HD=264mg vs LD=145mg qmo | HD-CKD (new last 12mos); Age mean ~63; 65% males, 79% white race, ~45% had DM, ~72% had HTN. Included: ferritin <400ug/L, TSAT <30% & on ESA (stratified before rand'n by type of vascular access, DM, & HD during < or ≥5mos). | Hgb (g/L):~106 high vs ~105 low<br>Ferritin (ug/L): 214 high vs 217 low<br>TSAT (%): 20 high vs 20 low<br>ESA dose (IU/wk): 8000 high vs 8000 low | • Hard, patient-meaningful 1' end-point: composite (nonfatal MI/stroke, hospitalization for HF, or death)<br>• High-dose: 320 events (29.3%) vs low-dose: 338 (32.3%) (HR 0.85, 95% CI 0.73-1, P<0.001 for NI, P<0.04 for superiority); consistent across subgroups<br>• ESA median monthly dose 19.4% lower in high-dose group (~29,700 IU/mos vs ~38,800 IU/mos)<br>• Trend toward ↑vascular access thrombosis (NS), other safety parameters not noticeably different | |

**ESA**

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| **Revicki *et al.*** [9] ~48wks; n=83; RCT, OL, ITT | **Erythropoietin vs placebo** in ND-CKD pts on health-related QOL[HRQL] Initially erythropoietin 50u/kg/dose SC 3xweekly or untreated; all treated pts could have dosage ↑ (max 450u/kg/wk) until Hct reached 36, then titrated to target 35 | ND-CKD; Age mean ~57, ~67.5% female, mean GFR~10.1ml/min | Hct (%): 26.8 ESA & untreated gp Physical function score (/100): 44.3 ESA vs 49.1 untreated | • **HRQL** Physical function: +7.8 ESA vs -4.8 untreated; p=0.006 / all other tests NS<br>• △Hct (%): +4.7 ESA vs -1 untreated (P < 0.0001)<br>• Withdrawals: 53.5 % (23/43) ESA vs 62.5% (25/40) untreated |
| **Roth *et al.*** [10] (as with Revicki *et al.*) | **Erythropoietin vs placebo** in ND-CKD pts, effect on rate of CKD decline | Used same pt population as Revicki | GFR (ml/min): 10.2 ESA vs 10 untreated | • △GFR (ml/min): -2.1 ESA vs -2.8 untreated; NS p=0.376 |
| **Levin *et al.*** [11] ~24mos; n=152; RCT, OL, ITT | **Early&High vs Delayed&Low ESA** in ND-CKD pts Erythropoietin 2000IU/wk initial dose given to: 1) study group to maintain Hgb 120-140g/L, 2) control group with a Hgb of 90g/L or less before treatment with a target of 90-105g/L | ND-CKD; Age mean ~57, ~30% female, 38% DM, GFR mean ~29 ml/min; all pts "iron replete" (TSAT>20%, ferritin>60 ug/L) | Hgb (g/L): 117.3 delayed vs 117.6 early **LVMI (g/m²): 98.3 delayed vs 100.6 early** | • △Hgb (g/L): -3 delayed vs 9.8 early<br>• **△LVMI@24mos(g/m²):+5.2 delayed vs +0.4 early; NS p=0.28** |
| **CREATE** [12] ~3yrs; n=603; RCT, OL | **Early/High-Hgb vs Late/Low-Hgb Erythropoietin** in CKD pts Erythropoietin beta given to target: 1) start when Hgb 110-125g/L, target 130-150g/L 2) start when Hgb 100g/L, target 105-115g/L | Stage 3-4 ND-CKD; Age mean ~59, ~46% female, 26% DM Included: CrCl=15-35 ml/min, Hgb<110 g/L Excluded: uncontrolled HTN **Of Note:** Wt (kg): 74.7 early/high-Hgb vs 71.8 late/low-Hgb; p=0.05 | Hgb (g/L): 116 early/high vs 116 late/low Ferritin (ug/L): 174 early/high vs 189 late/low TSAT (%):25.6 early/high vs 38.1 late/low LVMI (g/m²): 120 early/high vs 118 late/low GFR (ml/min): 24.9 early/high vs 24.2 late/low | • CV Composite (sudden death, MI, acute HF, stroke, TIA, hosp'n for angina, complication of PVD, or hosp'n for arrhythmia): 18% [58 events] early/high vs 14% [47 events] late/low; HR=0.78, NS p=0.20<br>• △LVMI @2yrs(g/m2): -4.6 early/high vs -3.3 late/low; NS<br>• △QOL@2yr(SF-36): better general health with early/high p=0.008 & **vitality** p=0.01<br>• △eGFR (ml/min/yr): -3.6 early/high vs -3.1 late/low; NS<br>• **Dialysis: 127 early/high vs 111 late/low; p=0.03**<br>• **HTN (sys>160): 89 early/high vs 59 late/low; p=0.005** |
| **CHOIR** [13] Median 16mos; n=1432; RCT, OL **EARLY TERMINATION** | **Erythropoietin to High- 130 (130-135) vs Low-Hgb 113 (105-110)** in CKD pts | Stage 3-4 ND-CKD; Age mean ~66, ~55% female, GFR~27 ml/min Included: CrCl=15-50 ml/min, Hgb<110 g/L Excluded: uncontrolled HTN **Of Note:** HTN (%): 95.8 high-Hgb vs 93.2 low-Hgb; p=0.03 CABG (%): 17.4 vs 13.5; p=0.05 | Hgb (g/L): 101 high vs 101 low Ferritin (ug/L): 168 high vs 179 low TSAT (%): 25.2 high vs 24.6 low | • Composite (death, MI, hosp'n for HF, stroke): 125 events (18%) high vs 97 events (14%) low; HR=1.34, **p=0.03**, **NNH=25** over 16months (driven by death & hosp'ns)<br>• Death: 52 high vs 36 low; NS, HR=1.48, **p=0.07**<br>• △QOL: significant differences in only 1 of 12 categories (emotional role)<br>• Any serious AE: 376 (54.8%) high vs 334 (48.5%) low; p=0.02<br>• Any serious AE assoc'd w/ESA: 10 (1.5%) high vs 3 (0.4%) low; p=0.05<br>• HF: 77 (11.2%) high vs 51 (7.4%) low; p=0.02; [? ↑CKD [Inrig'12]] |
| **ND-CKD PEARL** n=983, ≥52wks peginesatide monthly vs darbepoetin q2wk: Hgb target 110-120g/L, peg ↑CV mortality HR=1.32 | | | | |
| **Canadian EPO Study group** [14] ~6mos; n=118; RCT, DB | **Erythropoietin to high-Hgb 115-130 vs Erythropoietin to low-Hgb 95-110 vs Placebo** in HD-CKD pts Initially erythropoietin 100u/kg/dose 3xweekly; all pts with ferritin<250ug/L received oral or IV iron 1 month prior, & prn during the study | HD-CKD; Age mean ~43-44 EPO vs 48 placebo; Hgb<90g/L | Hgb (g/L): 71 high vs 69 low vs 71 placebo | • △Sickness impact profile: 7.8 high vs 5.3 low vs 2.9 placebo<br>• △ Stress test m walked: 51 high vs 33 low vs 19 placebo<br>• Mean dose (units/kg/wk): 248 high vs 204 low<br>• Hgb (g/L): 117 high vs 102 low vs 74 placebo<br>• Dialysis access site clots: 7/38 high vs 4/40 low vs 1/40 placebo<br>• △BP (sys/dia): 0/+7 high vs 0/+2 low vs -4/-1 placebo |
| **Parfrey *et al.*** [15] ~96wks; n=596; RCT, DB | **Erythropoietin to High 135-145- vs Low 95-115 Hgb** in dialysis pts without symptomatic heart dx or LV dilation Arms divided into "concentric LVH" & "LV dilation" | HD-CKD; Age mean ~50.8, ~60% male **Of Note:** Age: 52.2 high-Hgb vs 49.4 low-Hgb; p=0.02 SBP mmHg: 144 high-Hgb vs 140 low-Hgb; p=0.02 | LVVI (ml/m²) gp: 296 high vs 300 low LVMI (g/m²) gp: 122 high vs 123 low Hgb (g/L): 110 high vs 110 low TSAT (%): 35.7 high vs 36.8 low | • %△LVVI (%): 7.6 high-Hgb vs 8.3 low-Hgb; NS<br>• %△LVMI (%): 16.8 high vs 14.2 low; NS<br>• Mean Hgb (g/L) @24wks: 133 high vs 109 low<br>• **△QOL @ (SF-36): 1.21 high vs -2.31 low; p=0.036**<br>• TSAT (%): 34.6 high vs 34.2 low |
| **Foley *et al.*** [16] ~48wks; n=146; RCT | **Erythropoietin to High135 (130-140) vs Low100 (95-105) Hgb** effect on cardiomyopathy in dialysis pts | HD-CKD; Age mean ~62, ~45% male in LVH group, ~78% male in dilation group | LVMI (g/m²): 147 high vs 139 low LVCVI (g/m²): 122 high vs 123 low | • △LVMI @48wks (g/m²): NS; p=0.35 Mann-Whitney *U*-test<br>• △LVCVI @48wks (g/m²): NS; p=0.13 Mann-Whitney *U*-test<br>• △Hgb (g/L): 122.5 high vs 104 low<br>• Improvement in high group: fatigue p=0.009, depression p=0.02, & relationship p=0.004 |
| **Besarab** [17] 1998 Median 14mos; n=1233; **EARLY TERMINATION** | **Erythropoietin to "Normal"- 42% vs Low-HCT 30%** in CKD pts w/ clinical evidence of HF or ischemic heart dx "Normal Hematocrit Study" | HD-CKD; Age mean ~65, ~50% female, Dialysis duration ~3.2yrs, ~44% DM, ~51% Class II NYHA HF (no class IV) | Hct (%): 30.5 high vs 30.5 low | • Time to death or 1st non-fatal MI: didn't reach SS, term'd early<br>• Death/1st non-fatal MI: 202 high vs 164 low; RR=1.3 95% CI 0.9-1.9; Deaths: 183 high vs 150 low; Non-fatal MI: 19 high vs 14 low<br>• reportedly improved physical functioning originally, but not confirmed in reanalysis<br>• reanalysis: ↑Death/MI 1.28 95% CI 1.06-1.56; ↑Death 1.27 95% CI 1.04-1.54 Coyne '12 |
| **Tonelli *et al.*** [18] | **Erythropoietin to High- vs Low- Hgb** in CKD pts: Cost-effectiveness Target Hgb g/L: 110-120, 120-125, 140 vs 95-105 | HD-CKD; "typical US dialysis centre" population | IV Dose (units 3X/wk) to achieve Hgb targets: 95-105=3523, 110-120=5078, 120-125=6097,140=9341 | • Cost/QALY: 110-120 vs 95-105 =$ 55,295; 120-125 vs 110-120 =$ 613,015; 140 vs 120-125 = $ 828,215 |
| **HD-CKD EMERALD** n=1608, ≥52wks peginesatide ~5mg/monthly vs epoetin 4600-9900 IU/1-3x/week: Hgb target 100-120g/L, peginesatide as effective as epoetin. | | | | |
| **TREAT** [19] Median 29mos; n~4038; RCT, DB, ITT, multi-centred | **Darbepoetin to High- vs Low-Hgb in CKD pts with type 2 diabetes** Target Hgb g/L: **130** in study group vs "placebo" control (≥**90** placebo or if <90, then darbepoetin to >90) | ND-CKD & diabetes Age mean ~68, ~56% female, eGFR ~33ml/min, BMI=30, CV hx ~65%, DM: 15yr history, A1C ~7%, on iron tx ~44% Included: eGFR MDRD 20-60 ml/min/1.73m^2, Hgb<110 g/L, TSAT>15% Excluded: uncontrolled HTN, kidney transplant, Ca, HIV, bleeding, preg | Hgb (g/L): 105 High vs 104 Low Ferritin (ug/L): 131 darbe vs 137 Low TSAT (%): 23 High vs 23 Low Heart Failure (%): 31.5 High vs 35.2 low; p=0.01 FACT-Fatigue score (0 least tired - 52 most tired): 30.2 High vs 30.4 Low. | • 1˚outcome (death or CV event nonfatal MI, HF, stroke, hosp'n for angina): 632 [31.4%] High 130 Target vs 302 [29.7%] Low 90 Target; NS<br>• 1˚outcome (death or ESRD): 652 [32.4%] High vs 618 [30.5%] Low; NS<br>• **↑stroke 101 [5%] High vs 53 [2.6%] Low, HR=1.92 95%CI 1.38-2.68; p<0.001, NNH=42 / 2.4yr**<br>• Hgb (g/L) achieved: **125** High vs **106** Low<br>• **Venous Thromboembolisms: 41 [2.0%] High vs. 23 [1.1%] Low; p=0.02**<br>• **Arterial Thromboembolisms: 178 [8.9%] High vs. 144 [7.1%] Low; p=0.04**<br>• **ESRD: 338 [16.8%] High vs. 330 [16.3%] Low; NS**<br>• **Transfusions: 15% High vs. 25% Low; p<0.001**<br>• **Fatigue: +4.2 High vs. +2.8 Low; p<0.001**<br>**Note: 46% "placebo" had darbepoetin rescue, but ↓QOL** |

**ESA Therapy:**

- Goal of treating iron-replete pts with ESAs is to improve QOL, while minimizing any AE of the drug & decreasing the need for transfusions
- ESAs: ↑ blood pressure; caution
- ESAs: ↓ need for blood **transfusions**, which come with their own set of complications
- No clinical benefit has been shown with tx with ESAs early Levin & CREATE, therefore **Tx should be withheld until Hgb is sustained below 100g/L & iron stores are repleted & other causes of anemia considered** CSN 2008 Guidelines
- LV mass: Pts treated to low or high Hgb targets do not show difference in progression of LV mass in HD-CKD Parfrey & Foley or ND-CKD Levin & CREATE
- QOL in HD-CKD: high Hgb showed improvement in quality of life, but the effect **waned** over time Parfrey & Foley
- QOL in ND-CKD: Varying results show few areas are improved by treating with ESAs early & to higher targets CREATE, CHOIR, & TREAT, & what effects are seen do **diminish** over time CREATE
- Worsening kidney function in ND-CKD: No studies have shown significant difference in tx to high vs low Hgb targets & the contribution to worsening eGFR Roth & TREAT (may ↑ dialysis if tx to higher targets CREATE, or may have no association TREAT)
- Hard endpoints in HD-CKD: Studies showing hard endpoints, such as time to death or 1st MI Besarab, show treating to high Hgb targets >130 may produce more **harm** than good FDA warnings
- Hard(er) endpoints in ND-CKD: Studies comparing composite CV endpoints show tx to high Hgb targets >130 may lead to **↑CV events** CREATE & CHOIR and stroke TREAT, though there are some limitations to studies {**CREATE**: ?under-powered, **CHOIR**: see "Of note"; no iron protocol used, **TREAT**: 46% of "placebo" group received study drug for rescue}
- Meta-analysis of 9 RCTs (all n>100, follow-up >12wks) with CKD patients who were randomly assigned to receive ESAs showed that targeting higher Hgb levels lead to ↑ all-cause mortality (RR=1.17, p=0.031) & AV access thrombosis (RR=1.34, p=0.0001)
- Results of **TREAT** reinforce that treating to higher i.e. physiologic Hgb levels Target: 130 g/L, achieved 125 may come with **significant risks** & only modest improvements in quality of life. Those with a poor initial hematopoietic response to darbepoetin had worse CV outcomes & death.
- ESA:FDA June/11 **if Hgb >110**, then assoc. ↑MI/stroke.

**CKD**=chronic kidney dx **C-G**=Cockcroft-Gault **dx**=disease **ESA**=Erythropoiesis stimulating agent **ESRD**=end-stage renal dx **FeSO4**=ferrous sulfate **Hct**=hematocrit **HD-CKD**=dialysis-CKD **HF**=heart failure **Hgb**=hemoglobin **HRQL**=health-related QOL **ITT**=intention to treat **LFT**=liver function tests **LVMI**=left ventricular mass index **LVVI**=left ventricular volume index **LVCVI**=left ventricular cavity volume index **MCV**=Mean corpuscular volume **MI**=myocardial infarction **ND-CKD**=non-dialysis CKD **OL**=open label **pt**=patient **QALY**=quality-adjusted life year **QOL**=quality of life **RCT**=randomized control trial **RDW**=Red cell distribution width **TIBC**=total iron binding capacity **TSAT**=transferrin saturation **TSH**=thyroid stimulating hormone ♀=female △=changes

# References: Anemia - Hemoglobin Control: Landmark Outcome Trials – Summary (www.RxFiles.ca)


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