Anaemia – Part 2

Rory McCulloch

Case Study

- 69 year female
- PC: Excessive fatigue
- HPC: Onset very gradual. No history of blood loss. No change in bowel habit. No weight loss, night sweats or bone pains.
- PMH: T2DM, CKD Stage 3, hypertension.
- DH: Statin, amlodipine, Ramipril, gliclazide, metformin.
- O/E: High BMI. No palpable lymph nodes or abdo masses.

FBC

	Value	Reference
Haemoglobin	**97** g/L	120-160
WCC	7.7 x 10^9/L	3.6-11
Platelets	237 x 10^9/L	150-400
Neutrophils	5.0 x 10^9/L	1.8-7.5
MCV	90.6 fL	82-98
MCH	29.7 pg	
Reticulocytes	50 x 10^9/L	50-100

Other blood tests

- Creatinine 130 (eGFR 39)
- Ferritin 21 mcg/L (13-150)
- Folate 9.6 mcg/L (4.6-18.7)
- B12 240 ng/L (>180)
- TSH 2.85 mu/L (0.35-4.5)
- Myeloma screen: No band protein on SPE, urine BJP negative

Differential diagnosis

- Anaemia of Chronic Kidney Disease
- Anaemia of Chronic Disease
- Iron deficiency anaemia
- Primary haematological disease (e.g. myelodysplasia)

Iron deficiency anaemia

- Specific questions in history:
    - Weight loss
    - Poor diet
    - Symptoms of malabsorption
    - Altered bowel habit
    - Bleeding symptoms
    - Family history (1 first degree <50, 2 first degree >50)

Investigations

- Full Blood Count
- Serum ferritin
- Iron studies: serum iron, TIBC, Transferrin saturations
- Consider therapeutic trial parenteral iron therapy

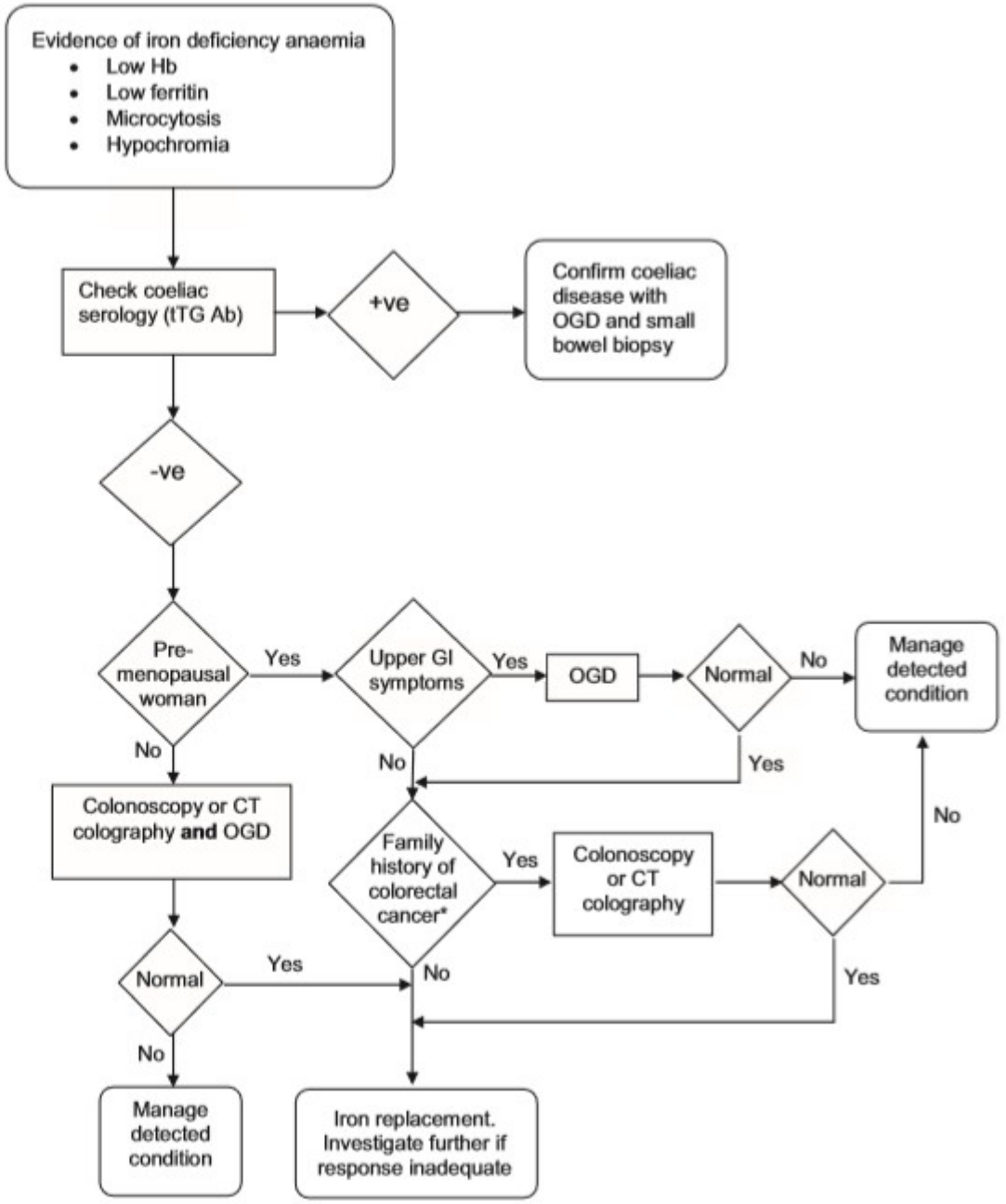
Table 1 Pathological contributors to iron deficiency anaemia in the UK with prevalence as percentage of total[4–9]

Contributor	Prevalence
Occult GI blood loss	
Common	
Aspirin/NSAID use	10–15%
Colonic carcinoma	5–10%
Gastric carcinoma	5%
Benign gastric ulceration	5%
Angiodysplasia	5%
Uncommon	
Oesophagitis	2–4%
Oesophageal carcinoma	1–2%
Gastric antral vascular ectasia	1–2%
Small bowel tumours	1–2%
Cameron ulcer in large hiatus hernia	<1%
Ampullary carcinoma	<1%
Ancylomasta duodenale	<1%
Malabsorption	
Common	
Coeliac disease	4–6%
Gastrectomy	<5%
Helicobacter pylori colonisation	<5%
Uncommon	
Gut resection	<1%
Bacterial overgrowth	<1%
Non-GI blood loss	
Common	
Menstruation	20–30%
Blood donation	5%
Uncommon	
Haematuria	1%
Epistaxis	<1%

Other tests to consider

- Urinalysis
- Coeliac screen: tTG antibodies
- OGD and colonoscopy

Figure 1 An abbreviated flow chart of the investigation of iron deficiency anaemia. GI, gastrointestinal; Hb, haemoglobin; OGD, oesophagogastroduodenoscopy; tTG Ab, tissue transglutaminase antibody. *See text for details of significant family history.



Guidelines for the Management of Iron Deficiency Anaemia

Andrew F Goddard, Martin W James, Alistair S McIntyre, Brian B Scott, on behalf of the British Society of Gastroenterology

Gut 2011;60:1309–1316. doi:10.1136/gut.2010.228874

Treatment

- Oral iron:
  - Ferrous sulphate 200 mg BD
  - Ferrous fumarate
  - Ferrous gluconate (better tolerated)
- If not tolerated IV monofer
- Transfusion only if severe and symptomatic
- Checks:
  - Monthly until anaemia corrected
  - 3 monthly for 1 year

Pregnancy

- Mild IDA common in pregnancy
- Investigations not usually required unless anaemia severe
- Enquire FH: Coeliac disease and GI neoplasia
- Majority can be managed with oral iron supplementation

Anaemia of Chronic Kidney Disease

Prevalence of Anemia in Chronic Kidney Disease in the United States

Melissa E. Stauffer[1]*, Tao Fan[2]

1 SCRIBCO, Effort, Pennsylvania, United States of America, 2 Merck & Co., Inc., Whitehouse Station, New Jersey, United States of America

Group	Number (12,077)	%	Prevalence of anaemia	%
All CKD	2,125	14.0	410	15.4
Stage 1 (GFR >90)	507	3.1	57	8.4
Stage 2 (GFR 60-89)	489	3.4	68	12.2
Stage 3 (GFR 30-59)	1,028	7.0	231	17.4
Stage 4 (GFR 15-29)	70	0.4	37	50.3
Stage 5 (GFR <15)	31	0.1	17	53.4
No CKD	9,952	86.0	729	6.3

Citation: Stauffer ME, Fan T (2014) Prevalence of Anemia in Chronic Kidney Disease in the United States. PLoS ONE 9(1): e84943. doi:10.1371/journal.pone.0084943

Aetiology

- Iron deficiency:
  - dietary, reduced intestinal absorption, GI bleeding.
  - ~50% stage 2-5 have absolute or relative iron deficiency.
- EPO deficiency:
  - reduced renal mass
- EPO hyporesponsiveness:
  - ?inflammatory/ autonomic
- Nephrotic syndrome:
  - Non-albumin proteins excreted (e.g. ferritin, transferrin)

Management

- Refer to Chronic Kidney Disease Service

Treatment

NICE guidelines [CG114] Published date: February 2011

- Optimise iron levels
  - Maintain ferritin > 200 *(150)* mcg/L, transferrin sats >20%

- Erythropoietin Stimulating Agents (e.g. darbopoietin)
  - Initiate for patients likely to benefit in quality of life
  - Co-morbidities or prognosis negate benefit
  - Start dose 20-40 mcg SC once weekly

ESAs

- Aim Hb 100 to 120 g/L
- Aim for 10 to 20 g/L increase per month
- Reduce dose if Hb > 115 g/L
- Increase if < 105 g/L

- Check FBC 2-4 weekly during induction
- 1-3 monthly during maintenance

Side effects

- Need blood pressure monitoring
- Local pain at site of injection
- Flu like symptoms
- Rare: Pure red cell aplasia
- ?Increased risk of thrombotic events

Aims of therapy

- Improve quality of life:
  - Cognitive function, sexual function, exercise capacity, reduce need for transfusions.

- Does it improve outcome?
  - Progression of CKD?
  - Cardiovascular events?
  - Mortality rate?

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 19, 2009 VOL. 361 NO. 21

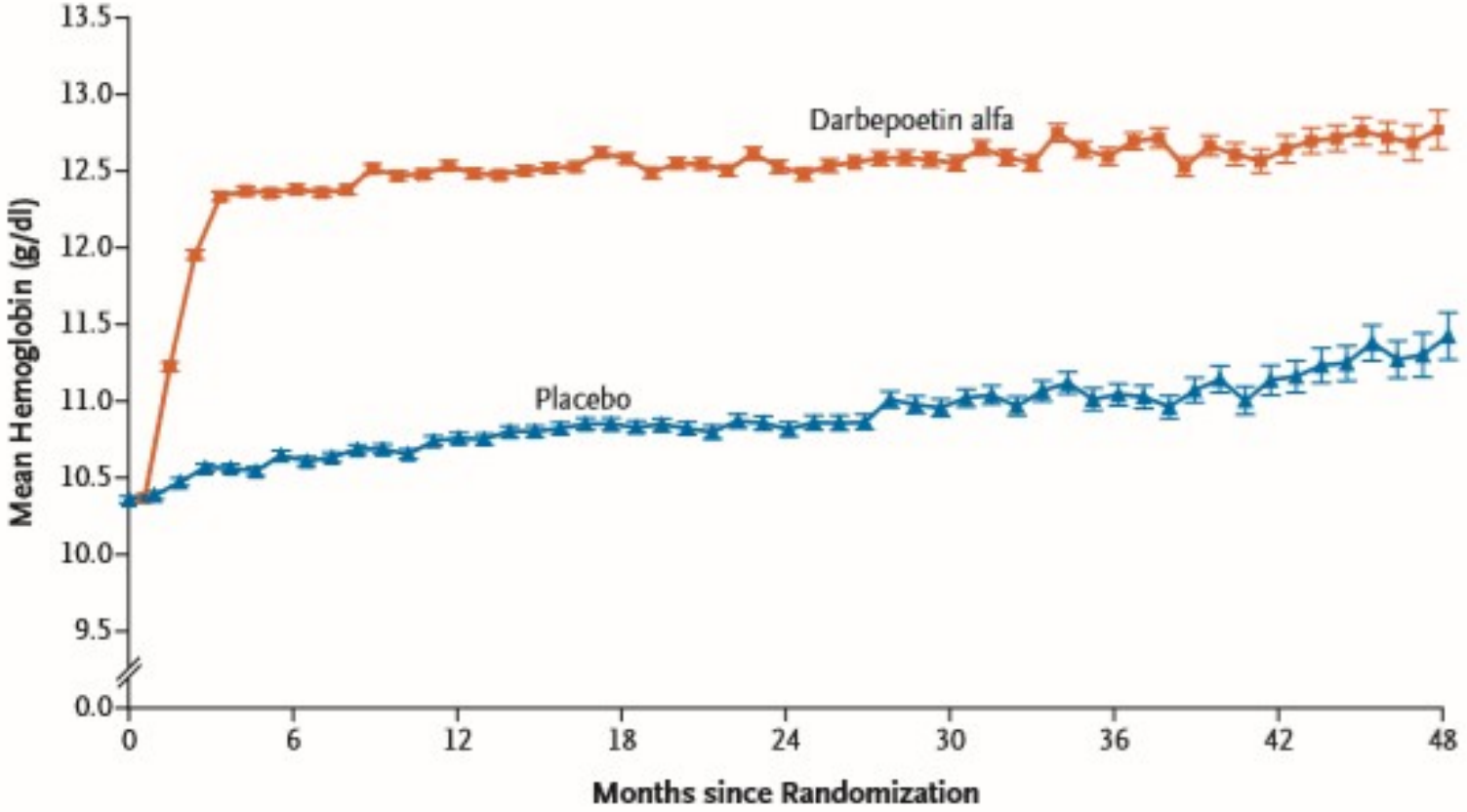
A Trial of Darbepoetin Alfa in Type 2 Diabetes and Chronic Kidney Disease

Marc A. Pfeffer, M.D., Ph.D., Emmanuel A. Burdmann, M.D., Ph.D., Chao-Yin Chen, Ph.D., Mark E. Cooper, M.D.,

Study

- 4,038 patients with diabetes, CKD 3 and anaemia (Hb <110 g/L)
  - 2,012 received darbopoietin alfa – aim Hb 130 g/L
  - 2,026 received placebo, rescue darbopoietin alfa when Hb <90 g/L

- Median follow-up 29.1 months



No. of Patients									
Darbepoetin alfa	2004	1768	1503	1300	946	635	404	253	97
Placebo	2019	1742	1460	1221	887	620	356	216	79

Figure 1. Mean Hemoglobin Levels through 48 Months among Patients Who Were Assigned to Receive Darbepoetin Alfa or Placebo.

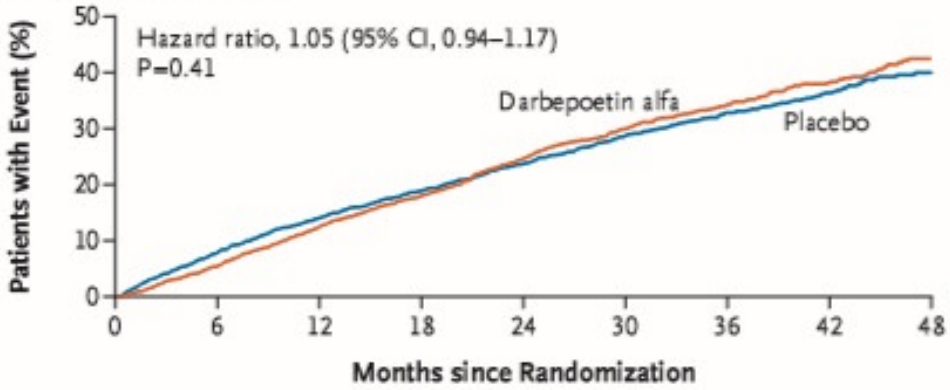
I bars represent standard errors.

Table 2. Composite and Component End Points.*

End Point	Darbepoetin Alfa (N=2012)	Placebo (N=2026)	Hazard Ratio (95% CI)	P Value†
	number (percent)			
Primary end points				
Cardiovascular composite end point‡	632 (31.4)	602 (29.7)	1.05 (0.94–1.17)	0.41
Death from any cause	412 (20.5)	395 (19.5)	1.05 (0.92–1.21)	0.48
Myocardial infarction§	124 (6.2)	129 (6.4)	0.96 (0.75–1.22)	0.73
Stroke§	101 (5.0)	53 (2.6)	1.92 (1.38–2.68)	<0.001
Heart failure§	205 (10.2)	229 (11.3)	0.89 (0.74–1.08)	0.24
Myocardial ischemia	41 (2.0)	49 (2.4)	0.84 (0.55–1.27)	0.40
Renal composite end point (ESRD or death)	652 (32.4)	618 (30.5)	1.06 (0.95–1.19)	0.29
ESRD	338 (16.8)	330 (16.3)	1.02 (0.87–1.18)	0.83
Additional adjudicated end points				
Death from cardiovascular causes	259 (12.9)	250 (12.3)	1.05 (0.88–1.25)	0.61
Cardiac revascularization	84 (4.2)	117 (5.8)	0.71 (0.54–0.94)	0.02

* ESRD denotes end-stage renal disease.
† P values have not been adjusted for multiple comparisons.
‡ A patient may have had multiple cardiovascular events of different types. The cardiovascular composite end point reflects only the first occurrence of any of the components.
§ This category includes both fatal and nonfatal events.

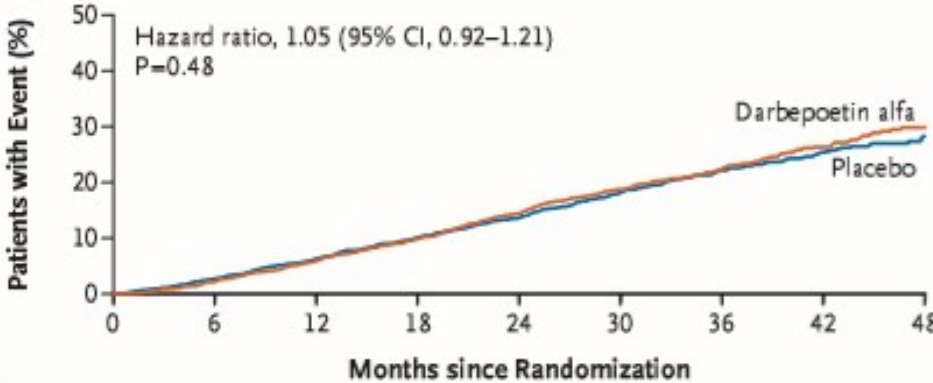
Cardiovascular Composite End Point



No. at Risk

Darbepoetin alfa	2012	1882	1717	1515	1180	817	551	318	130
Placebo	2026	1836	1687	1487	1178	834	529	319	122

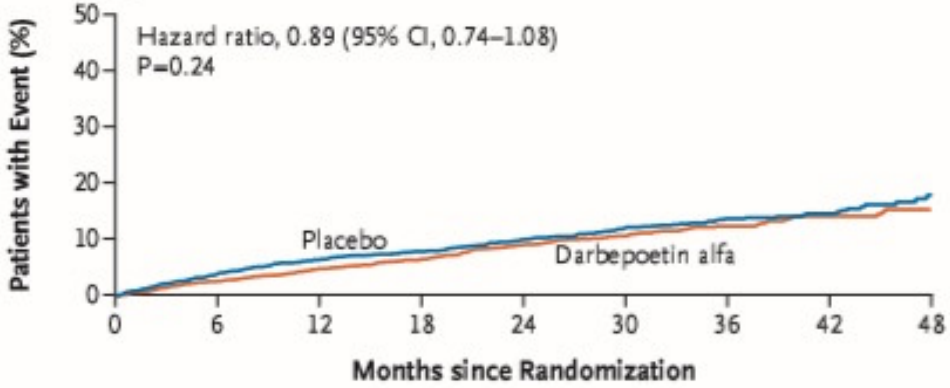
B Death from Any Cause



No. at Risk

Darbepoetin alfa	2012	1947	1847	1659	1337	945	655	386	164
Placebo	2026	1943	1839	1652	1345	970	636	385	156

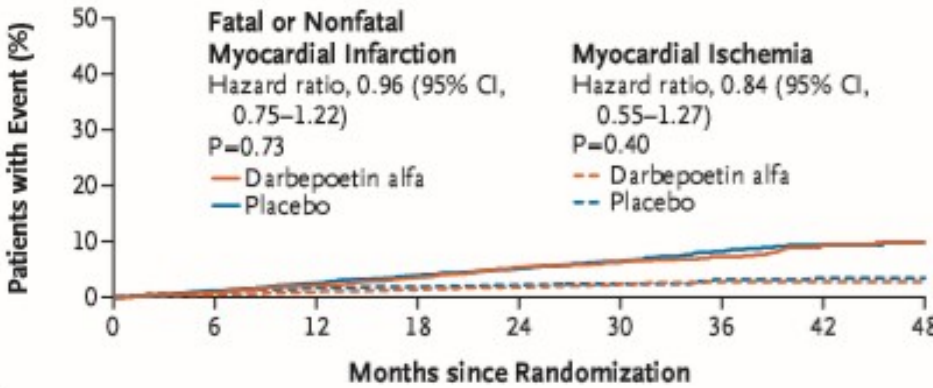
Fatal or Nonfatal Congestive Heart Failure



No. at Risk

Darbepoetin alfa	2012	1890	1742	1525	1191	819	555	319	136
Placebo	2026	1859	1702	1495	1187	835	519	307	115

D Fatal or Nonfatal Myocardial Infarction and Myocardial Ischemia



No. at Risk

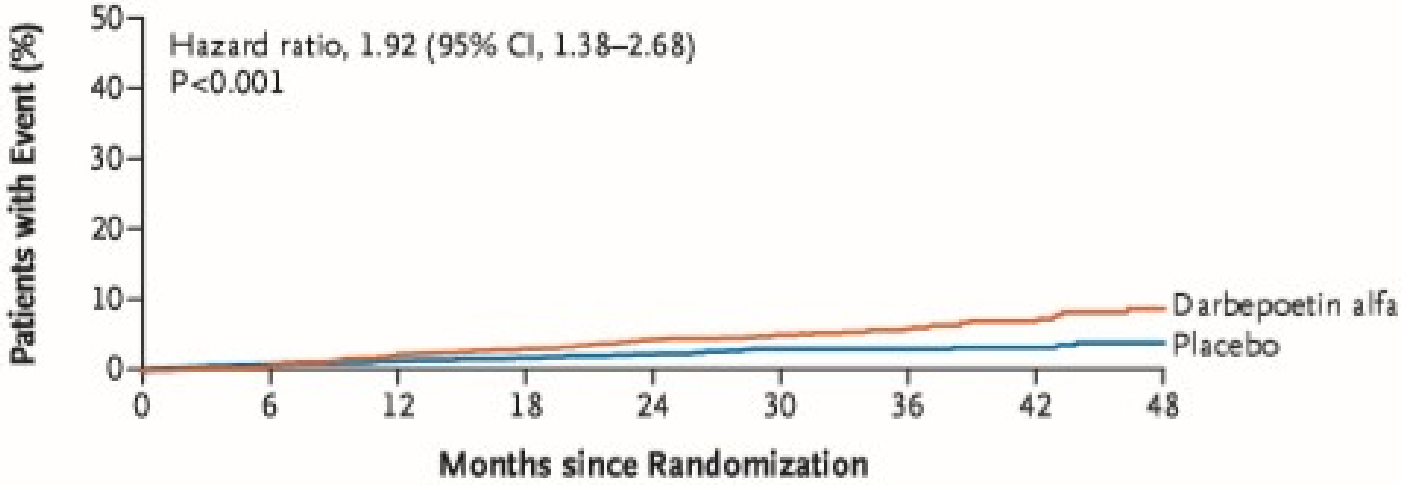
Fatal or Nonfatal Myocardial Infarction

Darbepoetin alfa	2012	1920	1785	1566	1232	851	577	325	137
Placebo	2026	1907	1765	1550	1235	863	539	324	123

Myocardial Ischemia

Darbepoetin alfa	2012	1924	1794	1583	1255	869	597	347	146
Placebo	2026	1906	1767	1561	1251	880	556	338	132

Fatal or Nonfatal Stroke



No. at Risk

Darbepoetin alfa	2012	1923	1787	1581	1247	863	590	341	141
Placebo	2026	1914	1783	1575	1262	886	561	338	132

Outcome

- No objective improvement in quality of life.
- Increased mortality rate in patients with known malignancy.

Other causes of anaemia

- Anaemia of Chronic Disease
- B12 and folate deficiency

Summary

- Cause of anaemia not always obvious
- Systematic approach should aim to exclude serious conditions
- A thorough approach should enable appropriate and decisive specialist referrals