



# The HERO trial

July 2011

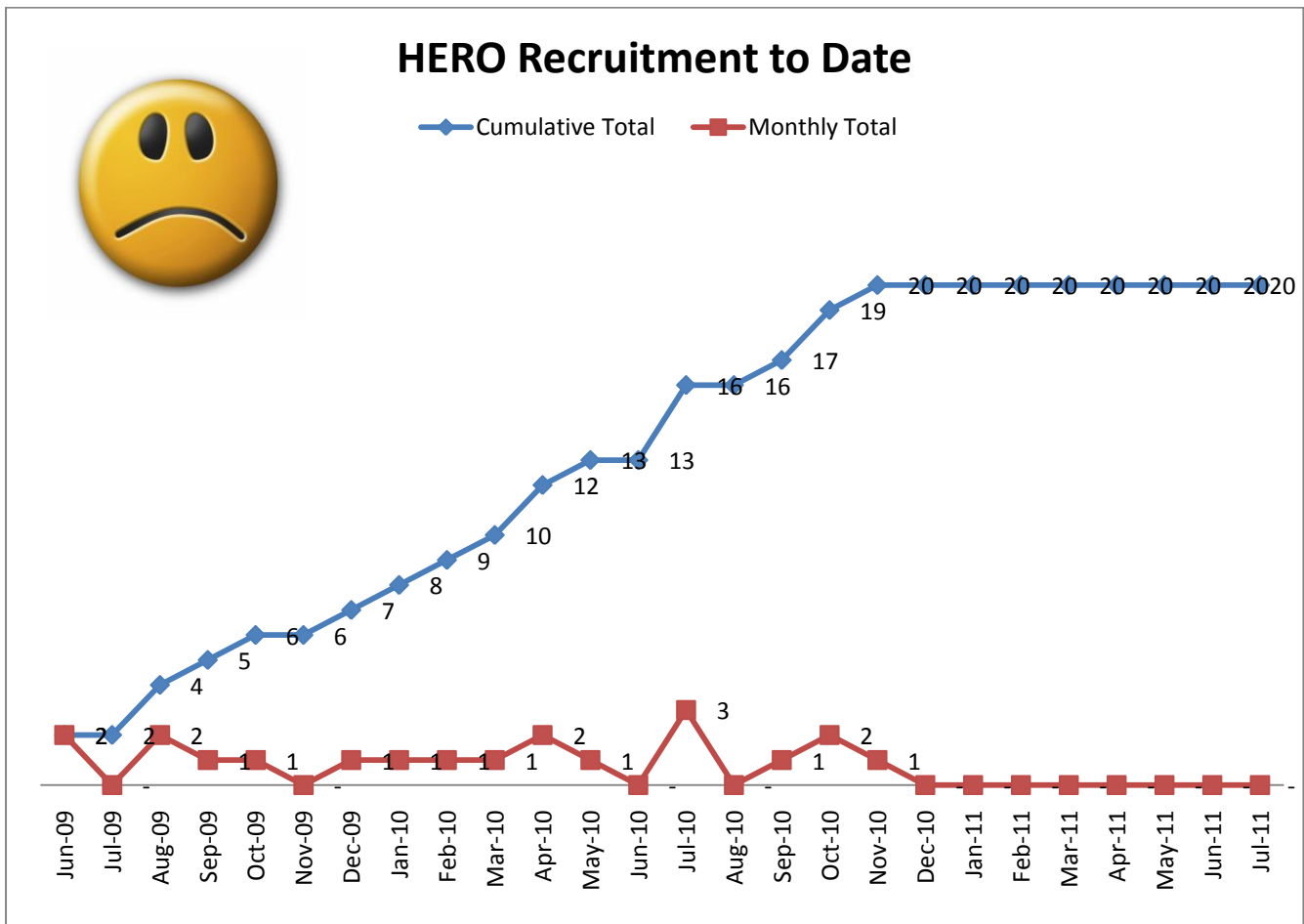
Monthly Update

Recruitment Target: .....110

Current Recruitment: .....20

National Required Recruitment Rate per Month (for a Dec 2012 finish): .....5

Each Site Required Recruitment Rate (for a Dec 2012 finish): .....1 every 2 mths



Dear HEROes

Welcome to the July Monthly Update for 2011.

As we move into the second half of the year it is timely to remind sites of the key changes that have been made to V2.1 of the HERO protocol. Poor recruitment has dogged the trial and after extensive consultation several changes (documented in Table 1 below) were made to the trial. It is expected these changes will double the available patient population and reduce the number of participants excluded due to concurrent illness. I have also attached a checklist which may be of use to sites when screening potential patients for the trial.

Kind regards

*Donna*

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Clinical Project Manager

Table 1: Changes to HERO Protocol V2.1 March 2011

V2.0	V2.1
<p><b>Inclusion Criteria:</b> ERI ≥ 2.0 IU/kg/week/gHb for erythropoietin treated patients and ≥ 0.01 µg/kg/week/gHb for darbepoetin treated patients</p> <p><b>Exclusion Criteria:</b> Major surgery, infection, acute myocardial infarction or malignancy within the last 12 weeks;</p> <p><b>ESA Doses:</b> Erythropoietin (EPO) or darbepoetin (DPO) dosages will not be increased during the study, and will only be reduced if haemoglobin levels rise above 125 g/L. Iron supplementation will be performed according to usual protocol.</p> <p><b>Iron Doses:</b> Iron supplementation will be performed according to usual protocol.</p> <p><b>Quality of Life Data:</b> Not collected</p>	<p><b>Inclusion Criteria:</b> ERI ≥ 1.0 IU/kg/week/gHb for erythropoietin treated patients and ≥ 0.005 µg/kg/week/gHb for darbepoetin treated patients</p> <p><b>Exclusion Criteria:</b> Any surgery within the last 6 weeks; infection within 6 weeks of the last antibiotic dose; acute myocardial infarction or malignancy within the last 6 weeks</p> <p><b>ESA Doses:</b> Erythropoietin (EPO) or darbepoetin (DPO) dosages will be reduced if haemoglobin levels rise above 120 g/L or the rate of rise in haemoglobin is &gt; 10 g/L per month. Change in ESA dose will be allowed according to the local protocol at the discretion of the treating physician. An algorithm for dose titration of ESA dose will be provided as guidance.</p> <p><b>Iron Doses:</b> Dose of iron should not be changed during the 4-month follow up, irrespective of current dose, route of administration, and the results of iron studies. The site investigators are advised not to change the iron dose for 6 weeks before randomisation.</p> <p><b>Quality of Life Data:</b> Information on quality of life will be collected using the generic health status instrument, the Short Form 36, at baseline and final follow-up of 4 months.</p>

<b>Inclusion Criteria</b>		√
<b>IC1</b>	Willing to participate and has signed the Participant Information and Consent Form	
<b>IC2</b>	Stage 4 or 5 chronic kidney disease	
<b>IC3</b>	Haemoglobin concentration $\leq 120$ g/l	
<b>IC4</b>	ERI $\geq 1.0$ IU/kg/week/gHb for EPO treated patients and $\geq 0.005$ $\mu$ g/kg/week/gHb for darbepoetin treated patients	
<b>IC5</b>	EPO/DPO dose stable during last 8 weeks	
<b>IC6</b>	Aged 18 years or over	
<b>Exclusion Criteria</b>		
<b>EC1</b>	History of psychological illness or condition which interferes with ability to understand or comply with the requirements of the study	
<b>EC2</b>	Pregnancy, intent to become pregnant, or breastfeeding	
<b>EC3</b>	Known sensitivity to or intolerance of oxpentifylline or other methylxanthines, such as caffeine, theophylline or theobromine	
<b>EC4</b>	History of major gastrointestinal bleeding or any gastrointestinal bleeding in the past 12 weeks	
<b>EC5</b>	Absolute or functional iron deficiency (ferritin $< 100$ microgram/l and/or transferrin saturation $< 20$ percent)	
<b>EC6</b>	Vitamin B12 or folate deficiency (test results from previous 4 weeks may be used)	
<b>EC7</b>	Parathyroid hormone $> 100$ pmol/l (test results from previous 4 weeks may be used)	
<b>EC8</b>	Serum Aluminium $> 2$ micromol/l (test results from previous 4 weeks may be used)	
<b>EC9</b>	Urea reduction ratio $< 65$ percent OR single pool Kt/V $< 1.0$ (haemodialysis patients) OR total weekly Kt/V $< 1.7$ (peritoneal dialysis patients) (test results from previous 4 weeks may be used)	
<b>EC10</b>	Presence of systematic haematological disease (including antibody-mediated pure red cell aplasia) or known haemoglobinopathy	
<b>EC11</b>	Active haemolysis	
<b>EC12</b>	Any surgery within the last 6 weeks; infection within 6 weeks of the last antibiotic dose; acute myocardial infarction or malignancy within the last 6 weeks	
<b>EC13</b>	Melatonin treatment, androgen therapy or blood transfusion within the previous 4 weeks	
<b>EC14</b>	Vitamin C therapy at dose greater than 1000mg/day or at a dose which has changed within the last 12 weeks	
<b>EC15</b>	Haemorrhagic stroke or severe haemorrhage within the last 12 weeks	
<b>EC16</b>	Current immunosuppressant use, or immunosuppression during previous 4 weeks	