EFFICACY OF ERYTHROPOIETIN (R-HUEPO) IN THE CRITICALLY ILL PATIENT: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Objective: To assess the efficacy of recombinant human erythropoietin (r-HuEPO) in reducing the exposure to allogeneic RBC transfusions in critically ill patients.

Study Design: Adult patients who met eligibility criteria and signed informed consent were randomized on ICU day three to receive either placebo or 40,000 IU of r-HuEPO subcutaneously weekly for three doses. Patients remaining in the ICU at study day 21 received a fourth dose. All patients received oral iron. Patients were followed for 28 days for efficacy and 42 days for safety. All patients enrolled were analyzed by intent to treat.

Results: Thirteen-hundred two patients (650 r-HuEPO, 652 placebo) from 65 US centers (trauma, medical, surgical, and multidisciplinary ICUs) were randomized, stratified by center. Baseline characteristics and demographics were similar between the two groups (average age 51yrs; male 62%; APACHE II score 19.6±7.8 SD). Primary efficacy result: 60.4% of placebo vs. 50.5% of r-HuEPO patients were transfused ($p=0.0004$ two sided Fisher's exact test). Placebo patients were transfused median of 2.0 units vs 1.0 for r-HuEPO patients ($p=0.0008$ Wilcoxon-Mann-Whitney test) and had a lower increase in hemoglobin of 0.94 vs 1.32 g/dl as compared to the r-HuEPO group ($p=0.001$ two sided T-test). There was a 19% reduction in total RBC units transfused (1963 vs 1590 placebo vs r-HuEPO groups). Mortality and other adverse events including thrombovascular events were similar between the two groups. There were no statistically significant differences between the groups in key analyses such as mechanical ventilation free days, new onset ventilation for patients not ventilated on admission, ICU readmission, or ICU LOS although each of these analyses favored the r-HuEPO group.

Discussion: This large randomized trial conducted in a diverse group of intensive care unit settings demonstrates the efficacy of r-HuEPO in reducing allogeneic RBC transfusions in the critically ill patient, consistent with the findings of a previous three-center trial1. It demonstrates the efficacy of r-HuEPO administered subcutaneously weekly at a dose of 40,000 IU. r-HuEPO may be considered as part of an overall blood management strategy in long term ICU patients.

Summary: Treatment with r-HuEPO resulted in a statistically significant increase in the proportion of ICU patients who were transfusion free and an almost 20% reduction in the total number of allogeneic transfusions administered. Despite fewer patients transfused and less allogeneic blood received , there was a greater increase in hemoglobin in r-HuEPO treated-patients than in placebo-treated patients. The treatment was well-tolerated with no differences overall between r-HuEPO and placebo groups with regard to mortality or other adverse events.

Ref: 1. Corwin, H., Gettinger, A., Rodriguez, R., et al. Efficacy of Recombinant Human Erythropoietin in the Critically Ill Patient: A Randomized Double Blind Placebo-Controlled Trial. Critical Care Medicine. 1999;27:2346-2350

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