

Effects of Epoetin Alfa in Hematologic Malignancies

**Timothy Littlewood, M.D.
Bone Marrow Transplant Service
John Radcliffe Hospital
Oxford, England**



VIENNA

Littlewood et al.: Subanalysis in HM Patients

- **Placebo-controlled trial evaluating efficacy of epoetin alfa in 375 anemic patients with solid tumors or HM receiving nonplatinum chemotherapy**
- **Subgroup analysis of patients ($n = 173$) with HM**
- **Primary endpoint: percent of patients transfused after 28 days**
- **Secondary endpoints included change in Hb level, proportion of responders, change in scores on 5 cancer-specific, Hb-sensitive QOL scales**
- **Results for HM subgroup similar to those for total population**

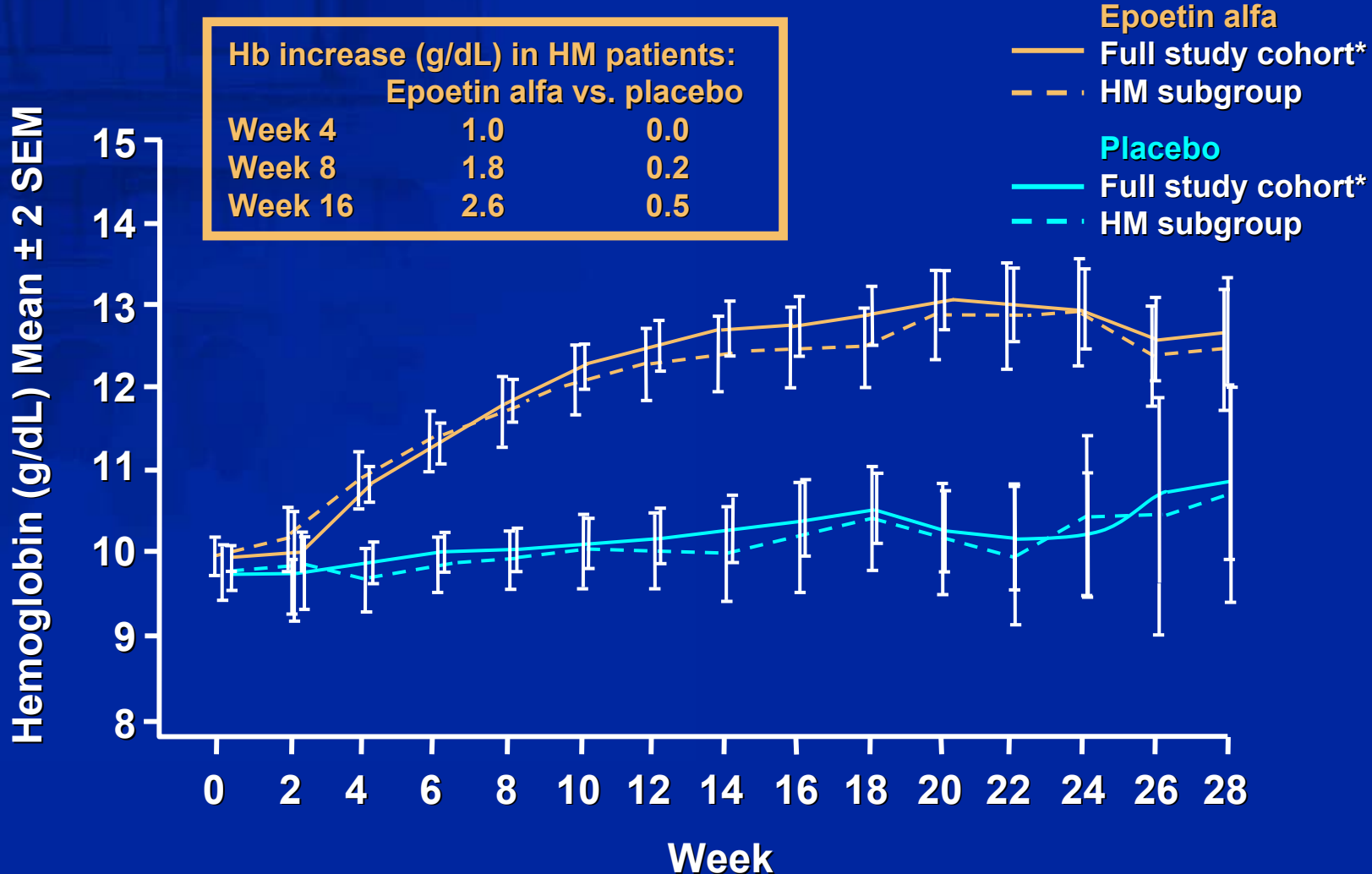
Note: Although not presented in full at the symposium, these data provide valuable information regarding managing anemia in patients with HM

HM Patient Demographics (*n* = 173)*

	Epoetin alfa (<i>n</i> = 115)	Placebo (<i>n</i> = 58)
Female, <i>n</i> (%)	56 (49)	26 (45)
Male, <i>n</i> (%)	59 (51)	32 (55)
Mean age (years)	59.4	63.9
Mean baseline Hb ± SD (g/dL)	9.9±1.22	9.7±1.21
Required transfusions, <i>n</i> (%)[†]	41 (36)	20 (35)
HM, <i>n</i> (%)		
Non-Hodgkin's lymphoma	41 (36)	21 (36)
Myeloma	37 (32)	25 (43)
Hodgkin's disease	19 (16)	6 (10)
Chronic lymphocytic leukemia	16 (14)	5 (9)
Other	2 (2)	1 (2)

*Intent-to-treat (ITT) population; [†]Within 3 months prior to study entry

Epoetin Alfa Steadily Increased Hb Levels



*p < .001 for epoetin alfa vs. placebo (full study population)

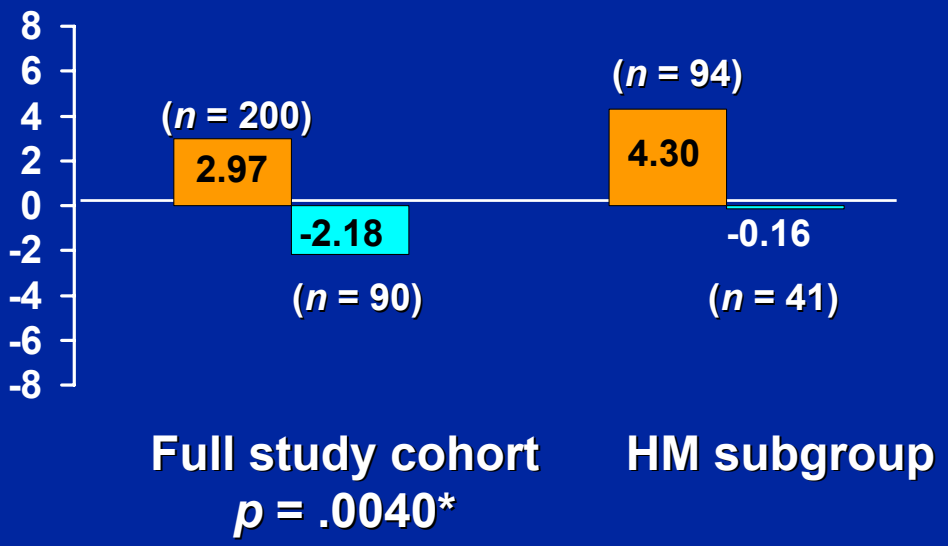
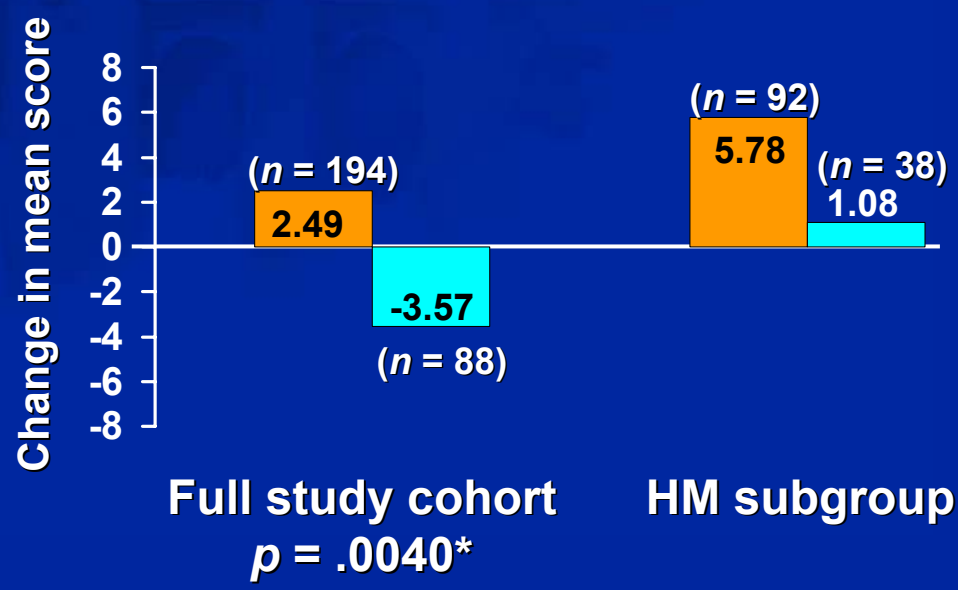
Littlewood, Hematol J (2000); Littlewood, J Clin Oncol (2001)

Epoetin Alfa Improves QOL— FACT-An Scores

■ Epoetin alfa ■ Placebo

FACT-An: FACT-G scale, range: 0–108

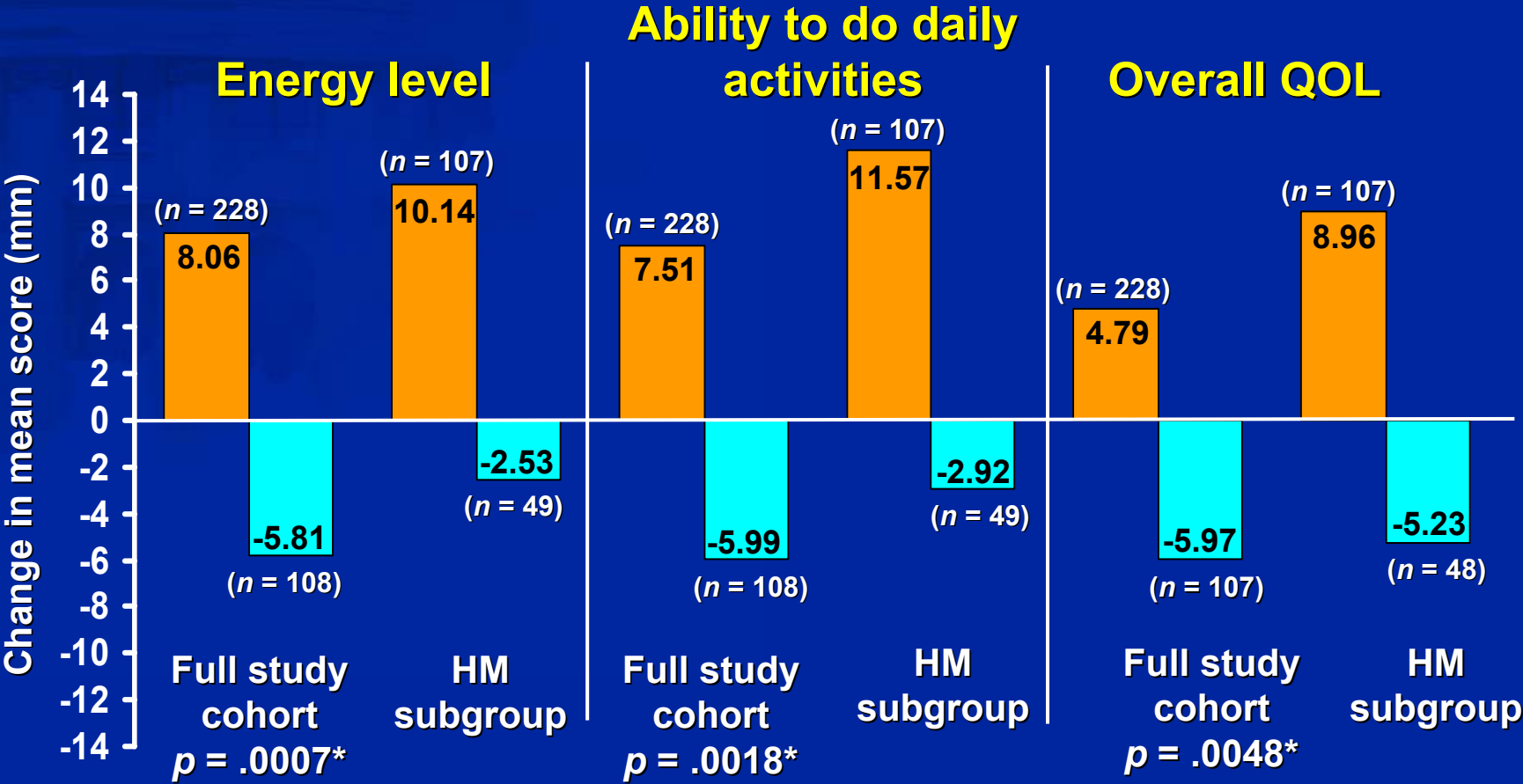
FACT-An: Fatigue subscale, range: 0–52



*adjusted for multiple comparisons

Epoetin Alfa Improves QOL—CLAS Scores

■ Epoetin alfa ■ Placebo



*adjusted for multiple comparisons

Recommendations for Use of Epoetin in Patients With HM (I)

ASCO/ASH recommendations (<i>Rizzo 2002</i>)	Panel of experts recommendations (<i>Ludwig 2002</i>)
Criteria for initiation	
<ul style="list-style-type: none">▪ Hb <10g/dL▪ Certain clinical circumstances if Hb is 10-12 g/dL	<ul style="list-style-type: none">▪ Hb <10 g/dL▪ Hb \leq12 g/dL and WHO performance status \geqIII due to anemia▪ Hb \leq12 g/dL and decrease in Hb of \geq1.5 g/dL per month during ongoing chemotherapy
Starting dose	
<ul style="list-style-type: none">▪ 150 IU/kg three times weekly for \geq4 weeks OR <ul style="list-style-type: none">▪ 40,000 IU once weekly	<ul style="list-style-type: none">▪ 10,000 IU three times weekly or 40,000 IU once weekly

Recommendations for Use of Epoetin in Patients With HM (II)

ASCO/ASH recommendations (Rizzo 2002)	Panel of experts recommendations (Ludwig 2002)
Dose escalation	
<ul style="list-style-type: none">▪ Dose escalation to 300 IU/kg three times weekly for an additional 4-8 weeks in those not responding to initial dose at week 4*	<ul style="list-style-type: none">▪ Dose escalation to 20,000 IU three times weekly or 60,000 IU weekly if no response at 4 weeks*
Dose titration	
<ul style="list-style-type: none">▪ Dose titration to maintain Hb around 12 g/dL	<ul style="list-style-type: none">▪ Dose titration to maintain Hb ≥ 12 g/dL

*Dose response defined as an increase in Hb of ≥ 1 g/dL

Recommendations for Use of Epoetin in Patients With HM (III)

ASCO/ASH recommendations (<i>Rizzo 2002</i>)	Panel of experts recommendations (<i>Ludwig 2002</i>)
Discontinuation	
<ul style="list-style-type: none">▪ Discontinue after 6-8 weeks if there is no response (<1-2 g/dL increase in Hb)▪ Discontinue if Hb >12 g/dL▪ Restart when level falls to near 10 g/dL	<ul style="list-style-type: none">▪ Discontinue if at 4 weeks after dose escalation Hb level has not increased by 1 g/dL▪ Discontinue if Hb >14 g/dL▪ If Hb falls to <12 g/dL, restart with a 25% reduction in dose

Recommendations for Use of Epoetin in Patients With HM (IV)

ASCO/ASH recommendations (<i>Rizzo 2002</i>)	Panel of experts recommendations (<i>Ludwig 2002</i>)
Iron repletion	
<ul style="list-style-type: none">▪ Baseline and periodic monitoring of iron, total iron binding capacity, transferrin saturation, or ferritin levels and instituting iron repletion when indicated may be valuable in limiting the need for rHuEpo[‡]	<ul style="list-style-type: none">▪ If transferrin saturation < 20%

[‡]The guidelines note that there is inadequate evidence to specify optimal timing, periodicity, or testing regimen for such monitoring

Epoetin alfa—Standard of Care for Anemia Management in Hematologic Malignancies

- Rapidly and effectively increases Hb
- Reduces transfusion requirements
- Improves QOL