

Hemoglobin as a Prognostic Factor in NSCLC

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Anemia Is Defined as...

- Hemoglobin (Hb) less than 8 or 9 g/dL
- Hb less than 10.5 g/dL (*Littlewood study*)
- Hb less than 10.5 g/dL with symptoms (eg, dyspnea, dizziness, fatigue)
- Hb less than 12 g/dL
- Any level of Hb at which patient is functioning below normal

Grading of Anemia

	Grade	WHO (g/dL)	NCI/CTC/etc (g/dL)
0	0	≥ 11	12–16F, 14–16M
Mild	1	9.5–10.9	10–WNL*
Moderate	2	8.0–9.4	8–10
Severe	3	6.5–7.9	6.5–7.9
Life threat	4	<6.5	<6.5

13 g/dL = 8.06 mmol/L M, **12 g/dL** = 7.44 mmol/L F

*WNL: within normal limits

Groopman (1999)

What Are the Outcomes?

- **Survival**
- **Time to progression**
- **Response rate – objective**
- **Response rate – symptoms**
- **Toxicity**
- **Quality of life (QOL)**
- **Cost effectiveness – value**

Hb Level and Survival

■ SWOG Study

- $n = 2531$ with advanced NSCLC
- Cisplatin treated

Results

- Best OS: Good performance status
 - Hb >11 g/dL positively correlated with survival ($p < .001$)
 - Age >47 years
- ## ■ Mild to moderate anemia associated with poor survival in cancer patients regardless of treatment

Non-Small Cell Lung Cancer

■ Study Design

- $n = 143$, local and advanced disease, influence of collagen degradation markers as prognostic factors

■ Results

- OS related to collagen degradation marker, sedimentation rate and Hb level

Non-Small Cell Lung Cancer

- $n = 96$
- Local and advanced disease
- Treated by irradiation
- Results
 - Hb level only prognostic factor for OS

Anemia Perioperatively

- Colon cancer
- Lung cancer
 - $n = 330$, 169 transfusion
 - More deaths and recurrences
- Lung cancer
 - $n = 352$, transfusion more in >60 years
 - No effect on outcome
 - >60 also shown in platinum chemotherapy study
- Is it cause or effect?

Anemia: Independent Prognostic Factor for Survival in Cancer Patients

- **Anemia is common in cancer patients**
- **Studies have compared the survival of patients with or without anemia and have shown reduced survival times in various malignancies in patients with anemia**
- **Obtain an overall estimate of the effect of anemia on survival in patients with malignant disease**

Results (I)

- Patients received chemotherapy and/or radiotherapy treatment at the time that the Hb or anemia status was established - literature search - 60 papers
- Anemia defined as present or absent, or stratified by Hb levels, which varied from 8.5–14.0 g/dL
- Anemic patients had median survival
 - 4 months (lung and MM) to 96 months (prostate)
- Nonanemic patients had median survival
 - 7 months (lung) to 120 months (prostate)

Results (II)

- **Relative risk of death in anemic cancer patients increases by**
 - 19% in lung cancer patients
 - 75% in head and neck cancer patients
 - 47% in prostate cancer patients
 - 67% in lymphoma patients

- **Overall estimate increase in risk was 65% (54%–77%)**

Survival Conclusions

- **Anemia is a strong predictor of poorer survival**
- **Additional studies are necessary to determine whether treating low hemoglobin levels improves survival**

Data Interpreted With Caution

- Placebo-controlled study, $n = 375$
- Study not originally designed or powered to evaluate survival
- Other survival influences not controlled for or stratified in study
 - Stage of disease
 - Bone marrow involvement
 - Intensity of chemotherapy
 - Disease progression

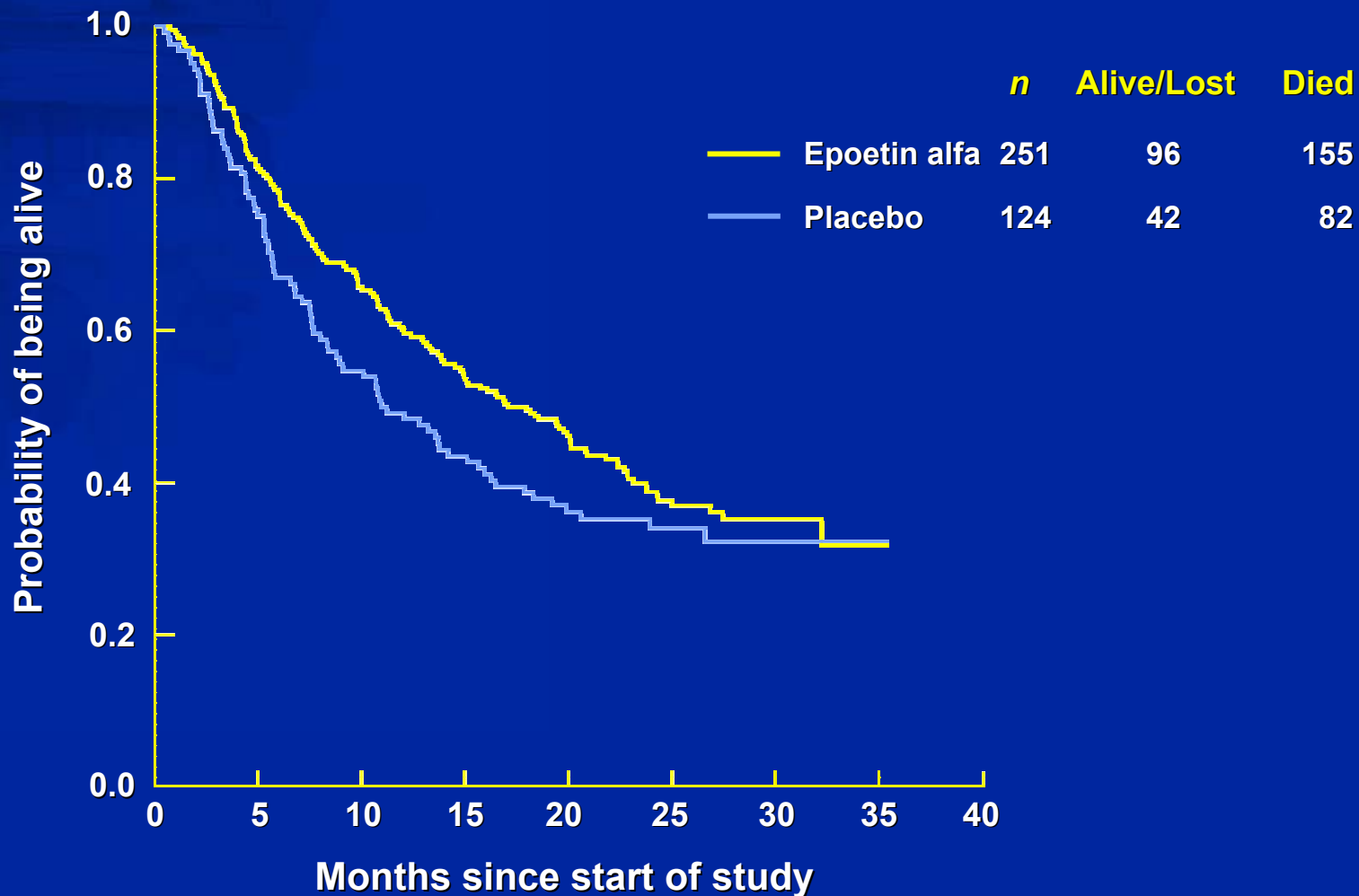
Survival Analysis

- Assessed at 12 months following study completion by last patient
- Patient status
 - 135 patients alive
 - epoetin alfa 94/251 (37%)
 - placebo 41/124 (33%)
 - 237 patients died
 - epoetin alfa 155/251 (62%)
 - placebo 82/124 (66%)
 - 3 patients lost to follow-up
 - 2 epoetin alfa (1%)
 - 1 placebo (1%)
- Median follow-up 26 months

Kaplan-Meier Estimates of Survival

	Epoetin alfa	Placebo
Kaplan-Meier estimates of 12-month survival rate	60%	49%
Median survival times (months)	17	11

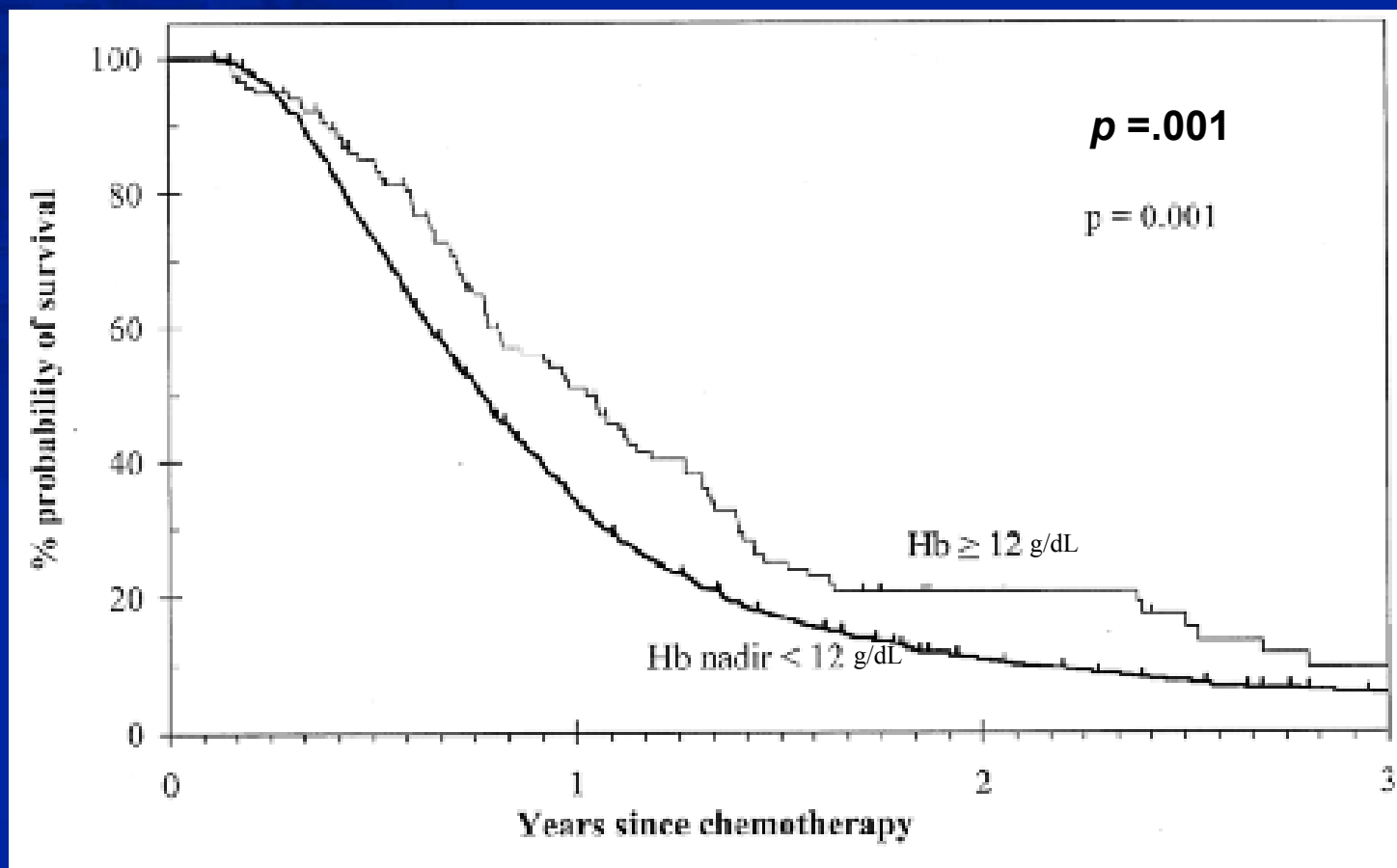
Kaplan-Meier Estimates of Survival



($p = .126$, log-rank test)

Littlewood (2001)

Lung Cancer Patients—Survival by Nadir Hb



Kaplan-Meier survival curves for 906 patients treated with chemotherapy for small-cell or non-small-cell lung cancer according to lowest recorded hemoglobin (Hb g/dL) level during treatment

Anemia and Weight Loss

MVA 1994–2001

	SCLC	NSCLC
<i>n</i> =	290	418
Hb <12 g/dL		86%[†]
Weight loss	59%	58%
Anemia as toxicity		<i>p</i> =.0003

[†]Survival: 9 months vs. 12 months, *p* =.001

Chemotherapy/Radiotherapy

- Carboplatinum/Taxol + radiotherapy concurrently weekly
- $n = 115$

Hb decline

- <10% decrease on Tx
- 10-30% decrease on Tx
- >30% decrease on Tx

MS

- 26.4 months
- 15 months
- 9 months

2-year survival

- 51%
- 26%
- 0

- Hb independent $p = .015$

Prognostic Factors for Mesothelioma

- $n = 111$, median survival 5.1 months
- Poor prognosis if
 - Age >49 years
 - Hb <14 g/dL
 - Platelets >400
 - Sarcomatous¹
- Same for CALGB with PS, weight loss high WCC¹
- Same for Andreopoulou
- Hb, NS with Curran for EORTC²

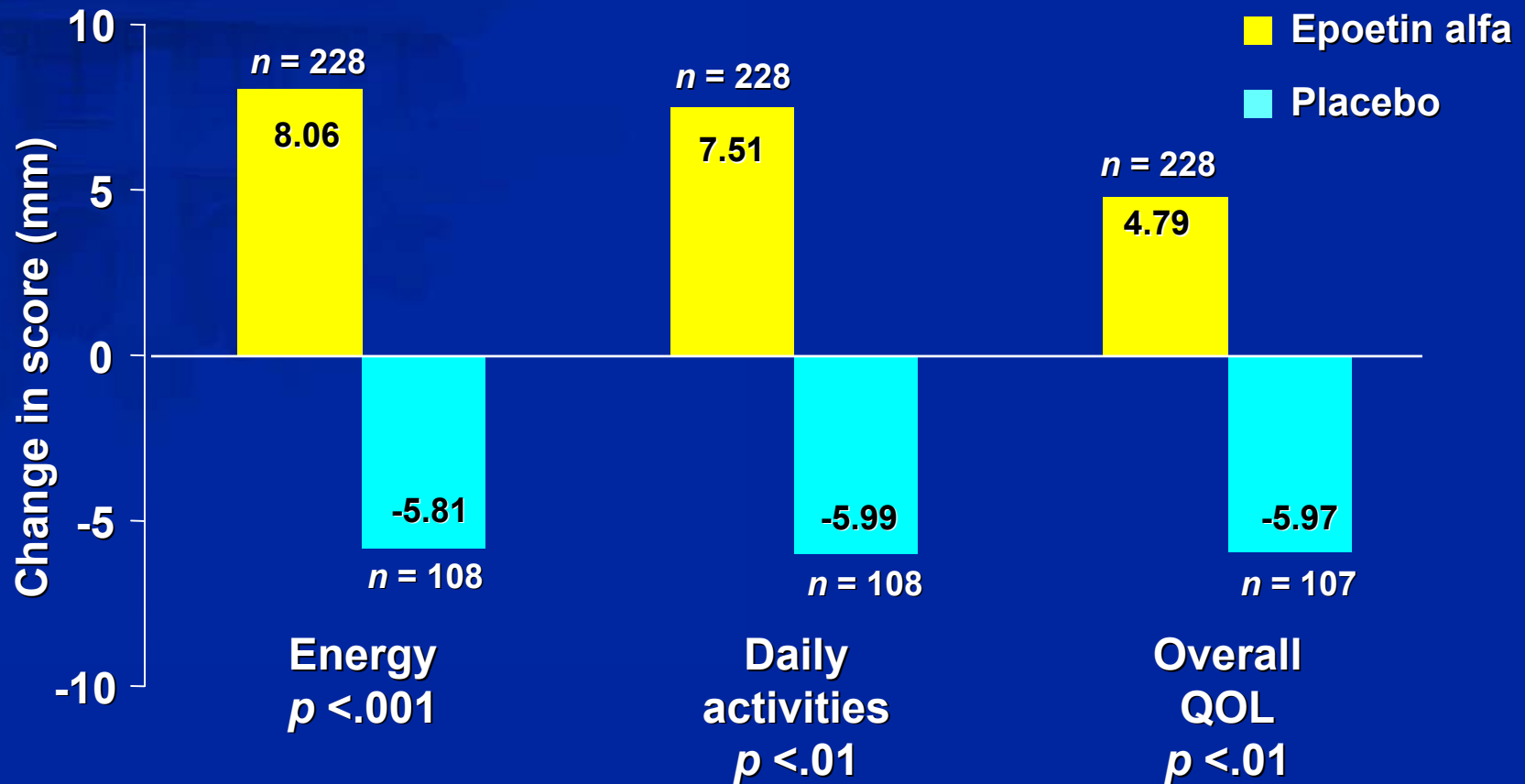
¹Edwards (Thorax 2000)

²Curran (JCO 1998)

Hb Correlates With Quality of Life

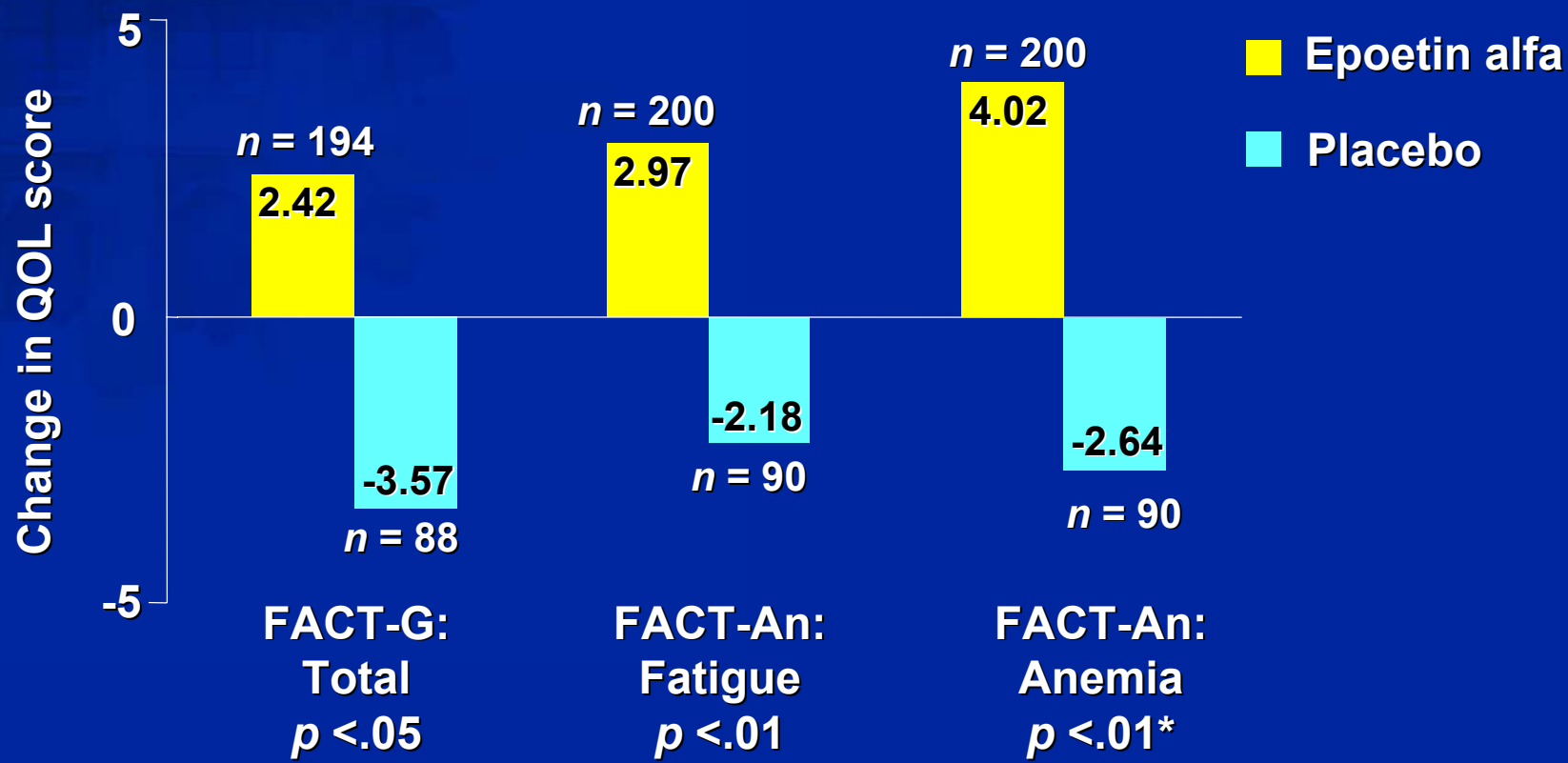
- **Definition of anemia**
 - Hb <12 g/dL (F)
 - Hb <13 g/dL (M)
- **FACT-An, SF-36**
- **Breast, ovary, lung, and multiple myeloma**
- **Mean Hb 10.6 g/dL, no epoetin alfa**
- **For each gram Hb, 8 points on FACT-An and 7 on SF-36**

Change in CLAS* Score From Baseline to Last Assessment



*Cancer Linear Analog Scale, also known as Linear Analog Scale Assessment or LASA

Change in FACT-G and FACT-An From Baseline to Last Assessment



*Not adjusted for multiple comparisons

Low Hb – Poor Prognosis

- **Correcting anemia makes 30% of patients feel better**
- **Is this inherent tumor biology – more aggressive or extensive tumor burden?**
- **What is the QOL with transfused Hb >12 g/dL?**
- **Does correcting Hb reverse the prognostic implications?**