

# **Efficacy Evaluation of Anemia Treatments**

**Pere Gascón  
Spain**



ANEMIA

# Epoetin Alfa Studies: Defining Efficacy

- Hemoglobin
  - Change from baseline to final
- Transfusions
  - Number of patients transfused
  - Number of units
- Quality of life
  - Energy level, daily activity, overall QOL

# Defining Efficacy: Hemoglobin

# Treatment With Epoetin Alfa Produces Reliable and Predictable Increases in Hb

- Duration of chemotherapy (CT) is often short<sup>1</sup>
- Hemoglobin (Hb) decreases in early CT cycles are expected<sup>1</sup>
- Community-based clinical trials of epoetin alfa in anemic patients showed that Hb increased<sup>2,3</sup>
  - ~ 1 g/dL in 4 weeks
  - ~ 2 g/dL in 8 weeks
- Reliable and predictable Hb increases needed to assure quality-of-life (QOL) benefit

<sup>1</sup>Ludwig (EJC in press)

<sup>2</sup>Demetri (J Clin Oncol 1998)

<sup>3</sup>Gabrilove (J Clin Oncol 2001)

# Hb Meta-analysis Methods

- Retrospective analysis of 7 randomized studies\* (N = 1,639) in anemic cancer CT patients receiving either epoetin alfa 150–300 IU/kg or placebo 3 times weekly
- A subset analysis was performed for 1,285 patients with Hb values for baseline and each of the next 10 weeks
- Analysis of one of the included studies was performed to further assess the effect of different analytic techniques

4 randomized published studies<sup>1-4</sup>; 3 unpublished studies

<sup>1</sup>Abels (*Eur J Cancer* 1993)

<sup>2</sup>Rose (*BLOOD* 1994 )

<sup>3</sup>Dammacco (*Br J Haematol* 2001)

<sup>4</sup>Littlewood (*J Clin Oncol* 2001)

# Hb Meta-analysis Results

- Mean changes in Hb values from baseline to each subsequent week showed significantly ( $P < 0.001$ ) greater increases in Hb for the epoetin alfa group than for the placebo group
- In the epoetin alfa group Hb levels increased
  - 1.0 g/dL by Week 4
  - 1.7 g/dL by Week 8
  - 1.8 g/dL by Week 10
- In the placebo group Hb levels increased
  - 0.2 g/dL by Week 10

# Results of Analysis of Analytic Techniques

- Hb outcomes calculated using ITT, EFF, and PP populations are comparable
- Censoring of Hb values within 28 days of transfusion resulted in higher Hb estimates (0.1 to 0.3 g/dL) than not censoring

# Hb Meta-analysis Conclusions

- Hb decreases during CT are expected; timely Hb response to epoetin alfa early during CT is clinically important<sup>1</sup>
- Results of the meta-analysis of 7 randomized, controlled trials of anemic cancer patients undergoing CT (N = 1,624) agree with those of previous nonrandomized, community-based studies<sup>6,7</sup>
- Epoetin alfa therapy increased Hb levels ~1g/dL by week 4 and ~2 g/dL by Week 8 in this large population

<sup>1</sup>Cella (*J Clin Cancer* 2003); <sup>2</sup>Fallowfield (*Br J Cancer* 2002); <sup>3</sup>Littlewood (*J Clin Oncol* 2001); <sup>4</sup>Crawford (*Cancer* 2002); <sup>5</sup>Nortier (ESMO 2000) <sup>6</sup>Demetri (*J Clin Oncol* 1998); <sup>7</sup>Gabrilove (*J Clin Oncol* 2001)

# Defining Efficacy: Transfusion

# Cancer and Treatment-Related Anemia

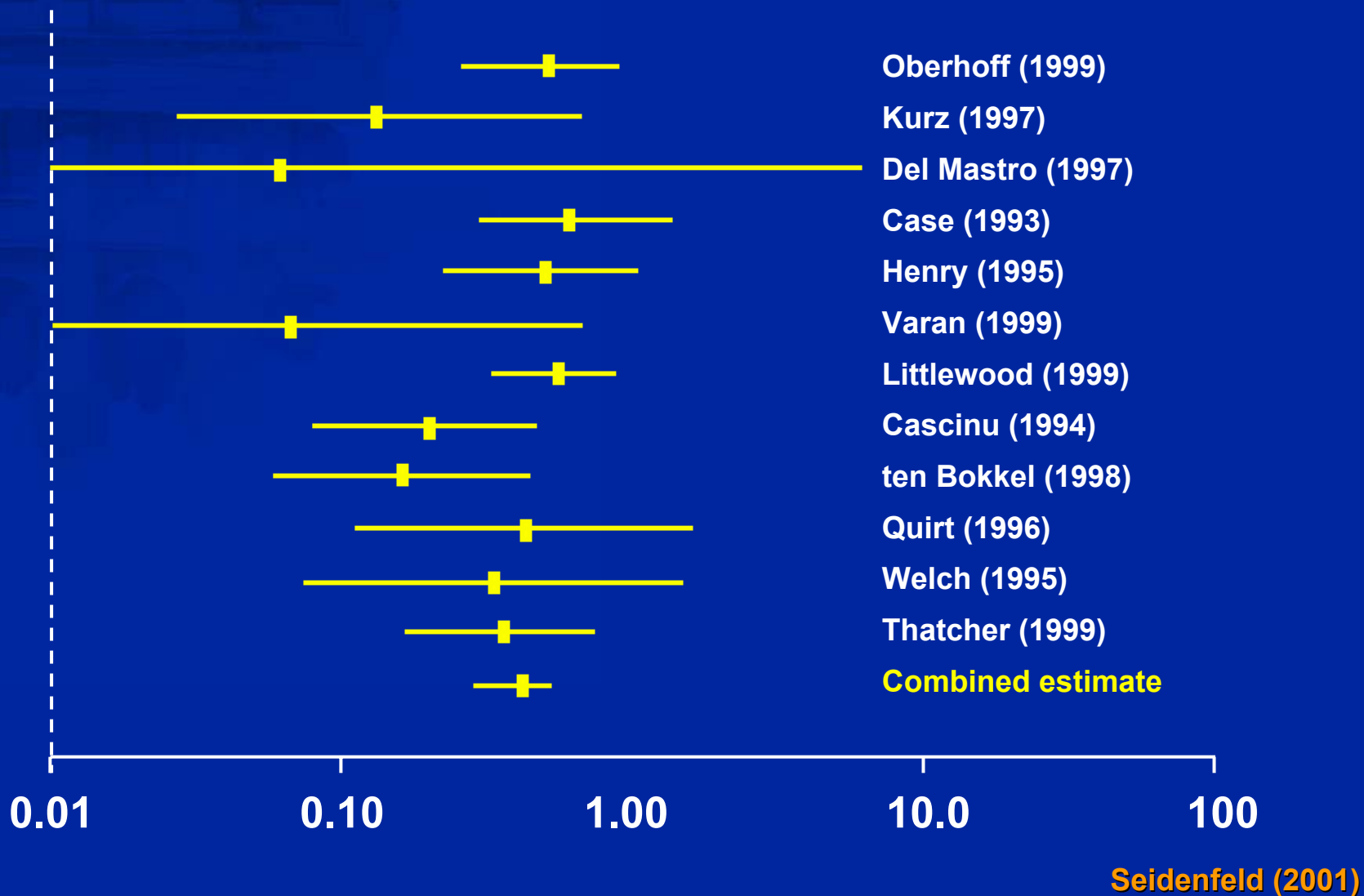
## Transfusion reduction

- Agency for Healthcare Policy and Research (AHRQ)
  - “Epoetin in oncology” (1998)
    - Evidence-based review
  - Epoetin treatment of anemia associated with cancer therapy: a systematic review and meta-analysis of controlled clinical trials

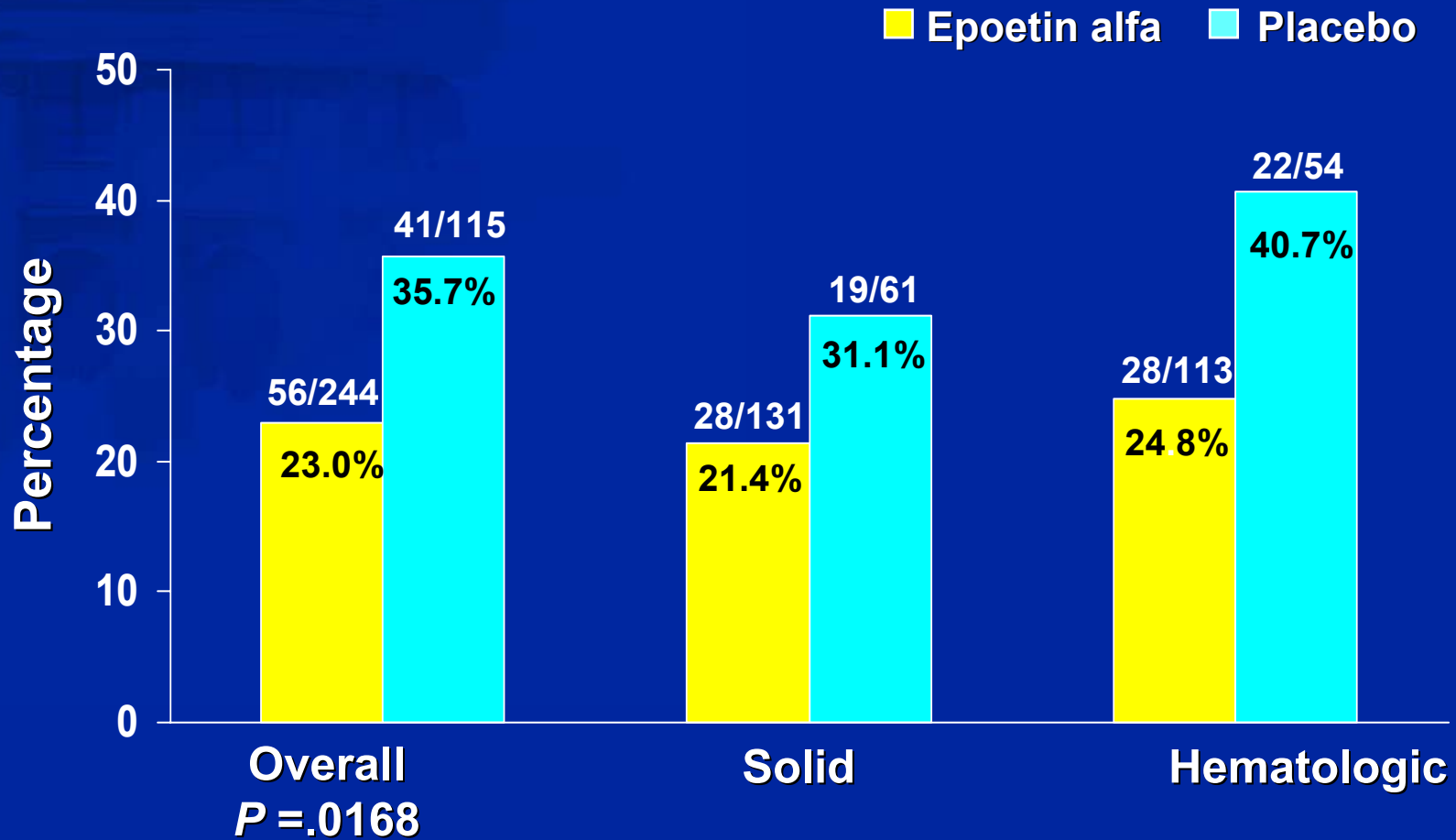
# AHRQ Meta-Analysis: Odds of Transfusion

- 12 controlled trials, 1390 evaluable patients
  - Combined odds ratio = 0.38
  - 95% CI = 0.28–0.51
  - NNT = 4.4 (95% CI = 3.6–6.1)

# AHRQ Meta-Analysis: Odds of Transfusion



# Randomized Data: Transfusion Endpoint



# Defining Efficacy: Quality of Life

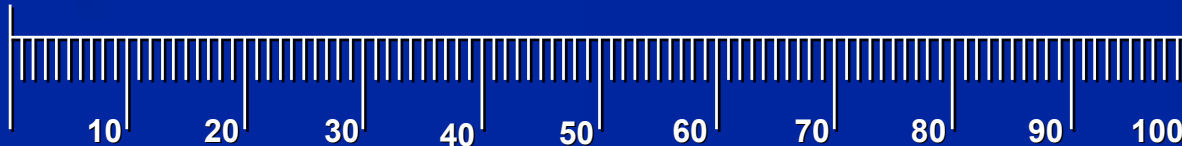
# Epoetin Alfa Clinical Studies: QOL

## Linear Analog Scale Assessment\*

TO BE COMPLETED BY THE PATIENT

**HOW WOULD YOU RATE YOUR ENERGY LEVEL  
DURING PAST WEEK?**

AS LOW AS  
COULD BE



AS HIGH AS  
COULD BE

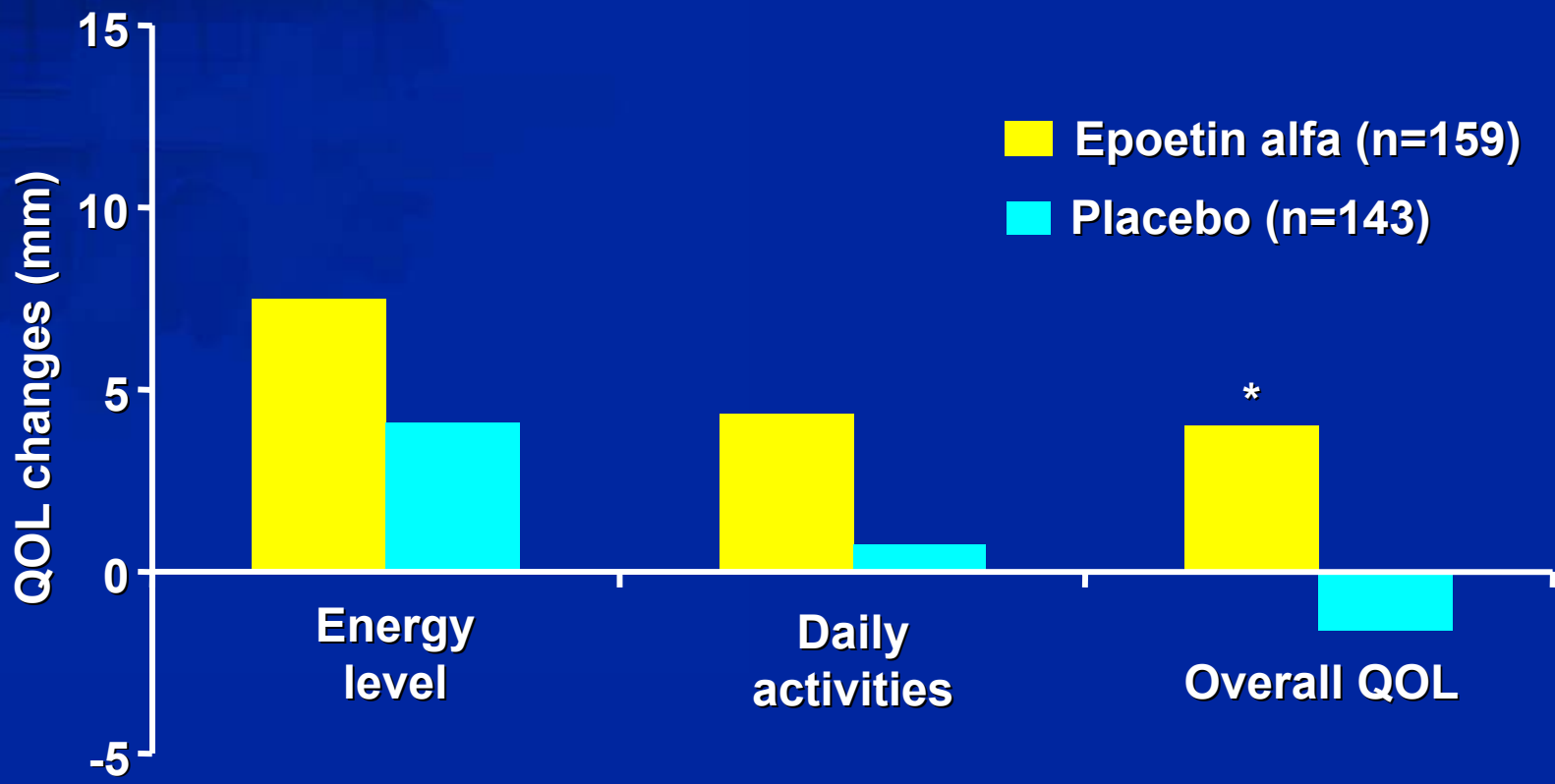
SAME SCALE FOR:

- ABILITY TO DO DAILY ACTIVITIES
- OVERALL QUALITY OF LIFE

\*LASA, also known as Cancer Linear Analog Scale or CLAS

# Epoetin Alfa Studies

## Change in QOL measures



\*Significantly ( $P < .05$ ) different from corresponding placebo response

# Epoetin Alfa Nonrandomized Studies: QOL

## Glaspys study (N=2342)

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- Open-label, nonrandomized
- Anemic
- Initial dose: 10,000 IU sc tiw
- Retrospective tumor response analysis
- LASA
- FACT-An

## Demetri study (N=2370)

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- Open-label, nonrandomized
- Anemic (Hb <11.0 g/dL)
- Initial dose: 10,000 IU sc tiw
- Prospective tumor response analysis
- LASA
- FACT-An

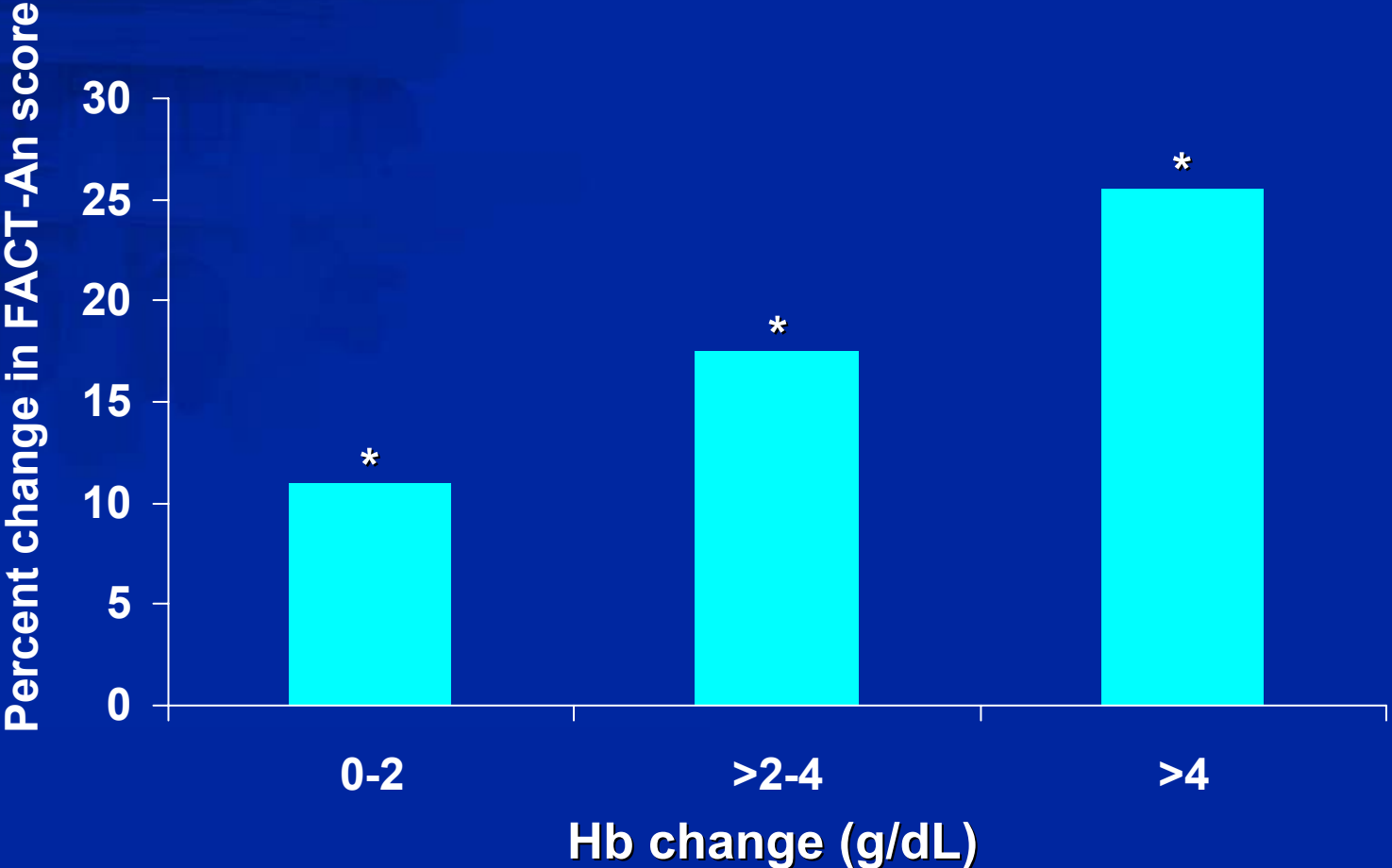
## Gabrilove study (N=2869)

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- Open-label, nonrandomized
- Anemic (Hb <11.0 g/dL)
- Initial dose: 40,000 IU sc qw
- Prospective tumor response analysis
- LASA
- Anemia subscale of FACT-An

# Once-Weekly Dosing Study

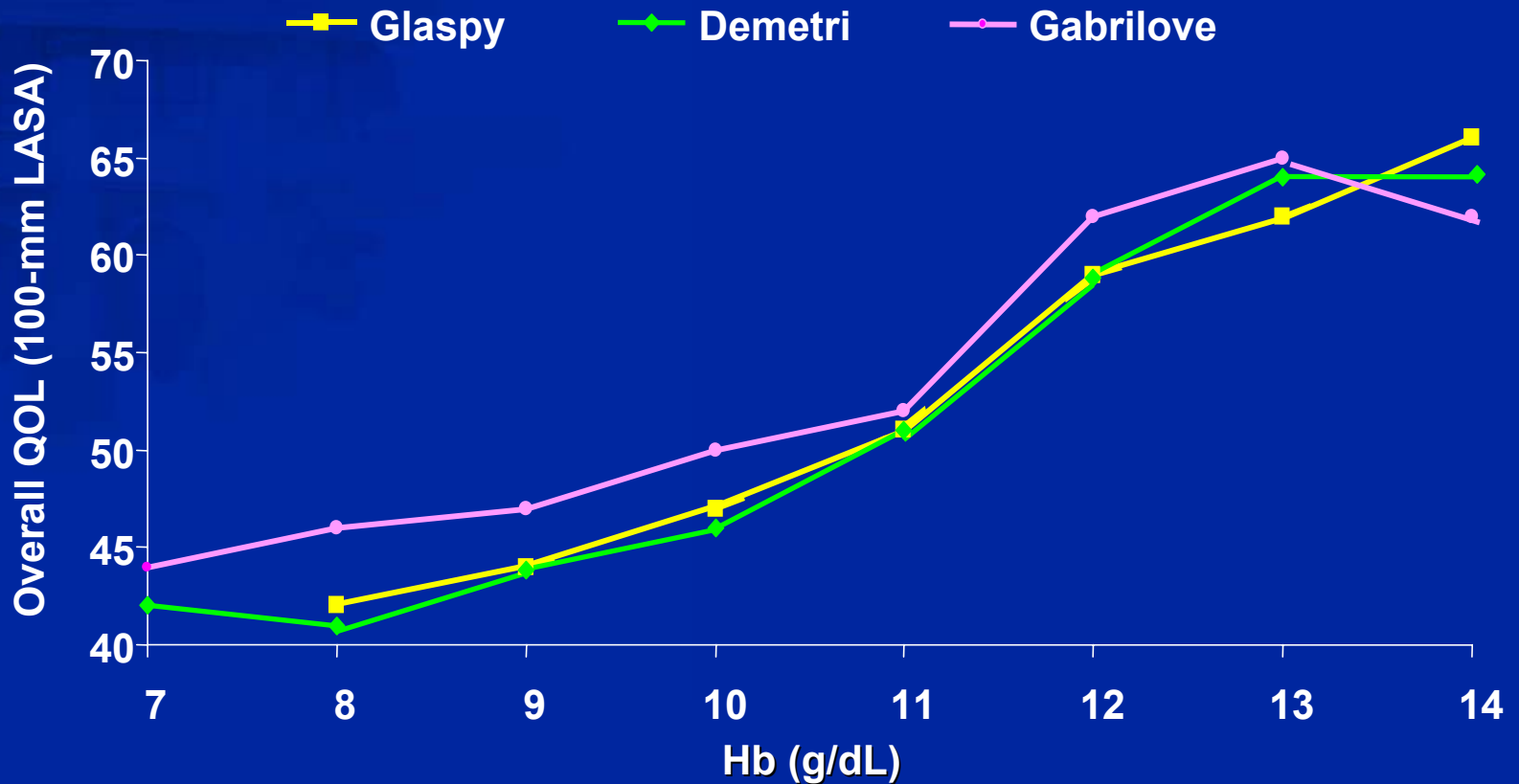
## Percent change in FACT-An



\*P <.001

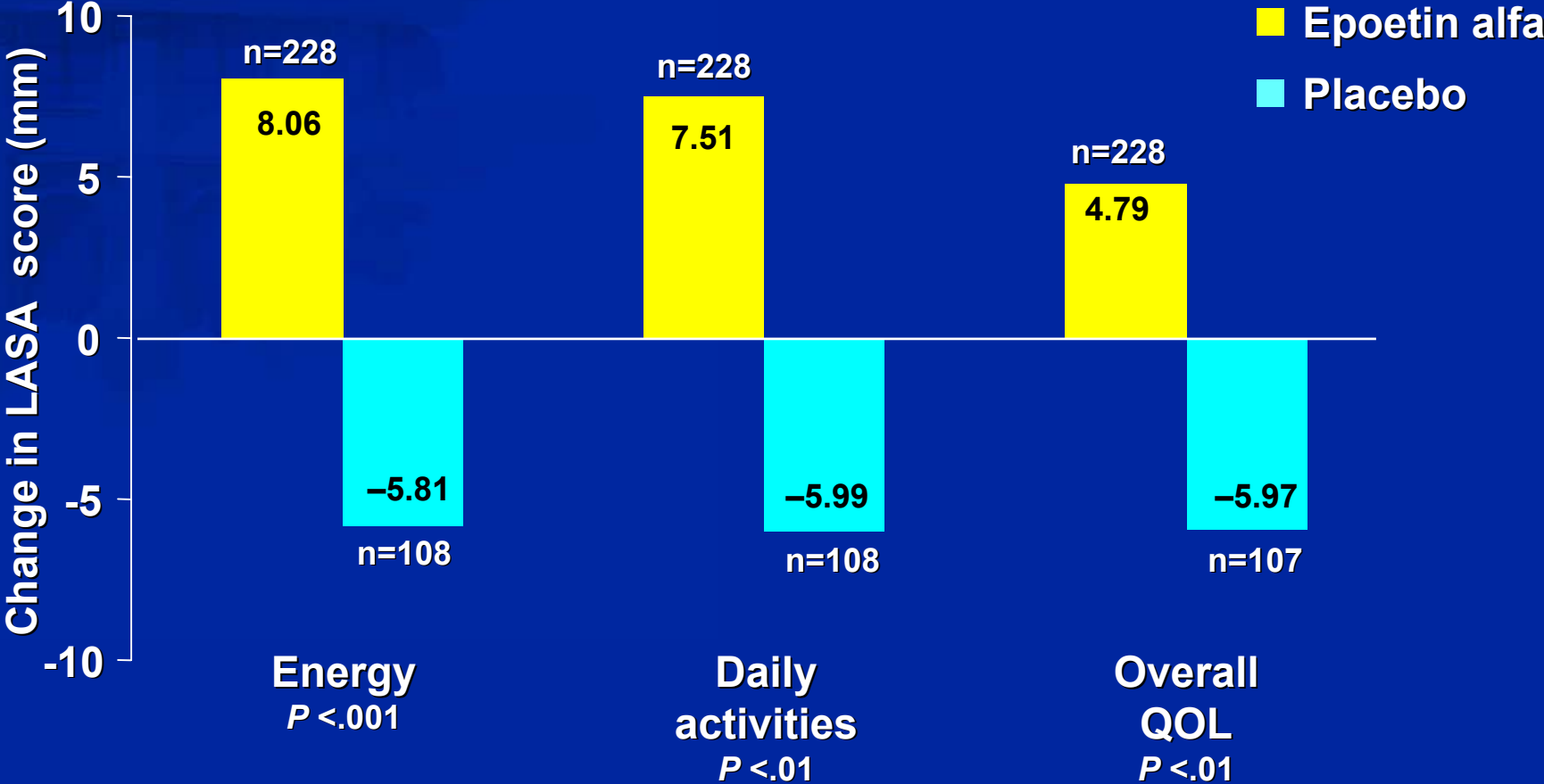
# Epoetin Alfa Nonrandomized Studies: QOL

LASA scores according to Hb levels

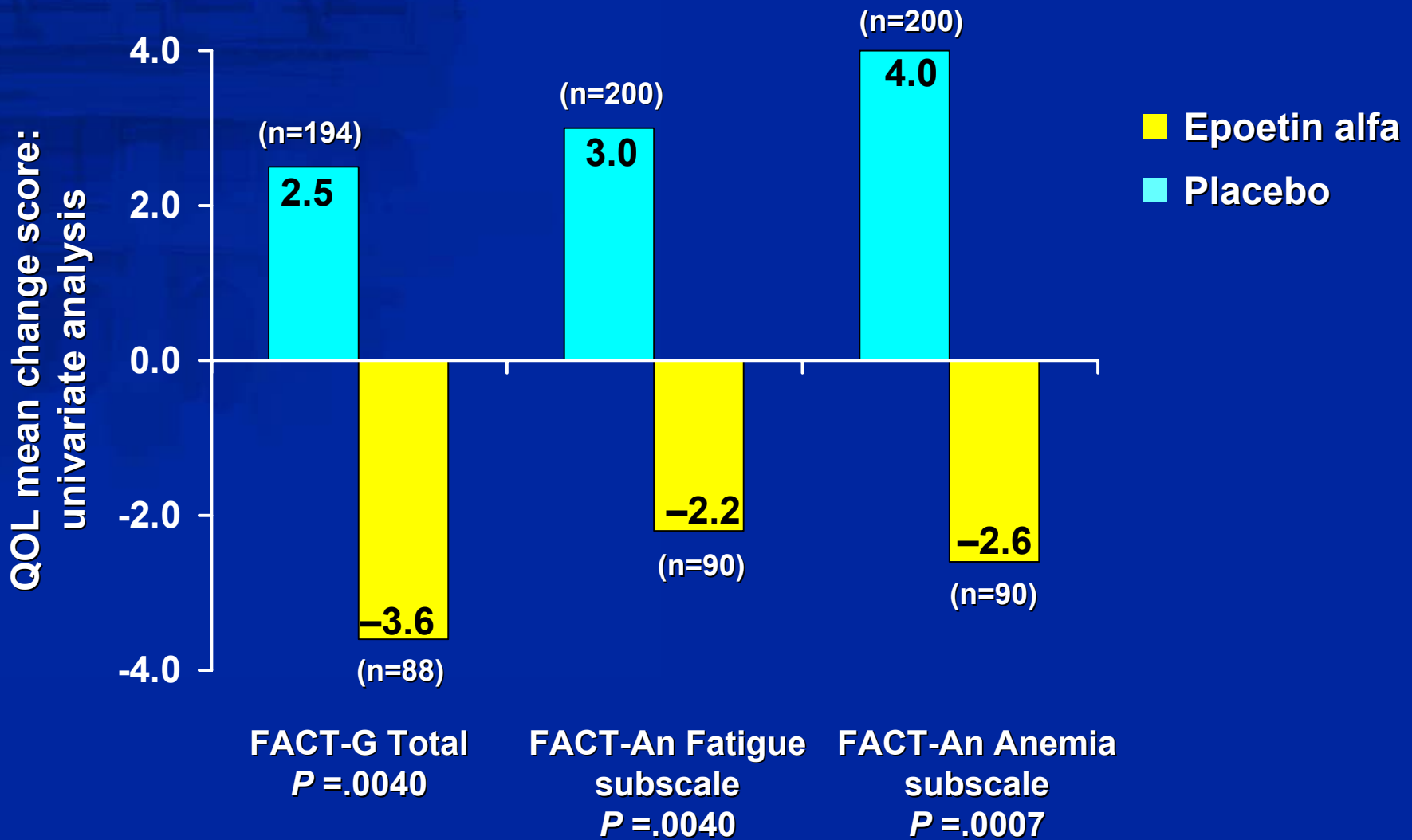


<b>Glaspy</b>	—	267	740	918	833	308	287	223
<b>Demetri</b>	59	352	770	753	547	391	313	160
<b>Gabrilove</b>	156	466	1134	1426	844	544	410	168

# Randomized Data: Epoetin Alfa and QOL



# Randomized Data: Epoetin Alfa and QOL



# Epoetin Alfa: Proven Efficacy

- **Clinical trials enrolling over ten thousand cancer patients have demonstrated that epoetin alfa reliably and predictably:**
  - increases Hb levels: ~ 1 g/dL at 4 weeks; ~ 2 g/dL at 8 weeks
  - reduces transfusion use
- **Results have been confirmed by meta-analysis**
- **Correlation between increased Hb and improved QOL**