

Epoetin Alfa Dosing Strategies to Maximize Efficacy

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Maximizing Efficacy of Epoetin Alfa in Cancer Patients: Goals

- ... to treat mild-to-moderate anemia promptly, before severe anemia develops
- ... to increase clinical response in patients with hemoglobin (Hb) <9 g/dL
- ... to improve compliance of patients eligible for chemotherapy even with low Hb levels
- ... to reduce time to response in order to minimize transfusion needs

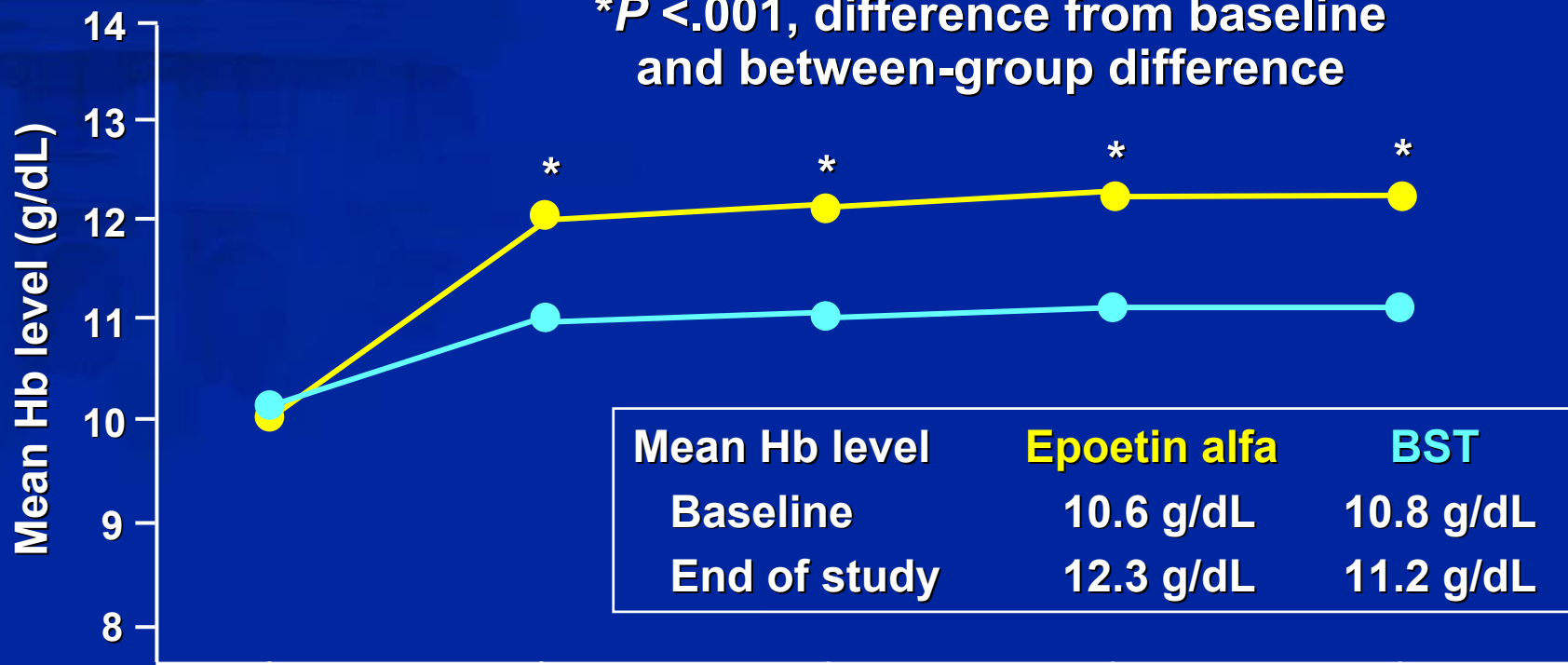
Maintaining Hb Levels During CT: Earlier Treatment With Epoetin Alfa

Study Design

- Randomized (1:1), multicenter, open-label, Phase IIIb trial
- Patients scheduled for myelotoxic CT for ≥ 12 weeks for breast cancer
 - Hb ≤ 12.0 g/dL
 - ECOG performance score 0, 1, or 2
- Epoetin alfa (n=107): 10,000 - 20,000 IU tiw up to 24 weeks during CT and 4 weeks after CT
- Control (n=107): best standard treatment (BST)

Earlier Treatment Maintains Hb Above 12 g/dL Throughout Entire Study

* $P < .001$, difference from baseline and between-group difference



Mean Hb level	Epoetin alfa	BST
Baseline	10.6 g/dL	10.8 g/dL
End of study	12.3 g/dL	11.2 g/dL

Baseline

After 4-6 weeks

After 8-9 weeks

After 12 weeks

Up to 28 weeks

Epoetin alfa n=107
BST n=107

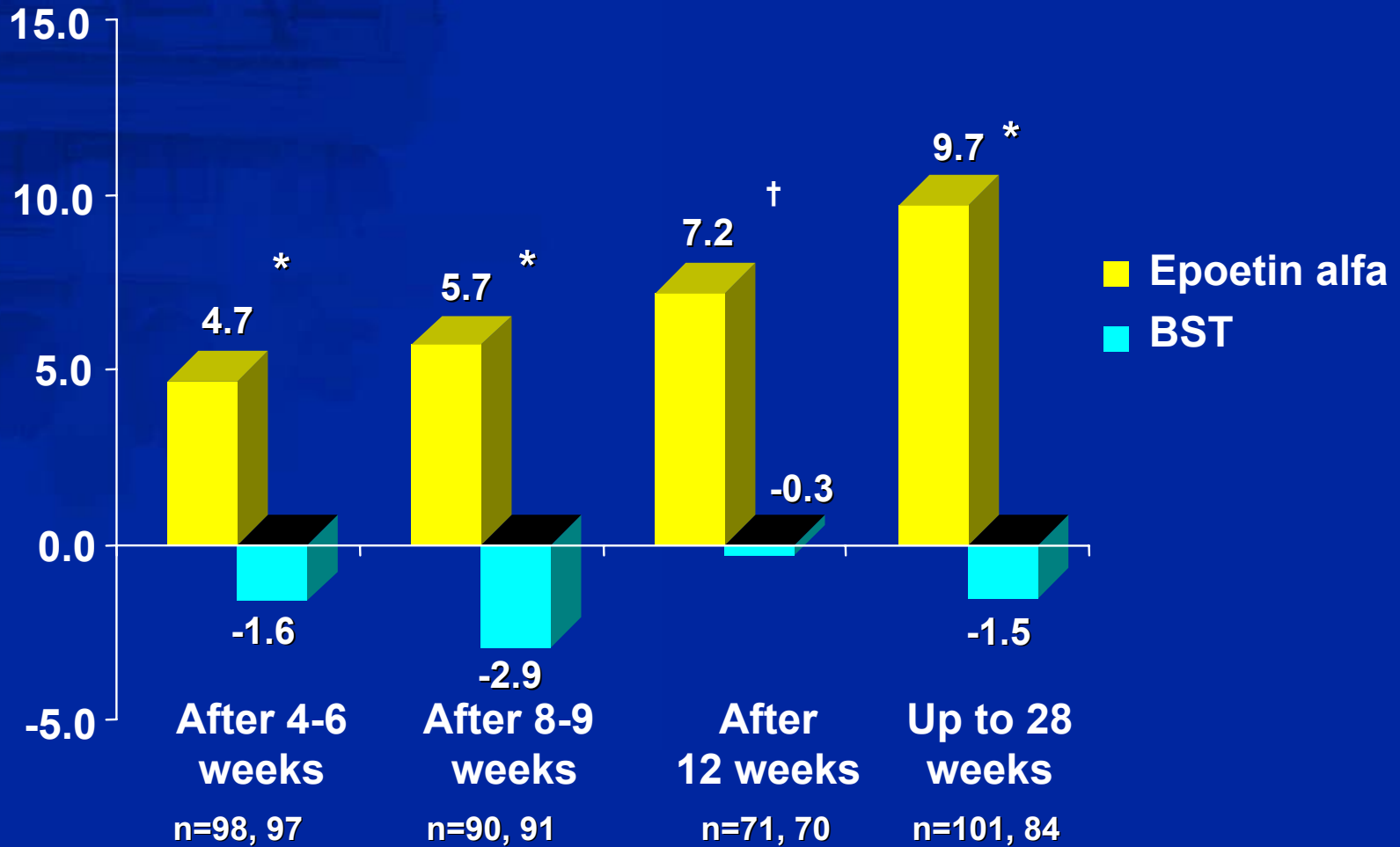
n=98
n=103

n=90
n=96

n=69
n=74

n=93
n=89

Mean QOL Change Between Baseline and All Time Points



* $P < .001$, † $P = .002$; between-group difference

Earlier Treatment Study Conclusions

- **Early intervention (Hb 10-12 g/dL) with epoetin alfa during CT in patients with breast cancer**
 - increased Hb levels rapidly and significantly ($P < .001$)
 - improved QOL rapidly and significantly ($P < .01$) as measured by FACT-An and CLAS
- **84% overall response rate to epoetin alfa**
 - response seen as early as Weeks 4-6
 - regardless of disease stage

Efficacy of Dose -dense Epoetin Alfa in Cancer Patients With Hb <9 g/dL

Our pilot study design

- Epoetin alfa 40,000 IU sc treatment on days 1, 4, 7, 10, 13
- Single IV dose of 125 mg elemental iron
- Hematologic parameter evaluation on days 15 and 45*
- Historic parallel control group: epoetin alfa 10,000 IU sc tiw (no dose increase for nonresponders)

*Previous studies measured parameters at 4 weeks and 8 weeks

Average Hb Increases

Comparison with Littlewood tiw data

Change in Hb (g/dL) Cortesi (2003)

	Day 15 ¹	Day 45 ²
10,000 IU tiw	0.38	0.80
40,000 IU x 2/wk	1.68	2.90

¹ $P = .0042$ between groups; ² $P = .0001$ between groups

Change in Hb (g/dL) Littlewood (2001)

	Week 4 (day 28)	Week 8 (day 56)
150-300 IU/kg tiw	0.9	1.8

Response Rates

Comparison with other historical data

	15 days		45 days	
	40,000 IU x 2/wk	10,000 IU tiw	40,000 IU x 2/wk	10,000 IU tiw
Hb \geq2 g/dL	37%	16%	82%	21%
	40,000-60,000 IU qw Gabrilove 2001 (N=2964)		150-300 IU/kg tiw Littlewood 2001 (N=375)	
Overall response (Hb\uparrow \geq2 g/dL)*	68.0%		70.5%	

* Treatment period: Gabrilove, 16 weeks; Littlewood, 12-24 weeks

Chemotherapy: Maintenance of Dose Intensity During 45 Days of Treatment

Administered dose	40,000 IU x 2/wk	10,000 IU tiw
100%	74%	47%
75%–100%	26%	16%
50%–75%	0%	32%
<50%	0%	5%

High Initial Dose Conclusions

- With Hb ≥ 10.5 g/dL, standard dosing is effective in 80% of cases (responders)
- With Hb < 9 g/dL, induction therapy allows
 - Rapid response (1.7 g/dL in 15 days)
 - Increase in percentage of responders (74% increase Hb levels > 1 g/dL in 15 days)
 - Transfusion needs to be reduced
- Chemotherapy can always be performed according to treatment plan