

Anemia has a Prognostic and Clinical Impact in Hematologic Malignancies

Joan Bladé
Department of Hematology
Hospital Clinic
Barcelona, Spain



ANEMIA

Mechanisms of Cancer-Related Anemia

- Bone marrow replacement
- Relative erythropoietin deficiency
- Renal insufficiency
- Decreased erythropoiesis (cytokine-mediated [$\text{TNF}\alpha$ and IL-1])
- Chemotherapy/radiation therapy
- Dysregulated cell apoptosis (erythroblast cytotoxicity)
- Others (B_{12} or folate deficiency, hemolytic autoimmune)

Anemia as a Prognostic Factor in Hematologic Malignancies

	Disease	Prognostic system
Clinical stage	CLL MM	Rai, Binet, Durie & Salmon
Prognostic index	Follicular NHL HD MDS	FLIPI Hasenclever IPSS
Unfavorable significance	WM IM CMML	

Multiple Myeloma

Hemoglobin Levels

Hb (g/dL)	1960-1971 ¹	1985-1998 ²
< 12	62%	69%
< 10	—	34%
< 8	8%	—

¹Kyle, Mayo Clinic Proc (1975); ²Kyle, Mayo Clinic Proc (2003)

Multiple Myeloma

Prognostic Factors

Author, year	<i>n</i>	Hb (g/dL)	Associated variables
<i>Carbone et al., 1967</i>	112	≤ 9	Ca ≥12, BUN ≥30, ECOG ≥2
<i>Durie & Salmon, 1975</i>	71	< 8.5	Ca ≥12, Cr ≥2, M ↑↑↑, X-ray+++
<i>Alexanian et al., 1975</i>	482	< 8.5	Ca ≥12.5, BUN >40, M ↑, IgA, ↓ Alb, response
MRC, 1980	485	≤ 7.5	Urea >10mM, ECOG >1
<i>San Miguel et al., 1989</i>	220	≤ 8.5	Cr >2, ECOG >2, M-index ≤.09

Hodgkin's Disease

Hasenclever Prognostic Index

Feature	Relative risk
Albumin <4 g/L	1.49
Hb <10.5 g/dL	1.35
Sex (male)	1.35
Stage IV	1.26
Age \geq 45 yrs	1.39
WBC count $>15 \times 10^9/L$	1.41
Lymphocyte count $<0.6 \times 10^9/L$	1.38

Non-Hodgkin's Lymphoma

Variable	DFS (n = 678)	OS (n = 704)
Age \geq 60 years	<0.0001	<0.0001
ECOG \geq 2	0.038	<0.0001
Anemia	0.0048	0.0001
LDH>N	0.0014	0.0005
\uparrow β -2m	0.031	0.0014
BM (+)	0.012	-
Liver involvement	-	0.036

Follicular Lymphoma

International Prognostic Index (FLIPI)

- 1795 patients
- Prognostic model
 - Aged ≥ 60 years
 - Ann Arbor III-IV
 - LDH $>N$
 - Hg <12 g/dL
 - ≥ 4 extranodal sites

Clinical Trials With rHuEPO in Multiple Myeloma

Author	EPO	<i>n</i>	Response criteria	Response rate (%)
<i>Ludwig, 2002</i>	α	18	≥ 2 g/dL	76
<i>Barlogie, 1993</i>	α	41	≥ 2 g/dL	78
<i>Garton, 1995</i>	α	21	>38% Hto*	60 vs. 0
<i>Musto, 1998</i>	β	37	No transf	35
<i>Cazzola, 1998</i>	β	84	≥ 2 g/dL*	61 vs. 7
<i>Österborg, 1996</i>	β	65	≥ 2 g/dL*	55 vs. 20
<i>Littlewood, 2001</i>	α	58	No transf*	55 vs. 11
<i>Dammacco, 1998</i>	α	145	No transf*	47 vs. 23
<i>Österborg, 2002</i>	β	116	≥ 2 g/dL*	76 vs. 23

* Randomized