

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Löwenberg B, Ossenkoppele GJ, van Putten W, et al. High-dose daunorubicin in older patients with acute myeloid leukemia. *N Engl J Med* 2009;361:1235-48.

Ineligibility criteria as regards entry of patients in study

1. Previous induction treatment for AML/MDS
2. Prior chemotherapy within six months of study entry
3. Previous polycythemia rubra vera
4. Previous primary myelofibrosis
5. Blast crisis of chronic myeloid leukemia
6. AML-FAB type M3 or AML with cytogenetic abnormality t (15;17)
7. Hepatic or renal dysfunction as defined by:
 - a. Alanine Aminotransferase (ALT) and/or Aspartate Aminotransferase (AST) greater than 2.5 x normal value
 - b. Bilirubin greater than 2 x normal value
 - c. Serum creatinine greater than 2 x normal value (after adequate hydration), unless these are most likely caused by AML organ infiltration
8. Concurrent severe and/or uncontrolled medical condition (e.g., uncontrolled diabetes, infection, hypertension)
9. Cardiac disease as defined by:
 - a. myocardial infarction within the last six months of study entry, or
 - b. reduced left ventricular function with an ejection fraction less than or equal to 50% as measured by Multiple Gated Acquisition (MUGA) scan or echocardiogram (another method for measuring cardiac function being acceptable)
 - c. unstable angina
 - d. unstable cardiac arrhythmias

Cytogenetic Risk Categories

Favorable risk: core binding factor abnormalities: t(8;21) (q22;q22), inv(16)(p13.1;q22), or t(16;16)(p13.1;q22).

Very unfavorable risk: a monosomal karyotype, defined by the presence of two autosomal monosomies or one autosomal monosomy in combination with at least one structural abnormality other than core binding factor¹⁶.

Unfavorable risk: complex cytogenetic abnormalities (at least three unrelated cytogenetic abnormalities), monosomies or partial deletions of chromosomes 5 or 7 (del(5q), del(7q), -5, -7), abnormalities of the long arm of chromosome 3 (q21;q26), t(6;9)(p23;q34), t(9;22)(q34;q11.2) or abnormalities involving the long arm of chromosome 11 (11q23)¹⁷ unless the criteria of a monosomal karyotype were fulfilled.

Supplementary Table 1 Causes of death in first complete remission

	Induction treatment arm	
	A; Conventional DNR 45 mg/m ²	B: Escalated DNR 90 mg/m ²
	[numbers and percentages]	
Death in first CR	24	46
Death after cycle I or II		
infection/septicaemia/pneumonia	11	15
hemorrhage	4	1
neutropenic enteritis	-	2
intestinal perforation	-	1
second malignancy	1	4
cardiac arrest/failure	1	2
multiple organ (liver, renal a.o)	1	3
acute pulmonary embolism	-	1
hypoxic encephalopathy	-	1
unknown	1	2
Death after further postremission therapy		
infection/septicaemia	2	3
cardiac arrest/infarction	-	-
hemorrhage	-	1
second malignancy	-	1
acute liver failure after GO	-	1
neutropenic enteritis	1	-
complications after alloSCT	1	6
aneurysma aorta rupture after alloSCT	-	1
unknown	1	1

LEGEND

CR - complete remission

alloSCT: allogeneic hematopoietic stem cell transplantation

GO -geintuzumab ozogamicin