

# First Complete Remission versus other- than- First Complete Remission in Acute Myelogenous Leukemia with Allogeneic Hematopoietic Stem Cell Transplantation

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## Abstract

**Introduction:** The traditional goal of the treatment of Acute Myelogenous Leukemia is to produce and maintain a complete remission (CR). The difference in survival time was entirely attributable to the duration of time spent in CR. In this study, the outcome of AML patients with allogeneic HSCT in CR1 versus other than CR1 was compared.

**Patients and Methods:** Since March 1991 until November 2008, from 420 AML patients, 312 patients in CR1 with a median age of 28 years and 108 patients in other- than- CR1 with a median age of 27 years, have undergone allogeneic HSCT. The male/female ratio was 168/144 in the CR1 group and 55/53 in other- than- CR1. In totals 391 patients received Peripheral Blood, 27 patients Bone Marrow and 2 patients, Cord Blood as sources of HSCT.

**Results:** At present, 266 (85%) patients in CR1 and 73 (68%) patients in other- than-CR1 are living. The most common cause of death in CR1 group was Graft Versus Host Disease and in the other- than CR1 group was relapse. Median follow up time was 17 months (range: 1-158 months). Six month Disease Free Survival (DFS) and Overall Survival (OS) in CR1 was 86% and 91% (SE=2%). 2-years DFS and OS in CR1 was 78% (SE=3%) and 85% (SE=2%). Six month DFS and OS in other- than- CR1 was 64% (SE=5%) and 75% (SE=4%). In this groups 2 years DFS and OS was 50% and 64% (SE=5%). It is to be noted that six month DFS and OS in transplanted patients with CR1 was significantly higher than in other- than- CR1 ( $p<0.001$ ). Furthermore, 2-years DFS and OS in patients with CR1 were better than the second group ( $P<0.001$ ).

**Conclusion:** Although the results of HSCT in other than first complete remission is not as good as in first complete remission, it seems that it is good enough to advise doing allogeneic HSCT for these patients.

**Key words:** Hematopoietic Stem Cell Transplantation, Acute Myelogenous Leukemia, Allogeneic.

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## Introduction

Acute myeloid leukemia (AML) is not a single disease but rather a group of neoplastic disorders characterized by the proliferation and accumulation in the bone marrow and peripheral blood of immature Hematopoietic cells. These malignant cells gradually replace and inhibit the growth and maturation of normal erythroid, myeloid and megakaryocytic precursors.(1)

AML represents approximately 90% of all acute leukemias(1) and accounts for 15 to 20% of the acute leukemia in children.(2)

Remission rates have improved dramatically but remission, 5-year survival and cure rates are most depend on the patient's age when AML occurs(3) and cytogenetic changes.

The traditional goal of treatment of AML is to produce and maintain a complete remission (CR). The difference in survival time was entirely attributable to the duration of time spent in CR. Better survival has been reported for young patients who have received allogeneic bone marrow transplantation in the first remission.(1) The incidence of AML increases with age and most patients are over 60 years at present.(4)

Also, incidence rates are greater in developed countries and industrialized cities. Studies reveal an increased risk for Eastern European Jews and decreased risk for an Asian population.(5)

The role of hematopoietic cell transplantation (HCT) for AML has progressed from early reports of syngeneic marrow transplantation to the

extensive data now available on allogeneic HCT from matched-sibling donors with evidence of a beneficial graft-vs-leukemia (GVL) effect.(6) Here we have a retrospective study of patients who underwent allogeneic stem cell transplantation and the effect of some factors such as age, sex, being in first or other than first complete remission status before stem cell transplantation as well as sources of stem cell transplantation on overall survival (OS) and disease-free survival (DFS).

### Patients and methods

This study includes 420 patients with AML who received allogeneic stem cell transplantation from March 1991 until November 2008, at the Hematology- Oncology and Stem Cell Transplantation Research Center (HORCSCT) of Tehran University of Medical Sciences in Shariati Hospital.

The patients were divided into two groups before receiving stem cell transplantation included first and other- than- first- CR, such as second and third complete remission or primary induction failure or relapse.

Also, there were several sources for HSCT for transplantation including peripheral blood, bone marrow and cord blood.

In this study, the outcome of the AML patients with allogeneic HSCT in the first CR versus other- than- first complete remission was compared with Log-Rank test.

### Results

Four hundred twenty patients (223 male and 197 female) with allogeneic stem cell transplantation were analyzed in this study. There were 312 patients with a median age of 28 years (range: 2-57) in first complete remission and 108 patients with a median age of 27 years (range: 3-56) in other- than- first complete remission status who had undergone allogeneic hematopoietic stem cell transplantation (HSCT).

In total, the stem cell source of transplantation for 391 recipients was peripheral blood (PB) and for 27 recipients was bone marrow (BM). Just two recipients had Cord Blood (CB) as a source for their transplantation. In the first complete remission group, 294 patients (94.2%) had a PB source and 17 patients (5.4%) had a BM source for their transplantation. In the other- than- first complete remission groups 97 patients (89.8%) had a PB source and 10 patients (9.3%) had a BM source. In both groups, just one patient had a source of CB for transplantation.

The main conditioning regimen for the 354 AML patients was busulfan associated with cyclophosphamide. The result was that 265 (74.8%) of them were in first complete remission. Other drugs used as conditioning were fludarabine, ATG, melphalan, etoposide and campath.

The median time for absolute neutrophil count  $\geq 0.5 \times 10^9$  L was +12 and the median time for the platelet count  $\geq 20 \times 10^9$  L was +16 in the first complete remission group. It was +17 in the other- than- first complete remission group.

At the end of this study, 339 patients were living 266 of them had first complete remission status and 73 of them were in other- than- first complete remission status.

Also, 81 patients died; 46 of them had first complete remission status and 35 patients were in other- than- first remission status.

The greatest cause of death in the first complete remission group was Graft Versus Host Disease (GVHD) (18 patients) and in other- than- first complete remission group was relapse (14 patients). The other causes of death were infection, cardiac and pulmonary toxicity, VOD and others. The median follow-up time was 17 months.

As a result of this study, the 6 months overall survival in patients who were in their first complete remission status before allogeneic stem cell transplantation was 90.6% (SE=2%) and for patients in other- than- first complete remission status was 75.1% (SE= 4%). A two- year overall survival for patients in the first complete remission status was 85.1% (SE=2%) and for patients in other- than- first complete remission status was 64.2% (SE=5%) ( $p < 0.001$ ).

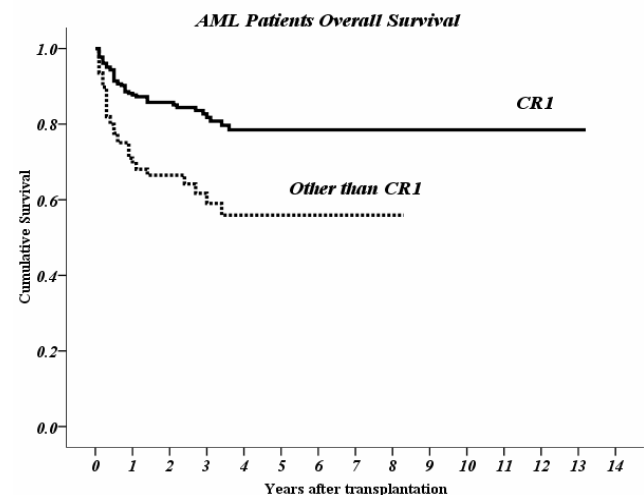
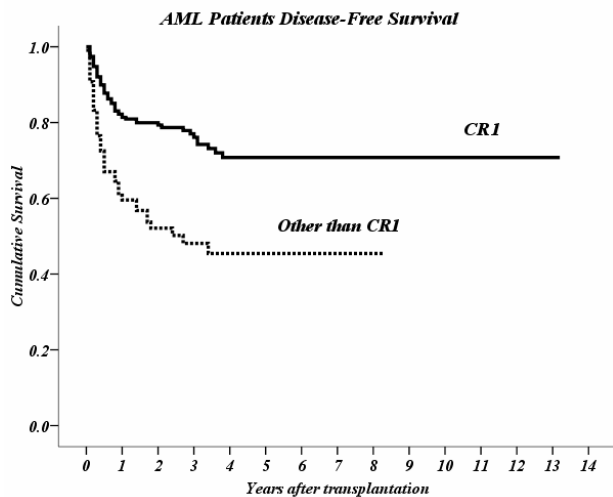


Figure 1. Probability of Overall survival by disease status at transplant



**Figure 1. Probability of disease free survival by disease status at transplant**

Also a 6 months DFS for patients in the first complete remission status was 86.2 % (SE=2%) and for patients in other- than- first complete remission status was 64.5 % (SE=5%).

A two- year DFS for patients in the first complete remission status was 78.7 % (SE=3%) and for patients in other- than- first complete remission status was 50.2 % (SE=5%) (P<0.001).

## Discussion

Allogeneic bone marrow transplantation from an HLA- matched sibling has been an established practice for 15 to 20 years and cures 50 to 60 percent of recipients. It is the most active antileukemic treatment currently available.(7)

Disease status at transplantation was very important where as the relative risk of relapse in patients who received their stem cell transplantation in the second complete remission (RR=2) or in other statuses (RR= 1.84) was greater than in the patients who received stem cell transplantation in their first complete remission status; the relative risk of treatment failure in patients in the second complete remission (RR=1.68) or in other statuses (RR=1.92) which was greater than the patients in the first complete remission.(2)

According to a study of The American Society of Hematology from October, 1987 to December, 1996, on 101 patients with AML in the first complete remission with a preparative regimen, including cytoxan with total body irradiation (CYTBI) or busulfan followed by allogeneic bone marrow transplantation (BMT) from an HLA- identical sibling, 2 years DFS was (72% v 47%) (P<0.01) and 2 years OS was (75% v 51%) (P<0.02).(8)

Also, the International Bone Marrow Registry (IBMTR) reported the results of 647 patients

receiving an unmanipulated BMT from a matched – sibling donor between January, 1989, and December, 1993. The conditioning regimen was cyclophosphamide and TBI-based in the remainder, DFS was 60 % (95% CI= 56-64%) at 3 years. These results are similar to data from the European Group for Blood and Marrow Transplantation (EBMT) on 516 patients, 69% of whom received TBI. The four- year DFS was 55±3%.(9)

In this study, we could see significant differences between the overall survival of recipients in the first complete remission and overall survival of recipients in other- than- first complete remission. Also, we could see a significant difference concerning the disease- free survival of those patients. This means the overall survival and disease- free survival of patients who received their stem cell transplantation in the first complete remission status was significantly higher than those who received transplantation in the other- than- first complete remission status.

The DFS and OS are better in patients in the first complete remission versus other- than- first complete remission group. Also, in this study, the result of allogeneic HSCT in the other- than- first complete remission group is better than in conventional chemotherapy and might be advised for those patients if they fit into stem cell transplantation.

## References

1. Kenneth B. Miller, Daoust PR. Clinical Manifestations of Acute Myeloid Leukemia. In: R. Hoffman, E. J. Benz, S. J. Shattil, B. Furie, L. E. Silberstein, McGlave P, Heslop H, editors. Hematology basic principles and practice. 5 ed: Churchill Livingstone; 2009. p. 1071.
2. Ghavamzadeh A, Masnavi A, Khatami F, et al. A Comparison of Allogeneic and Autologous Hematopoietic Stem Cell Transplantation for Acute Myeloblastic Leukemia. International Journal of Hematology-Oncology and Stem Cell Research. 2009; 3(1): 12-6.
3. Jane L. Liesveld, Lichtman MA. Acute Myelogenous Leukemia. In: M. A. Lichtman, E. Beutler, T. J. Kipps, U. Seligsohn, Kaushansky K, Prchal JT, editors. Williams Hematology: Mc.Grow-Hill; 2006. p. 1183.
4. Scott Solomon, Malkovska V. Acute Myelogenous Leukemia. In: G. P. Rodgers, Young NS, editors. Bethesda handbook of clinical hematology: Lippincott Williams & Wilkins; 2005. p. 135.
5. Thai M. Cao, Coutre SE. Acute Lymphoblastic Leukemia in adults. In: J. P. Greer, J. Foerster, J. N. Lukens, G. M. Ropgers, Paraskevas F, Glader B, editors. Wintrobe's clinical hematology: Lippincott Williams & Wilkins; 2004. p. 2077.
6. Keith E. Stockerl-Goldstein, Blume KG. Allogeneic hematopoietic cell transplantation for adult patients with acute myeloid leukemia. In: Karl G. Blume, Forman SJ, Applebaum FR, editors. Thomas' Hematopoietic cell Transplantation. 3 ed: Blackwell; 2004. p. 1025.

7. Lowenberg B, Downing JR, Burnett A. Acute Myeloid Leukemia. *The New England Journal of Medicine*. 1999; 341(14): 1051-62.

8. Blaise D, Maraninchi D, Archimbaud E, et al. Allogeneic Bone Marrow Transplantation for Acute Myeloid Leukemia in First Remission: A Randomized Trial of a Busulfan-Cytosin versus Cytosin- Total Body Irradiation as Preparative Regimen: A Report from the Group d' Etudes de la greffe de Moelle Osseuse. *Blood*. 1992; 79: 2578- 82.

9. David R. Simpson, Armand Keating. Acute Myelogenous Leukemia. In: E. D. Ball, Lister J, Law P, editors.

*Hematopoietic Stem cell Therapy*: Churchill Livingstone; 2000. p. 15.