Treatment of Adult Acute Myeloblastic Leukemia

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The introduction of combination chemotherapy in the treatment of adult acute leukemia has had a profound impact on the response and duration of survival of patients with adult acute myeloblastic leukemia. In the past decade, the combination of cytosine arabinoside with an anthracycline antibiotic, either daunorubicin, adriamycin, or rubidazone, has been responsible to a large degree for the success.

In a study done at the M.D. Anderson Hospital in 1973, a combination of adriamycin, vincristine, Ara-C and prednisone (Table 1) was utilized for initial induction therapy for 58 adults between the age of 15 and 76 with a diagnosis of acute myeloblastic leukemia. 43 (74%) of the patients achieved a complete remission with 31 of 35 (89%) patients under the age of 50 achieving a complete remission [4]. Median duration of survival in this group of patients was 58 weeks. Nine patients remain alive between 4 and 5 years from diagnosis. These 9 are all in their original first complete remission and represents 9 of 31 Patients (29%) under the age of 50 who achieved remission.

Table 1. AD-oap. Acute myeloblastic leukemia

Entered	58		
Complete remission	43	(74%)	
Complete remission	<50	31/35	(88.5%)
	≥ 50	12/23	(51%)

Because of the initial success of this program, the same combination of agents was utilized in the Southwest Oncology Group for remission induction therapy. A total of 420 patients were entered, 224 achieved complete remission (54%). The survival of all patients and survival of those patients achieving a complete remission is shown in Fig. 1. The vertical lines on these survival curves represent patients still alive and can still effect the overall survival of these patients. The median duration of survival of all patients entered is 50 weeks and the projected median duration of survival of the patients who achieved complete remission is almost double this to 2 years [5].

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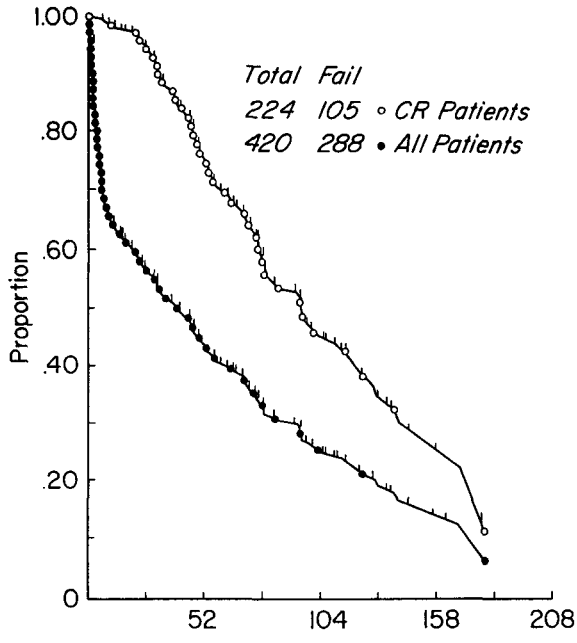

Fig. 1. Swog 7416/17. Acute myeloblastic leukemia survival from first treatment

In addition to adriamycin, rubidazone, a new anthracycline antibiotic related to daunorubicin, has been utilized in combination with cytosine arabinoside in the management of patients over the age of 50. The program is shown in Table 2. A total of 56 patients have been entered on this program with an overall response rate of 49% which is similar to the response rate seen in patients utilizing a combination of adriamycin, Ara-C, vincristine and prednisone [3].

Table 2. Roap. Acute myeloblastic leukemia. >50 years of age

Entered	57
Complete remission	28 (49%)

In an attempt to prolong remission, a late intensification program has been used in patients who have been in maintained complete remission for one year or longer. Late intensification therapy utilizes drugs that they have not been previously exposed to, the majority of the patients in this program received a combination of 6-mercaptopurine, methotrexate, vincristine and prednisone. A total of 62 patients have undergone late intensification therapy and 29 (47%) remain in unmaintained complete remission. The majority of the patients that relapsed, relapsed in the first six months and 31 of the 33 patients that have relapsed have done so within the first 24 months following discontinuous of chemotherapy (Table 3). The risk of relapse sub-

Table 3. Late intensification therapy in acute leukemia

Patients entered	62
Patients still in CR	29 (47%)
Relapsed by 6 months	21 (64%)
Relapsed by 24 months	31 (94%)

sequent to this time is less than 10% [1]. Of the 36 patients who are in continuous complete remission one year from complete remission, 9 (25%) had relapsed whereas 12 patients now have been discontinued from chemotherapy four years or longer from the late intensification and none of these have relapsed (Table 4). The overall risk of subsequent relapse after one year of continuous complete remission without chemotherapy is less than 10%.

Table 4. Duration of unmaintained remission after late intensification therapy

Duration of CR (Yrs from LI)	Number of Patients	Subsequent Relapses
1	36	9 (25%)
2	25	2 (8%)
3	18	1 (6%)
4	12	0

The survival in AML after relapse is short, the median duration of survival of patients with AML who have achieved a complete remission and subsequently relapsed, the survival from relapse is less than 20 weeks (Fig. 2). Only 5% of these patients are projected to be alive in one year. Because of these poor results following relapse, a program of autologous bone marrow transplantation has been introduced using marrow collected and stored from patients with acute myeloblastic leukemia during periods of remission. This therapy offers a viable alternative to reinduction chemotherapy. We have used a combination of piperazinedione and total body irradiation therapy.

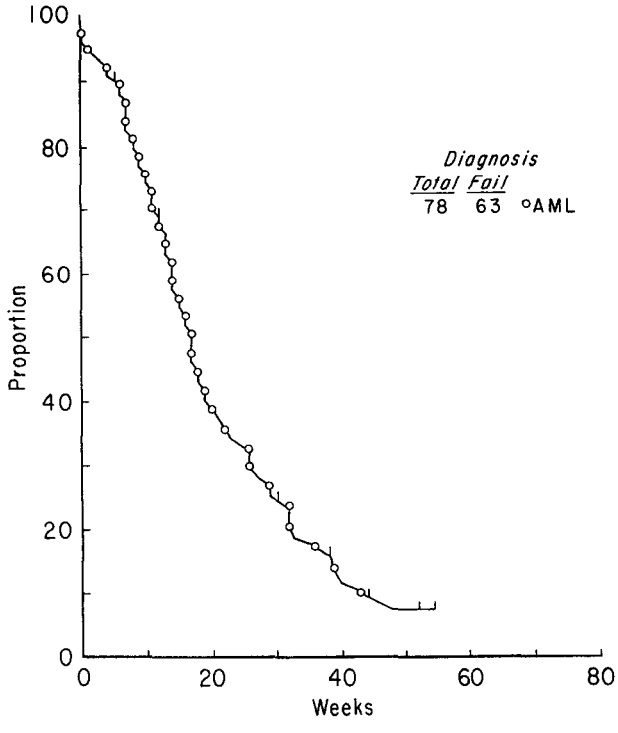

Fig. 2. Survival from relapse

This program has resulted in clearing of the leukemia and evidence of engraftment with normal myeloid recovery in 5 of 11 patients [2]. Survival of these patients, duration of remission and duration of bone marrow storage in months and interval between storage and relapse and the number of cells and the number of colony forming units reinfused is shown in Table 5.

Table 5. Autologous bone marrow transplantation

Number of Evaluable Patients	11
Number Showing Evidence of Engraftment	9
Number Achieving Complete Remission Survival (days) 17–320+	5
Interval Between Remission and Storage (months)	2–5 Median 12
Interval Between Storage and Relapse (months)	10–30 Median 19
Cells Transfused/kg b.w.	6.8×10^6–3.2×10^8 Median 1.2×10^8
CFU-C/10^5 Cells	0–15 Median 5

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