Symposium on Treatment of Cancer*

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1. Chemotherapy of Acute Leukemia in Adults

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Clinical effects of new agents in the treatment
of leukemia and lymphoma are presented.

1) N⁴-Behenoyl-1-β-D-arabinofuranosylcytosine
(BH-AC)¹⁾

In phase II study of BH-AC, significant re-
sponses were noted in AML patients with a CR
rate of 44.1%.

A phase III study of BH-AC in adult with
ANLL was conducted by a Cooperative Study
Group of the Treatment of Leukemia.

The regimen used and dosage schedules of

each drug were as follows: BH-AC, 170 mg/m²
per day, daunorubicin (DM) 25 mg/m² per day,
6-mercaptopurine (6-MP), 80 mg/m² per day,
and prednisolone (pred), 20 mg/m² per day,
both given orally (BH-AC·DMP regimen)²⁾. (Fig.
1)

The response of the patients to the BH-AC·
DMP regimen is shown in Table 1. Sixty-five
(74.7%) of the 87 patients with acute myelo-
blastic leukemia (AML), 29 (69.0%) of the pa-

Table 1. Effects of BH-AC·DMP Therapy in Adult
ANLL

Type	No. of Cases	CR	PR	F	CR Rate(%)
AML	87	65	2	20	74.7
AProL	12	9	0	3	75.0
AMoL	42	29	6	7	69.0
Total	141	103	8	30	73.1

Fig. 1. BH-AC·DMP Protocol for Adult ANLL

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tients with acute myelomonocytic leukemia (AMOL), and 9 (75.0%) of the 12 patients with acute promyelocytic leukemia (AproL) achieved complete remission (CR), respectively. Overall, 103 (73.1%) of the 141 patients with ANLL responded with complete remission. (Table 1)

The results obtained with the BH-AC•DMP therapy are superior to those in previous reports³⁾, in terms of rate of complete remission, remission duration and survival.

2) N⁴-palmitoyl-arabinofuranosylcytosine (PLAC)⁴⁾

Forty-six adults with acute leukemia were entered in phase II study of oral use of PLAC. PLAC 100–200 mg/m²/d was given orally for more than 30 days.

Responders with CR were noted with an overall rate of 10.1%, and those with PR were 15.9%. Of the patients who received PLAC orally, 5 of 30 patients (12.5%) with AML and 1 of 6 with BC of CML (16.6%) responded with CR. Two of 30 with AML, 3 of 6 with AMoL and each one of 3 with ALL and of 6 with CML-BC responded with PR.

Oral use of PLAC is therapeutic in the treatment of AML, particularly for atypical type of the disease.

3) Aclacinomycin A (ACM-A)⁵⁾

After phase I trial in human, phase II–III study of ACM-A in adult acute leukemia was conducted by a Cooperative Study Group. In phase II study, 38% of 21 patients responded with CR.

A phase III study of ACM-A in combination with BH-AC, 6-MP and prednisolone has been initiated (BH-AC•AMP regimen). The dosage schedule of each drug was as follows: ACM-A, 14 mg/m² per day intravenous infusion, BH-AC, 170 mg/m² per day intravenously, 6-MP, 80 mg/m² per day orally, and prednisolone, 20 mg/m² per day orally.

Of the 60 previously untreated patients, 66.7% responded with CR. There are 27 CRs in 37 patients with AML, 10 CRs in 14 patients with AMoL, 2 CRs in 3 patients with acute promyelocytic leukemia (APL) and 1 CR in 6 patients with erythroleukemia (EL).

Of the 65 patients who had had prior treatment

with chemotherapy, 66.7% responded with CR. There were 25 CRs in 41 patients with AML, 5 CRs in 10 patients with AMoL, and 11 CRs in 13 patients with APL. BH-AC•AMP therapy produced encouraging results in terms of response rate, particularly in patients who had had prior chemotherapy, since most of the responders were considered to be resistant to multicombination chemotherapy (BH-AC•DMP regimen)⁶⁾.

4) Tetrahydropyranil-adriamycin (THP-ADM)

THP-ADM is less toxic, particularly less cardiotoxic than other anthracyclines currently being clinically used and it has superior antitumor activity in experimental tumor systems to ADM.

The dose schedules employed were as follows: 15–20 mg/m² daily i.v. for 3 to 5 days for patients with acute leukemia, and 40 to 50 mg/m² once every 3 weeks i.v. for those with malignant lymphoma.

Each one of 6 patients with ALL and of 12 patients with AML achieved CR. Five of 22 patients had PR. Out of 19 evaluable patients with non-Hodgkin's lymphoma, 3 had CR and 5 had PR, response rate being 42.1%.

THP deserves further prospective study in leukemias and lymphomas.

5) Human Lymphoblastoid Interferon (HLBI)

The phase II clinical trial of HLBI in patients with multiple myeloma, leukemias and lymphomas was conducted by a Cooperative Study Group in Japan involving 24 institutions during a two year period.

Most of the patient received 3 mega international units of HLBI I.M. daily and in some patients, the dose was escalated to 6–12 mega units over a period of at least 4 weeks.

Of 73 evaluable patients with multiple myeloma, 1 CR and 13 PR cases were obtained which makes 19.2% of response rate. Of 53 patients with lymphomas including adult T cell leukemia, 2 CRs and 7 PRs occurred which makes 17.3% of remission rate. There were no CR in patients with leukemias, yet, one of 33 patients with acute leukemia and 2 of 9 patients with chronic leukemia responded with PR.

Of 32 patients with non-Hodgkin's lymphoma, 1 CR and 2 PR were seen, and it is noteworthy that of 10 patients with adult T cell leukemia,

1 responded with CR and 2 responded with PR.

HLBI deserves undoubtedly further prospective phase II–III clinical trials in multiple myeloma and lymphomas.

REFERENCES

- 1) Yamada K, et al: Pharmacologic and clinical studies of N⁴-Behenoyl-1-β-D-arabinofuranosylcytosine. Recent Results in Cancer Research 70: 219-229, 1980.
- 2) Yamada K, et al: Phase III study of N⁴-behenoyl-1-β-D-arabinofuranosylcytosine in adult acute leukemia. Current Chemotherapy and Immunotherapy II: 1308-1310, 1982.
- 3) Yamada K, et al: DCMP two-step therapy for acute myelogenous leukemia in adults. Jpn J Clin Oncol 8: 133-140, 1978.
- 4) Tsuruo T: Comparison of cytotoxic effect and cellular uptake of 1-β-D-arabinofuranosylcytosine and its N⁴-acyl derivatives using cultured KB cells. Cancer Research 39: 1063-1070, 1979.
- 5) Yamada K, et al: A phase II study of aclacinomycin A in acute leukemia in adults. Cancer Treatment Review 7: 177-182, 1980.
- 6) Umezawa H, et al: Tetrahydropyranil derivatives of daunomycin and adriamycin. J Antibiotics 32: 1082-1084, 1979.

2. Alternating Combination Chemotherapy with a Multimodality Approach for Small Cell Lung Cancer

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Small cell lung cancer (SCLC) is disseminated at the presentation in most patients. Chemotherapy is, therefore, the principal therapeutic modality in this disease. The application of aggressive chemotherapies has resulted in improved survival for patients with SCLC. Our previous study utilizing a four-drug combination of cyclophosphamide, vincristine, methotrexate, and procarbazine (COMP)¹⁾ resulted in; 1) response rate of 68% with a complete remission (CR) rate of 28%, 2) an overall median survival time of 9.5 months, with a significant prolongation of life in patients who achieved CR, 3) a fraction of long-term disease-free survivors, especially in those who had received concomitant chest irradiation, and 4) a high frequency (41%) of cerebral metastases in complete responders.

The current study outlined in Fig. 1 was undertaken to test a cyclic alternating chemotherapy with the four-drug combination of COMP (cyclophosphamide, 270 mg/m², on day 1–5; vincristine, 1.4 mg/m², on day 1; methotrexate, 6.5 mg/m², on day 1–5; and procarbazine, 65 mg/m², on day 1–5) and a three-drug combina-

tion of VAN (oral VP-16, 140 mg/m², on day 29–32; adriamycin, 40 mg/m², on day 29; and ACNU 40 mg/m², on day 29) which appeared non-cross-resistant to COMP. In this study, also included two randomized clinical trials to test the effectiveness of concomitant chest irradiation in patients with limited disease (LD) who received the intensive alternating chemotherapy, and to test the validity of prophylactic cranial irradiation (PCI) for patients who achieved CR.

Between March, 1981 and November, 1983, 69 patients with SCLC entered the study. After stratification for the extent of disease, 34 patients with LD were randomized to receive the alternating chemotherapy alone or to receive chest irradiation after the first cycle of COMP and VAN. Thirty-five patients with extensive disease (ED) received the chemotherapy alone. Twenty-eight patients who had achieved CR were randomized to receive PCI or to have observation only. Of 35 patients with ED, 13 (37%) achieved CR and 18 (51%) achieved partial remission (PR). The projected median survival time was 8.5 months for all patients with ED. Of 18 pa-