Relapse of Hairy Cell Leukemia After 2-Chlorodeoxyadenosine: Long-Term Follow-Up of the Northwestern University Experience

By Martin S. Tallman, David Hakimian, Alfred W. Rademaker, Connie Zanjig, Eric Wollins, Esther Rose, and LoAnn C. Peterson

Although 2-chlorodeoxyadenosine (2-CdA) is effective in inducing complete remissions (CRs) in the majority of patients with hairy cell leukemia (HCL), neither the actual relapse rate, the clinical factors that may predict relapse, the long-term outcome, nor the response rate to re-treatment at relapse has been clearly determined. Fifty-two consecutive patients with previously untreated or treated HCL were treated with 2-CdA at a dose of 0.1 mg/kg/d by continuous intravenous infusion for 7 days. Of 50 assessable patients, 40 (80%) achieved CR, and 9 (18%) achieved partial remission (PR). A total of 7 patients (14%) have relapsed, at a median duration of 24 months (range, 12 to 44). Of the 7 relapsed patients, 5 were re-treated with a second cycle of 2-CdA; 2 achieved a second CR and 3 attained a PR. The progression-free survival (PFS) rate is 72% at 4 years for all 52 patients and 83% for patients achieving CR. The overall survival (OS) rate is 86% at 4 years. Only prior therapy was predictive of relapse. The majority of patients achieve durable CRs with a single cycle of 2-CdA. The relapse rate is low and the long-term prognosis is excellent. The few patients who relapse can attain second remissions after re-treatment with 2-CdA.

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Hairy Cell Leukemia (HCL) is an uncommon chronic lymphoproliferative disorder manifested by pancytopenia and splenomegaly. Although the disease is relatively indolent, the majority of patients eventually require treatment for life-threatening pancytopenia or symptomatic splenomegaly. 2-Chlorodeoxyadenosine (2-CdA) has been shown to induce complete remissions (CRs) in the majority of patients, with only a single cycle and a paucity of toxicities. However, persistence of minimal residual disease in the bone marrow, detected either by immunohistochemistry or polymerase chain reaction using clonogenic probes derived from the immunoglobulin heavy-chain genes, suggests that some patients are at risk of relapse. Neither the actual relapse rate nor the clinical factors that may predict those patients destined to relapse has been determined. Furthermore, the optimal approach for patients who do relapse after achieving a CR with 2-CdA is not known. The purpose of this study is to determine the durability of remissions and relapse rate in patients with HCL treated with a single cycle of 2-CdA and to determine the outcome of patients following re-treatment with 2-CdA at relapse.

MATERIALS AND METHODS

Patient population. Between February 1991 and May 1995, 52 consecutive patients with HCL were treated at the Robert H. Lurie Cancer Center of Northwestern University, Northwestern University Medical School, Robert H. Lurie Cancer Center of Northwestern University, Chicago, IL; and R.W. Johnson Pharmaceutical Research Institute, Raritan, NJ. Submitted February 26, 1996; accepted May 2, 1996. Supported in part by R. W. Johnson Pharmaceutical Research Institute, Raritan, NJ. Presented in part at the American Society of Hematology Meeting, Seattle, WA, December 1-5, 1995. Address reprint requests to Martin S. Tallman, MD, Division of Hematology/Oncology, Department of Medicine, Northwestern University Medical School, Robert H. Lurie Cancer Center of Northwestern University, 223 E Erie St, Suite 700, Chicago, IL 60611.

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Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>52</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>52</td>
</tr>
<tr>
<td>Median Range</td>
<td>34-86</td>
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<td></td>
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<tr>
<td>Male</td>
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<tr>
<td>ACN (µL)</td>
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</tr>
<tr>
<td>Median</td>
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<tr>
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<td>45-3,080</td>
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<tr>
<td>Hgb (g/dL)</td>
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<tr>
<td>Median</td>
<td>10.6</td>
</tr>
<tr>
<td>Range</td>
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<tr>
<td>Pt (× 10^9/L)</td>
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<tr>
<td>Median</td>
<td>97.1</td>
</tr>
<tr>
<td>Range</td>
<td>11-466</td>
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</tbody>
</table>

Abbreviations: ANC, absolute neutrophil count; Hgb, hemoglobin; Pt, platelets.

A PR required all of the following: (1) reduction of greater than 50% of hairy cells in the bone marrow core biopsy specimen; (2) increase of greater than 50% of all abnormally low peripheral blood counts; and (3) reduction of greater than 50% in abnormal adenopathy or hepatosplenomegaly.

Patients who did not fulfill the criteria for CR or PR were classified as nonresponders (NR).

Relapse was defined as the reappearance of hairy cells in the bone marrow core biopsy specimen after achieving CR or the reappearance of hairy cells in the marrow of those classified as PR based on residual splenomegaly only or an increase in greater than 50% of the percentage of residual hairy cells in the bone marrow core biopsy specimen.

**Hairy cell index measurement.** The hairy cell index was defined as the cellularity of the bone core biopsy specimen (fraction) multiplied by the fraction of hairy cells present in the cellular portion of the bone core biopsy specimen.11

**Statistical analysis.** Progression-free survival (PFS) was defined for patients achieving CR or PR and was measured from the date of treatment until relapse or death from any cause. Observations of PFS were censored at the date of last contact for patients with no report of relapse who were last known alive. Overall survival (OS) was measured from the day of treatment until death from any cause. Observations were censored for patients last known to be alive. PFS and OS were estimated by the method of Kaplan and Meier.12 Toxicities were graded according to standard criteria.13

RESULTS

**Accrual.** Fifty-two consecutive patients were initially treated with a single cycle of 2-CdA. All patients were assessable for toxicity. Of 52 patients, 50 were assessable for response; 1 patient did not have a follow-up bone marrow biopsy, and a second patient did not have CT scans obtained. Results were analyzed as of July 1, 1995. The median follow-up duration was 33 months (range, 2 to 50). Of 50 patients assessable for response, 38 (76%) complied fully with the planned yearly bone marrow biopsies. The median time between the last date of contact and the last bone marrow biopsy was 11.5 months.

**Response.** Of 50 assessable patients, 40 (80%) achieved CR with a single cycle of 2-CdA; 9 patients (18%) achieved PR; and 1 patient was categorized as NR (2%). Therefore, the overall response rate with a single cycle was 98%. Of the 9 patients achieving PR, 4 had residual disease in the marrow; 5 had no disease in the marrow, but had either residual splenomegaly measuring ≥14 cm in craniocaudal length by CT scan (3 patients) or residual internal adenopathy ≥2 cm by CT scan (2 patients). Of the 4 patients achieving PR with residual disease in the marrow (10%, 30%, and 40% of the nucleated marrow cells were hairy cells), 3 were re-treated at 3 months with a second cycle of 2-CdA with the identical dose and schedule, and 2 achieved CR. The third patient had no further response. The fourth patient achieving PR with residual marrow disease had approximately 5% residual hairy cells and is being observed with normal peripheral blood counts. The 1 patient categorized as NR at 3 months had complete eradication of HCL from the marrow and an increase in the platelet count from 90,000/µL to 143,000/µL but had persistent leukopenia (1,900/µL).

A patient with hairy cell leukemia and a second with an inguinal furuncle before therapy who developed febrile neutropenia at the time the infusion was completed.

**Initial evaluation and serial studies.** At the time of study entry, all patients had a complete history and physical examination; complete blood cell count (CBC) with differential and platelet count; simultaneous multiple analysis-20 (SMA-20) biochemical profile; computed tomographic (CT) scans of the chest, abdomen, and pelvis; and unilateral marrow aspirate and bone core biopsy with tartrate-resistant acid phosphatase (TRAP). During the 7 days of treatment, all patients had a daily CBC and an SMA-20 biochemical profile on days 1 and 4. Thereafter, a CBC, differential count, and platelet count were performed weekly for 8 weeks, and an SMA-20 biochemical profile was obtained monthly for 3 months. An initial cohort of patients received daily allopurinol for 2 weeks beginning on the first day of treatment as prophylaxis against potential tumor lysis. Because tumor lysis was uncommon, allopurinol was subsequently not routinely administered.

Patients were monitored without other therapy and were then reevaluated at 3 months with a unilateral bone marrow aspirate and biopsy and CT scans of the abdomen and pelvis (and chest CT scan if pretreatment chest CT showed adenopathy). Patients achieving a partial remission (PR) were eligible to receive a second 7-day cycle. Patients then underwent CBCs at least every 6 months and a yearly unilateral bone marrow aspirate and biopsy.

**Response criteria.** Patients were evaluated for response 3 months after the initiation of 2-CdA. A CR required all of the following: (1) complete absence of hairy cells in the peripheral blood and bone marrow; (2) normalization of peripheral blood counts (hemoglobin level ≥12 g/dL, white blood cell count ≥3,000/µL, neutrophil count ≥1,500/µL and platelet count ≥100,000/µL); (3) absence of all palpable adenopathy and hepatosplenomegaly; (4) absence of constitutional symptoms; and (5) disappearance of all abnormal adenopathy and hepatosplenomegaly by CT scans. Patients with mild residual splenomegaly (≥12 cm, but ≤14 cm in craniocaudal dimension) or minimal soft-tissue abnormality (≥2 cm in diameter) were considered in CR.
and neutropenia (684/μL) at the 3-month evaluation, precluding categorization as PR. However, at 6 months, his peripheral blood counts had normalized, and he was categorized as having achieved CR. Therefore, the CR rate for all assessable patients receiving either one or two cycles of 2-CdA (43 of 50) was 86%.

The 2 patients not assessable for response had sustained complete normalization of peripheral blood counts. The first patient refused a 3-month bone marrow biopsy. He subsequently developed prostate cancer 24 months after treatment and concurrent anemia and thrombocytopenia but again declined a bone marrow biopsy. The second patient had complete eradication of hairy cells in the marrow and complete normalization of all peripheral blood counts but had no CT scans performed. He remains in apparent remission with normal blood counts at 28 months after treatment. Although these patients were not assessable for response, both clearly responded well.

Relapse. Seven patients (14%) have relapsed from either CR (5 patients) or PR (2 patients; 1 marrow and 1 spleen) after the initial treatment with 2-CdA at a median response duration of 24 months; 3 patients were previously untreated, and 4 were previously treated with either IFN only (3 patients) or with splenectomy, IFN, and then 2'-DCF (1 patient). Among the patients relapsing from CR, 1 relapsed at 12 months, 2 at 24 months, and 1 each at 25 and 34 months from the start of the first cycle of 2-CdA. Two patients relapsed from PR, 1 at 6 months and 1 at 45 months. Of the 7 relapsed patients, 6 developed peripheral cytopenias warranting therapy. One patient relapsed from PR after two induction cycles of 2-CdA. He was then treated with IFN and died of progressive disease. The seventh patient relapsed with minimal marrow disease and normal peripheral blood counts and is being observed without treatment.

Re-treatment at relapse with 2-CdA. Of the 7 relapsed patients, 5 were re-treated with 2-CdA (Table 2). The first patient relapsed at 12 months and achieved a PR of 9 months’ duration with the second cycle of 2-CdA. He subsequently received cyclophosphamide, hydroxydaunorubicin, oncovin, prednisone (CHOP) chemotherapy and died of pneumonia during the neutropenic period. The second patient relapsed at 24 months and remains in a second CR of 24+ months’ duration. The third patient relapsed at 24 months and was observed for 1 year until the peripheral blood counts decreased. This patient achieved a PR after the second cycle of 2-CdA and remains in PR more than 9 months after treatment. The fourth patient relapsed at 25 months, was observed for 8 months until his blood counts decreased, and then achieved a PR of 15+ months after re-treatment with 2-CdA. A fifth patient has relapsed at 45 months from a PR (residual splenomegaly) and achieved a second CR of 6+ months’ duration.

Deaths. Of the 52 patients, 4 have died, 2 of progressive disease and 2 in CR of unrelated causes. Of the 2 patients achieving a CR after two induction cycles of 2-CdA, 1 died with normal peripheral blood counts of a presumably unrelated cardiac event 7 months after treatment (no autopsy was performed). Another patient, 85 years old at the time of treatment, died of a ruptured abdominal aortic aneurysm 3 years after treatment. An autopsy showed evidence of disease in the marrow or spleen.

Acute toxicities. Acute toxicities among the first 26 patients have been previously described. The most common toxicities included myelosuppression and culture-negative fever. No additional acute toxicities were observed during treatment of subsequent patients. Notably, no acute extramedullary toxicities have developed in the 5 patients retreated at relapse with a second cycle.

Long-term toxicities. One patient, a 70-year-old man at the time of initial treatment, has developed prostate cancer. No other patients have developed a secondary malignancy. No patient has developed an opportunistic infection. One patient, acutely ill with Legionnaire’s disease at the time of presentation, developed a distal extremity sensorimotor polyneuropathy manifested by paresthesias, distal motor weakness, and a gait disorder characterized by a sensory ataxia. The neuropathy persisted for 6 months after treatment, then gradually improved with analgesics. No clear etiology of the neuropathy was established. Only one other case of neuropathy was observed. This 46-year-old man developed a bilateral lower-extremity sensory neuropathy 6 months after receiving a second cycle of 2-CdA. This neuropathy persisted until his unrelated cardiac death.

PFS. The estimated PFS rate for the 52 patients is 72% at 4 years (Fig 1). The PFS rate at 4 years for patients achieving CR is 83%. Among patients achieving PR, the PFS rate is 83% between 7 and 43 months (Fig 2) (P = .22 by log-rank test).

OS. The OS rate for all 52 patients is 86% at 4 years (Fig 3). The OS rate at 4 years for patients achieving CR is 87%. The OS rate at 44 months for patients achieving PR is 83% (P = .39 by log-rank test; see Fig 4).
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Fig 1. PFS for all 50 assessable patients.

Prognostic factor analysis. Clinical variables examined for prognostic value in predicting PFS included whether prior therapy had been administered, whether the patient had undergone prior splenectomy, duration of disease before treatment with 2-CdA, hairy cell index, pretreatment and posttreatment splenic indices, and percent change in splenic index (Table 3). Only prior therapy approached statistical significance for PFS ($P = .048$).

DISCUSSION

The relapse rate, PFS, OS, and curative potential associated with 2-CdA in patients with HCL are not well known, because initial reports of high CR rates had relatively short follow-up durations.\textsuperscript{2,4} Furthermore, several recent studies suggest that some patients in CR by routine evaluation have minimal residual disease, detected by immunohistochemistry or molecular evidence of clonal remission, that may result in recurrent disease.\textsuperscript{6-9} In this analysis, we wished to address several questions with respect to long-term follow-up evaluation. First, what is the long-term prognosis for patients achieving a remission with 2-CdA and what is the incidence of relapse? Second, are there any factors that can predict relapse? Third, are there any long-term complications of treatment with 2-CdA? Fourth, what is the response rate after re-treatment with 2-CdA for patients who do relapse?

The results reported here indicate that the majority of patients with either previously treated or untreated HCL achieve durable remissions with a single cycle of 2-CdA, and the relapse rate appears low. The criteria for CR reported here are stricter than those in most other studies.\textsuperscript{2,4} We required resolution of splenomegaly to $\leq 14$ cm in cranioctau- dal dimension and resolution of adenopathy to $\leq 2$ cm by both CT scan and physical examination. Most other studies have required resolution of splenomegaly by physical examination alone. In the present series, 5 patients were classified as having achieved PR because of either residual splenomeg- aly (one 15 cm, one 16 cm, and one 20 cm) or residual adenopathy (one 2.8 cm and one 2.5 cm). The patient with residual adenopathy of 2.8 cm at 3 months had a repeat CT scan 6 months after treatment, and the adenopathy had decreased to 2.2 cm. This issue is potentially important, because internal adenopathy may be more frequent than previously recognized, particularly in patients with a long duration of disease.\textsuperscript{14} Only 1 of these 5 patients (with residual splenomegaly of 17 cm) has relapsed. Similarly, only 1 of 4 patients with residual marrow disease has relapsed. If strict CT scan criteria had not been required and resolution of splenomegaly only by physical examination had been sufficient, the CR rate among all 50 assessable patients (47 of 50) would have been 94%. The PFS rate in the present study is 72% at 48 months. Only 7 of 50 patients (14%) have relapsed, and 6 of these 7 patients have developed progressive pancytopenia requiring re-treatment.
follow-up duration in the report by Piro et al was short and satisfactory peripheral blood counts may be preserved despite hairy cells in the marrow, OS may be the only variable associated with relapse that approached statistical significance. The power to predict relapse was limited because of the limited number of patients relapsing. We and others have detected minimal residual disease by a variety of sophisticated techniques. Preliminary data suggest the presence of minimal residual disease detected by immunohistochemistry on bone marrow core biopsy specimens at 3 months may be the best predictor of relapse.

Because therapy with 2-CdA is associated with prolonged suppression of CD4+ lymphocytes, the absence of opportunistic infections or of an increase in secondary malignancies in the present report is reassuring. In the report by Seymour et al only one opportunistic infection (dermatomal herpes zoster) was reported and no second malignancies were observed. Similarly, no long-term infectious sequelae have been found in the Scripps experience. Opportunistic infection has been reported by Juliusson and Liliemark. Of 16 patients, 5 (31%) developed either fungal (3) or cytomegalovirus (2) infections, of which 2 were fatal. The reason for the high incidence of infection in this particular series is not clear; however, 3 patients were treated with either 2'-DCF or IFN immediately before 2-CdA and may have been profoundly immunosuppressed. The only malignancy developing in patients in the current report was prostate cancer, which developed in a 79-year-old man 2 years after treatment. This malignancy was likely unrelated, given the prevalence of this disease in the elderly population. There were 3 patients who died of a second malignancy on the 2'-DCF arm of the prospective randomized trial reported by Grever et al. One patient was diagnosed with colon cancer 3 weeks after registration and likely had an unrelated second cancer. Two other patients treated with 2'-DCF developed melanoma (1 patient) and lung cancer (1 patient) approximately 2 years after completing 2'-DCF. One additional patient initially treated with IFN was crossed over to the 2'-DCF arm and subsequently developed small-cell lung cancer. Interestingly, Kampmeier et al have recently observed an unexpectedly high incidence of second neoplasms, particularly of hematopoietic origin, in patients monitored for a median of 91 months (range, 0.2 to 109 months) after treatment with IFN. Even longer-term follow-up data than reported here of patients treated with purine nucleoside analogs will be important to determine if these newer therapies are associated with an increased incidence of secondary malignancy.

Now that it appears that a subset of patients treated with 2-CdA relapse, it is important to identify effective treatment in this setting. All patients in this series responded well to a second cycle of 2-CdA. Indeed, 2 of 5 patients (40%) achieved a second CR. In the report by Seymour et al re-2 relapsing patients received a second course of 2-CdA and both achieved sustained PRs, but with residual hairy cells in the bone marrow. Lauria et al reported that among 4 patients who relapsed from PR after a first cycle of 2-CdA

| Table 3. Prognostic Factor Analysis for PFS |
|-------------------------------|------|------|-----|
| Variable                      | No. of Patients | No. of Relapses | P Value |
| Log-rank analysis             | Prior Therapy  | Splenectomy  | Cox regression analysis         |
| No                            | 29   | 2     | Disease duration                |
| Yes                           | 23   | 5     | Hairy-cell index                |
| Splenectomy                   | No    | 40    | Pretreatment splenic index      |
| Yes                           | 12   | 2     | Posttreatment splenic index     |
| % Change in splenic index     | 28   | 5     |                                |

These results compare favorably with those reported in the few other published reports. Seymour et al reported recurrent disease in 8 of 40 patients (20%) monitored for a median of 30 months. Regular follow-up bone marrow samples were obtained in both the present report and in that by Seymour et al, and these data suggest that not all patients will be cured. In a large cohort of 144 patients reported in abstract form, Piro et al reported that only 4 patients (2.7%) have relapsed, at 12, 12, 36, and 48 months. Furthermore, 3 of these 4 patients had only a minimal amount of hairy cells in the bone marrow, with normal peripheral blood counts. Only one patient had progressive pancytopenia. The median follow-up duration in the report by Piro et al was short (14 months), and it is not clear that serial bone marrow samples were obtained, which may explain the comparatively low relapse rate. Because HCL is an indolent disease in most patients and satisfactory peripheral blood counts may be preserved despite hairy cells in the marrow, OS may be the most important end point of treatment.

Because the CR rates attained with 2'-DCF appear comparable with those achieved with 2-CdA, it is important to compare the relapse-free survival and OS rates associated with both agents. Kraut et al have reported that 11 of 24 patients have relapsed after CR with 2'-DCF at a median follow-up time of 30 months. Golomb et al reported 12 relapses among 78 patients treated with 2'-DCF after failing to respond to IFN-α. The remission and survival rates at 36 months were 84% and 91%, respectively, for patients with a performance status of 0 to 2. Grever et al observed 10 relapses between 13 and 44 months among 117 patients achieving CR on the 2'-DCF arm of a prospective randomized study comparing 2'-DCF versus IFN-α. The relapse-free survival rate was 91% at 7 years. However, it is not clear if annual bone marrow examinations were performed in either study, and the actual relapse rate may be underestimated. Catoysky et al reported that the 5-year survival rate among 110 patients treated with 2'-DCF was 88% and 97% if nonleukemic deaths are excluded. Given the indolent natural history of the disease, even longer follow-up evaluation of patients treated with either purine nucleoside analog will be required to determine if one or the other agent offers a substantially longer remission duration or better OS. A prospective randomized comparison between 2-CdA and 2'-DCF seems unlikely, because the CR rates with each agent are so high, and many years and resources would be required to detect even small differences.

There is great interest in trying to identify factors predictive of relapse. We examined several variables, including prior therapy, duration of disease, presence of prior splenectomy, hairy cell index, and splenic index. Prior therapy was the only variable associated with relapse that approached statistical significance. The power to predict relapse was limited because of the limited number of patients relapsing. We and others have detected minimal residual disease by a variety of sophisticated techniques. Preliminary data suggest the presence of minimal residual disease detected by immunohistochemistry on bone marrow core biopsy specimens at 3 months may be the best predictor of relapse. Because therapy with 2-CdA is associated with prolonged suppression of CD4+ lymphocytes, the absence of opportunistic infections or of an increase in secondary malignancies in the present report is reassuring. In the report by Seymour et al only one opportunistic infection (dermatomal herpes zoster) was reported and no second malignancies were observed. Similarly, no long-term infectious sequelae have been found in the Scripps experience. Opportunistic infection has been reported by Juliusson and Liliemark. Of 16 patients, 5 (31%) developed either fungal (3) or cytomegalovirus (2) infections, of which 2 were fatal. The reason for the high incidence of infection in this particular series is not clear; however, 3 patients were treated with either 2'-DCF or IFN immediately before 2-CdA and may have been profoundly immunosuppressed. The only malignancy developing in patients in the current report was prostate cancer, which developed in a 79-year-old man 2 years after treatment. This malignancy was likely unrelated, given the prevalence of this disease in the elderly population. There were 3 patients who died of a second malignancy on the 2'-DCF arm of the prospective randomized trial reported by Grever et al. One patient was diagnosed with colon cancer 3 weeks after registration and likely had an unrelated second cancer. Two other patients treated with 2'-DCF developed melanoma (1 patient) and lung cancer (1 patient) approximately 2 years after completing 2'-DCF. One additional patient initially treated with IFN was crossed over to the 2'-DCF arm and subsequently developed small-cell lung cancer. Interestingly, Kampmeier et al have recently observed an unexpectedly high incidence of second neoplasms, particularly of hematopoietic origin, in patients monitored for a median of 91 months (range, 0.2 to 109 months) after treatment with IFN. Even longer-term follow-up data than reported here of patients treated with purine nucleoside analogs will be important to determine if these newer therapies are associated with an increased incidence of secondary malignancy.

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(at 6, 12, 18, and 24 months), 2 achieved CR, 1 achieved PR, and 1 was too early to evaluate. Because few patients treated with purine nucleoside analogs relapse after achieving CR, the identification of patients likely to respond to 2-CdA at relapse will require many years of observation. However, given the potential for severe immunosuppression, caution regarding repetitive cycles of 2-CdA must be exercised in this setting. Patients relapsing after previous exposure to 2'-DCF may achieve CR with 2-CdA. Whether the reverse is true has not yet been determined. The roles of 2'-DCF and IFN in patients failing to respond to 2-CdA will need to be explored. Indeed, to avoid exacerbation of persistent CD4+ lymphopenia, investigators from the M.D. Anderson Cancer Center recently reported that CR can be attained with IFN-a (2 of 3 treated patients) in patients relapsing after 2-CdA. However, when IFN was discontinued, the disease recurred within 4 months.

The results in the present report indicate that a single cycle of 2-CdA induces durable CRs in most patients with HCL and with minimal toxicity. Despite the potential for prolonged suppression of CD4+ lymphocytes, no long-term complications clearly attributable to 2-CdA have yet been observed. The relapse rate appears low, and no variable studied here clearly predicts relapse. Most patients respond well to re-treatment with 2-CdA at relapse, and CR is achieved in approximately 40% of cases. The optimal therapy for patients who relapse after an initial cycle of 2-CdA is unknown. Given the indolent natural history of the disease, very long follow-up durations will be required to determine if any patients achieving CR with 2-CdA are actually cured.

REFERENCES


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