ABSTRACT

2-chlorodeoxyadenosine (2-CdA), a purine analogue, has become universally accepted as the agent of choice in treating hairy cell leukemia (HCL). However, few studies have reported long-term outcomes after 2-CdA treatment. Between January 1990 and June 2003, 86 consecutive patients with HCL were treated with a single 7-day course of 2-CdA by continuous infusion at a dose of 0.1 mg/kg/day. Of the 86 patients (mean age: 49 years), 67 patients (79%) achieved a complete response (CR), 18 patients (21%) a partial response (PR), and 1 patient’s response was unable to be assessed. The progression-free survival (PFS) for initial relapse after 12 years was 54%. At a median follow-up of 9.7 years (range: 0.3-13.8 years), 31/85 patients (36%) relapsed. Twenty-three relapsed patients were treated with a second cycle of 2-CdA, 2 patients with alternative agents, and 6 patients were observed. Of the 23 relapsed patients retreated with 2-CdA, 12 (52%) achieved a CR and 7 (30%) patients achieved a PR (overall response rate: 83%). The overall survival (OS) rate after 12 years was 87%. Fifteen patients (17%) developed other malignancies. Long-term follow-up of up 14 years (median of 9.7 years) showed an excellent PFS and OS for HCL patients after 2-CdA treatment.
INTRODUCTION

Hairy cell leukemia (HCL) is a chronic lymphoproliferative disorder characterized by varying degrees of cytopenias and the presence of a malignant clone of B cells with irregular cytoplasmic projections.1 Although HCL generally has an indolent course, the majority of patients require treatment for cytopenias or symptomatic splenomegaly.2 Treatment options have evolved over the past 20 years and now include the purine analogues 2-chlorodeoxyadenosine and 2’-deoxycoformycin.2 Initial studies demonstrate that treatment with 2-chlorodeoxyadenosine (2-CdA) leads to complete remissions in the majority of patients with minimal toxicities.3-6 Few studies have reported long-term outcomes of patients with HCL treated with 2-CdA. Four-year follow-up data has previously been reported.7 However, given the indolent natural history of the disease, long-term follow-up of patients with HCL treated with 2-CdA is important.

METHODS

Patient Population

Between January 1990 and June 2003, 86 consecutive patients with HCL were treated at the Feinberg School of Medicine and the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. Patients were followed for a median follow-up of 9.7 years (range: 0.3 – 13.8 years). Diagnosis was established by morphologic review of the peripheral blood smear and bone marrow aspirate and biopsy. In each case, an immunophenotype characteristic of HCL was demonstrated by flow cytometry, or the neoplastic cells were documented to be B-lineage by immunohistochemistry and tartrate-
resistant acid phosphatase (TRAP) positive by cytochemical stains. Pathology slides were reviewed by a single hematopathologist (LP). Characteristics of the patients are listed in Table 1. Of the 86 patients, 60 were previously untreated. Twenty-six patients were previously treated with the following therapies: 7 had undergone splenectomy, 11 were treated with interferon (IFN) only, 4 had undergone splenectomy followed by IFN, 2 had undergone splenectomy followed by IFN and 2'-deoxycoformycin (2’-DCF), 1 was treated with IFN followed by 2’-DCF, and 1 patient was treated with only 2’-DCF. Some follow-up complete blood counts (CBCs) and bone marrow aspirates and core biopsies were obtained from referring institutions until August 2004 under the approval of the Institutional Review Board of Northwestern University.

Eligibility

Eligibility criteria for treatment with 2-CdA included the following: (1) pathologically confirmed diagnosis of HCL based on bone marrow aspirate, core biopsy, and peripheral blood smear obtained within 2 weeks of study entry; (2) evidence of active disease including any of the following—neutropenia (neutrophil count <1,500/µL), anemia (hemoglobin <12 g/dL), thrombocytopenia (platelet count <100,000/µL), or symptomatic splenomegaly or adenopathy; (3) no evidence of active infection; (4) no prior treatment within 4 weeks of receiving 2-CdA; and (5) normal renal and hepatic function.

Administration of 2-CdA

All patients received a single cycle of 2-CdA at a dose of 0.1 mg/kg/day by continuous intravenous infusion for 7 days. Until the drug became commercially available in February 1993, 2-CdA was provided by the R.W. Johnson Pharmaceutical
Research Institute (Raritan, NJ), and patients were treated on an institutional phase II protocol after informed consent was obtained according to procedures approved by the Institutional Review Board of Northwestern University. The first 43 patients received 2-CdA as study participants while the subsequent 43 patients were treated with the commercial drug under the same protocol. In the majority of cases, patients received 2-CdA on an outpatient basis using the computerized ambulatory drug delivery (CADD) portable infusion pump (Pharmacia Deltec Inc., St. Paul, MN).

**Supportive Care**

At the beginning of the study, all patients who developed neutropenic fevers were hospitalized, cultured, and given broad-spectrum antibiotics. All blood cultures remained sterile without evidence of infection. Subsequent patients who developed neutropenic fevers were evaluated with collection of blood and urine cultures and treated with an oral antibiotic (usually ciprofloxacin or levofloxacin). Patients with sterile blood cultures after 48 hours also received a non-steroidal anti-inflammatory agent. Replacement blood products were administered for symptomatic anemia or platelet counts less than 15,000/µL. Growth factor was administered only to 2 patients who presented with life-threatening infections (1 with *Legionella* pneumonia and 1 with a symptomatic inguinal furuncle).

**Initial Evaluation and Serial Studies**

Prior to treatment, all patients had a complete history and physical examination; CBC; hepatic and renal panel; computed tomographic (CT) scans of the chest, abdomen, and pelvis to assess for splenomegaly and adenopathy; and unilateral bone marrow aspirate and core biopsy with flow cytometric immunophenotyping or
immunohistochemistry and TRAP. The initial 43 patients registered to the phase II protocol were routinely followed with CT scans. After data from the first 43 patients were collected and evaluated, it was determined that obtaining routine CT scans was not essential in monitoring for relapse in patients after treatment with 2-CdA, and this practice was subsequently discontinued. During the seven-day treatment course, all patients had daily CBCs with liver and renal function panels collected on days 1 and 4. CBCs were repeated weekly for 8 weeks, and liver and renal panels were collected monthly for 3 months. Patients were also initially treated with allopurinol to prevent tumor lysis syndrome, but this practice was discontinued after it was discovered that tumor lysis was rarely observed.

Patients were evaluated for treatment response at 3 months with a unilateral bone marrow aspirate and biopsy. The decision to assess patients at 3 months after treatment in the phase II protocol was based on the timeframe for disease assessment used in the initial trials with 2-CdA. The initial 43 patients registered to the phase II protocol were offered a second cycle of 2-CdA (same dose and duration) after 3-month evaluation if a partial remission or no remission was obtained. After it was observed that the vast majority of the patients who achieved a partial remission after the first cycle maintained stable peripheral blood counts, subsequent patients were retreated with a second cycle of 2-CdA (same dose and duration) only at time of relapse. Patients who had 2 or more relapses were treated with other agents including Rituximab, BL-22 Immunotoxin, and 2'-DCF. Long-term follow-up consisted of review of yearly CBCs collected at our institution or referring institutions. Bone marrow aspirates and biopsy results were obtained yearly at first and then only when indicated, for example, if patients had
peripheral cytopenias. There were no studies performed on these patients to analyze immunological profile (T-cell and humoral immunity).

**Response Criteria**

At 3-month evaluation following treatment, a complete remission (CR) was defined as exhibiting all of the following: (1) complete absence of hairy cells in the peripheral blood and bone marrow; (2) normalization of peripheral blood counts [hemoglobin (Hgb) level >12 g/dL, white blood cell count (WBC) ≥ 3,000/µL, absolute neutrophil count (ANC) ≥ 1,500/µL, and platelet (Plt) 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.

Patients without morphologic evidence of hairy cells, but evidence of minimal residual disease by immunohistochemistry of bone marrow core biopsies, as previously defined, were included in the CR group. Patients with mild residual splenomegaly (>12 but ≤ 14 cm in craniocaudal dimension) or minimal soft-tissue abnormality (≤ 2 cm in diameter) were also considered in CR.

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

Patients who did not fulfill the criteria for CR or PR were classified as achieving no remission (NR).

Relapse was defined as having any of the following: (1) reappearance of hairy cells in the bone marrow core biopsy specimen after achieving CR; (2) reappearance of
hairy cells in the bone marrow of patients achieving PR who had residual splenomegaly only; or (3) increase of residual hairy cells in bone marrow core biopsy specimens by more than 50%.

**Statistical Analysis**

Progression-free survival (PFS) was measured from the date of first treatment until relapse date or death from any cause. Observations of PFS were censored at the date of last contact for patients with no known report of relapse who were last known to be alive. Overall survival (OS) was measured from the first day of treatment until death from any cause. PFS and OS were estimated by the method of Kaplan and Meier. Curves were compared using the log-rank test.

**RESULTS**

**Accrual**

Eighty-six patients were initially treated with a single cycle of 2-CdA. All patients were monitored for toxicities. Of the 86 patients, 85 were assessed for response; 1 patient did not undergo bone marrow biopsy evaluation at 3 months. Results were analyzed as of September 1, 2004. Eighty out of the original 86 patients had a recent CBC collected as of January 2003. Patient characteristics, including age (median: 49 years old, range: 25 – 86 years old), gender (86% male, 14% female), and prior treatment (30% yes, 70% no) as well as the median and ranges of patients’ WBC, ANC, Hgb level, and Plt counts at time of 2-CdA treatment initiation are listed in Table 1.

**Response**
Of the 85 assessable patients, 67 (79%) achieved a CR and 18 (21%) patients achieved a PR, for an overall response rate of 100% (Figure 1). Of the 18 patients achieving a PR, 11 had residual disease in the bone marrow, and 7 had no disease in the bone marrow, but had either residual splenomegaly measuring >14 cm in craniocaudal length by CT scan (4 patients) or residual internal adenopathy (3 patients). Six of the 18 patients who achieved a PR were retreated with a second cycle of 2-CdA after the initial 3-month assessment. At 3-month evaluation after cycle #2, 3 of these patients achieved a CR and the remaining 3 remained in PR. Five of the 18 patients who initially achieved a PR were retreated with a second cycle of 2-CdA at time of progression of disease. Six of the 18 patients who initially achieved a PR were simply observed with normal peripheral blood counts. The remaining patient who achieved an initial PR was treated with 2’-DCF and achieved a CR.

The one patient who was not assessed at 3 months after initial treatment for HCL with 2-CdA refused to undergo a bone marrow biopsy, but achieved normal peripheral blood counts. He subsequently developed prostate cancer 24 months after 2-CdA treatment and died of complications from metastatic prostate cancer.

**Relapse and Retreatment with 2-CdA**

At a median follow-up of 9.7 years (range: 0.3 - 13.8 years), 31 patients (36%) have relapsed from either CR (21 patients) or PR (10 patients) after the initial treatment with 2-CdA (Figure 1). The median time to first relapse for those patients who initially achieved a CR was 35 months and 10.5 months for those who initially achieved a PR. There was no statistical significance to the median time to first relapse in those who initially achieved a CR versus PR ($p = 0.54$ by log-rank).
Of these relapsed patients, 13 were previously treated and 18 were not. Of the previously treated patients who relapsed, 6 were treated with IFN only, 3 with splenectomy alone, 2 with splenectomy followed by IFN and then 2’-DCF, one with IFN followed by 2’-DCF, and one with 2’-DCF alone. The median time to first relapse for the 18 relapsed patients without previous treatment was 35 months and was 25 months for the 13 relapsed patients with prior treatment. There was no statistical significance between the median time to first relapse in those who were previously treated and those who did not receive prior therapy (p = 0.70 by log rank). Twenty-five of the 31 patients who had first relapse had cytopenias requiring therapy while the remaining 6 without cytopenias were observed. Twenty-three of the 25 were retreated with 2-CdA and 2 patients were retreated with alternative agents (1 with Rituximab and the other with 2’-DCF). The patients retreated with Rituximab and 2’-DCF both achieved a CR.

Of the 23 relapsed patients retreated with 2-CdA, 12 patients (52%) achieved a CR, 7 patients (30%) achieved a PR, 3 patients (13%) had NR, and 1 patient’s (4%) response remains to be determined. Of the 12 patients achieving CR, 2 subsequently relapsed (patient #1 after 27 months and patient #2 after 60 months). Patient #1 was retreated with the immunotoxin BL-22 and achieved a CR, and patient #2 was retreated with 2’-DCF which led to a PR. The second remission for patient #1 was shorter than the first remission; however, the second remission was longer than the first remission in patient #2. The other 10 patients have been monitored by peripheral blood count without evidence of disease with a mean follow-up of 9.4 years.

Four of the 7 patients who achieved a PR after retreatment with 2-CdA were also retreated. One was treated with Rituximab and 2’-DCF resulting in a PR, 1 was treated
with IFN which led to a PR, 1 was treated with Rituximab resulting in a PR, and 1 was treated with 2’-DCF achieved a CR. The remaining 3 patients were observed by regular monitoring of their peripheral blood counts.

Of the 3 patients who had NR after retreatment with 2-CdA, 1 died of complications from HCL and 1 died due to complications of metastatic prostate cancer. The third patient was treated with 2’-DCF and achieved a CR that lasted for 72 months (compared to the 35 months of CR after the first cycle of 2-CdA).

Of the 6 relapsed patients who were observed without treatment, 3 have been followed by monitoring of their peripheral blood counts for a mean follow-up of 10.8 years, 1 died of complications from metastatic prostate cancer, and 2 patients were lost to long-term follow-up.

Deaths

After long-term follow-up, 9 patients have died: 2 due to progressive disease, 5 due to complications of other malignancies (3 due to prostate cancer, 1 due to melanoma, and 1 due to colon cancer), and 2 in CR of nonmalignant causes (1 died with normal peripheral blood counts of a presumably unrelated cardiac event 7 months after treatment and the other patient, age 85, died of a ruptured abdominal aortic aneurysm 3 years later).

Malignancies

Fifteen of the 86 patients (17%) treated with 2-CdA developed other malignancies (9 prostate cancer, 1 colon cancer, 1 lung cancer, 1 melanoma, 1 thymoma, 1 basal cell cancer, and 1 breast cancer). These are detailed in Table 2. Of these patients, 5 patients were previously treated before 2-CdA (2 with IFN alone, 2 with splenectomy alone, and one with IFN followed by 2’-DCF).
Toxicities

Toxicities from 2-CdA have been previously reported. The majority of acute toxicities included myelosuppression and culture-negative fever. Patients retreated with 2-CdA had no acute extramedullary toxicities. Two patients developed neuropathies after treatment with 2-CdA.

PFS

The estimated PFS rate for the 86 patients treated with 2-CdA is 54% at 12 years (Figure 2). At 12 years, the PFS rate for the 26 previously treated patients is 45% and is 60% for the 60 previously untreated patients (p = 0.23, Figure 3). Patients who initially achieved a CR have a PFS rate of 60% at 12 years (Figure 4).

OS

The OS rate for all 86 patients is 87% at 12 years (Figure 5). At 12 years, the OS rate for the 26 previously treated patients is 88% and is 85% for the 60 previously untreated patients (p = 0.92, Figure 6). The OS rate at 12 years for the 31 patients who relapsed is 84% (Figure 7). Patients who initially achieved a CR have an OS rate of 90% at 12 years (Figure 8).

DISCUSSION

As reported here, all patients with HCL responded to initial treatment with 2-CdA with the vast majority of these patients (79%) achieving a CR. Over half of the patients (55%) with a PR following initial treatment with 2-CdA achieved a CR after retreatment with the drug. Thus, one to two cycles of 2-CdA are extremely effective in inducing a CR in most patients with HCL. This response is durable as well. The estimated PFS for
all patients treated with 2-CdA was 54% and the OS was 87% at 12 years, and patients
who initially achieved a CR have even higher PFS and OS rates at 12 years (60% and
90%, respectively). Prior treatment was not statistically significant as a factor in both the
PFS and OS. Of the patients who relapsed after 1 cycle of 2-CdA, the most commonly
used agent for retreatment was 2-CdA and the majority of these patients (83%) again
responded with over half of them achieving a CR. Thus, the prognosis of patients with
HCL treated with 2-CdA is excellent and is not affected by any history of prior therapy.

Extended follow-up of patients treated with 2-CdA has been previously reported.
Goodman et al. analyzed 207 patients with HCL treated with 2-CdA and had at least 7
years of follow-up.10 The CR rate was 95% and the PR rate was 5%, for an overall
response rate of 100%. The relapse rate was 37%, and the OS was 97% at 108 months.
In this study, shorter disease duration, lower hemoglobin, and higher WBC count at
baseline were predictors for treatment failure with 2-CdA. Zinzani et al. utilized two
different 2-CdA administration modalities (weekly and daily) and reported extended
follow-up.11 Of the 37 eligible patients, the CR rate was 81% and the PR rate was 19%
(overall response rate 100%). At a median follow-up of 122 months, the relapse rate was
27% and the projected 13-year overall survival was 96%. Jehn et al. treated 44
consecutive patients with 2-CdA.12 Ninety-eight percent of patients achieved a CR with
some of these patients having evidence of residual disease. One patient (2%) achieved a
PR (overall response rate 100%). At a median follow-up of 8.5 years, the relapse rate
was 39% and the overall survival at 12 years after the start of 2-CdA treatment was 79%.

Compared to prior studies,10-12 we observed a somewhat lower CR rate after the
first cycle of therapy with 2-CdA. This can partly be explained by the criteria for CR
reported here. Other studies have not required resolution of splenomegaly or lymphadenopathy by CT scan as criteria for CR. In this study, we required resolution of splenomegaly to $\leq 14$ cm in craniocaudal dimension and resolution of adenopathy to $\leq 2$ cm by both CT scan and physical examination. Several of our patients were classified as achieving a PR based on the presence of such organomegaly that was detected only by CT scanning and would have been missed if only physical examination was required.

Initially, patients who achieved a PR after the first cycle of 2-CdA were offered a second cycle as part of the phase II protocol. A total of six patients in our study were offered this treatment—2 died in CR, 1 remains in CR to this day, and the final 3 received other therapies with only 1 of the three patients achieving a CR. After evaluation of the data from the initial 43 patients, it was determined that most patients who achieved a PR after the first cycle normalized their peripheral blood counts. This led to offering a second cycle of 2-CdA only after they had documented relapse.

There are conflicting reports in the literature regarding the incidence of other malignancies in patients with HCL. In a study by Au et al., 44 separate malignancies were reported in a total of 36 patients from a cohort of 117 patients for a total incidence of 30.7%.$^{13}$ In the M.D. Anderson Cancer Center experience reported by Kurzrock et al., 36 patients (7.4%) developed malignancies after a median follow-up time after diagnosis of 7.1 years.$^{14}$ This was not statistically significant when compared to data derived from the Connecticut Tumor Registry.$^{14}$ In the Scripps Clinic experience reported by Goodman et al., 48 second malignancies developed in 22% of HCL patients treated with 2-CdA.$^{10}$ This represented a low to moderate (2.03-fold) increase in the development of a second neoplasm. However, only 3 patients developed a malignancy after exposure to
2-CdA, suggesting that factors other than 2-CdA were contributing to the risk of secondary malignancies.

In this study, 15 of the 86 patients (17%) treated with 2-CdA developed other malignancies. Most of these malignancies were solid tumors with prostate cancer being the most common. No hematologic malignancies developed after exposure to 2-CdA. The percentage of patients that developed malignancies in our population is somewhat lower than the percentage observed by Goodman et al.\textsuperscript{10} but is higher than what would be expected when compared to an age-matched cohort in the SEER database.\textsuperscript{15} Whether this is related to HCL, treatment of the disease, or the result of confounding variables is unclear.

As most patients with HCL continue to do well for many years without recurrence, one question that arises is whether they are cured of their disease or are simply in a long-term remission. This question continues to remain unanswered. In their study, Goodman et al. reported no obvious plateau of the time-to-treatment failure curve.\textsuperscript{10} We also observed no plateau in the PFS curve after follow-up of close to 14 years, suggesting that late relapses do occur. However, most patients with HCL continue to survive and do not die as a result of their disease. Additional studies following HCL patients treated with 2-CdA for even longer periods of time are needed. Meanwhile, care of these patients should be focused on detection of other malignancies and medical conditions as dictated by current screening and treatment guidelines.

Future directions for treatment of HCL continue to be investigated. Further investigation is warranted to determine whether PFS can be improved with eradication of minimal residual disease (MRD). We previously reported a relapse-free survival
difference between patients who had MRD in their bone marrow as compared with those who did not. Whether eradication of MRD with agents such as Rituximab would lead to improvements in PFS and OS is untested, but warrants further study. Rituximab has an advantage over purine analogues such as 2-CdA and 2’-DCF in that it is less immunosuppressive. Rituximab is also an option for patients with purine-analogue resistant disease. Thomas et al. reported an 80% overall response rate (53% CR, 13% CR-MRD, 13% PR) in patients with relapsed or primary refractory HCL after nucleoside analog therapy who received 8-12 doses of weekly Rituximab. Excellent results have been reported by Kreitman et al. with the use of BL22, a recombinant immunotoxin containing the variable portion (fv) of the monoclonal antibody to CD22 fused to a fragment of Pseudomonas exotoxin. In previously treated HCL patients given BL22, the overall response rate was 80% with 69% of patients achieving a CR. Toxicity in these patients included a cytokine release syndrome and the development of a reversible hemolytic-uremic syndrome in 2 patients.

In summary, long-term follow-up of patients with HCL treated with 2-CdA shows that this agent is safe and highly effective treatment for this disease. The majority of patients enjoy long-term remission. Patients who relapse have several options available including another cycle of 2-CdA, treatment with alternative purine analogues, or treatment with novel agents such as Rituximab and BL22. Based on this long-term experience with 2-CdA in HCL, purine analogues such as 2-CdA should be agents of choice in the initial treatment of HCL. Whether patients who continue to be in long-term remission after treatment with 2-CdA are cured of their disease remains to be determined. However, patients can be assured of excellent OS after treatment with 2-CdA.
REFERENCES


### TABLES

#### Table 1. Characteristics of 86 Patients with HCL

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<tr>
<th>Characteristic</th>
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<th>Range</th>
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<tr>
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<td>WBC ($x 10^3/\mu L$)</td>
<td>2.5</td>
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<td>ANC (/µL)</td>
<td>816</td>
<td>10 – 16022</td>
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<td>Hgb (g/dL)</td>
<td>11.2</td>
<td>5.9 – 14.7</td>
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<td>Plt ($x 10^3/\mu L$)</td>
<td>79</td>
<td>11 – 466</td>
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<tr>
<td>Follow-up (years)</td>
<td>9.7</td>
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<tr>
<td>Male</td>
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<table>
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<td>Yes</td>
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<td>No</td>
<td>60 (70%)</td>
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Abbreviations: WBC, white blood cell count; ANC, absolute neutrophil count; Hgb, hemoglobin; Plt, platelets
Table 2. Malignancies Developing in Patients with HCL Treated with 2-CdA

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<th>Malignancy</th>
<th>Number</th>
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<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Lung</td>
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<td>0</td>
<td>0</td>
</tr>
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<td>0</td>
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<td>Thymoma</td>
<td>1</td>
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<tr>
<td>Basal cell</td>
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</tr>
<tr>
<td>Total</td>
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<td>5</td>
<td>5</td>
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FIGURES

Figure 1. Diagram of Response and Relapse to Cycle #1 and Response to Cycle #2 in Patients with HCL Treated with 2-CdA

- 85 evaluable patients

- Cycle #1: 2-CdA
  - CR: 67/85 (79%)
  - PR: 18/85 (21%)
  - 21/67 relapsed (31%)
  - 10/18 relapsed (56%)

- Cycle #2: 2-CdA
  - 31/85 relapsed (36%)
  - 6/31 observed
  - 25/31* retreated

- * 1/25 retreated with Rituximab (CR) and 1/25 retreated with 2’-DCF (CR)
- † 1/23 (4%) response remains to be determined
Figure 2. PFS for All 86 Patients with HCL

Progression Free Survival (%)

No. Pts. At Risk   86  74  50  41  37  27  14  0

Dotted lines represent 95% confidence limits
Figure 3. PFS for Treated and Previously Untreated Patients with HCL

Progression Free Survival (%)

Years

No. Pts. At Risk
Not Prev. Tx. 60 53 33 25 23 16 10 0
Prev. Tx 26 21 17 16 14 11 4 0

p=0.23
Figure 4. PFS for Patients with HCL Achieving CR with 1 Cycle of 2-CdA

No. Pts. At Risk  67  62  41  35  31  22  13  0

Dotted lines represent 95% confidence limits
Figure 5. OS for All 86 Patients with HCL

No. Pts. 86 80 68 59 53 38 21 0
At Risk

Dotted lines represent 95% confidence limits
Figure 6. OS for Treated and Previously Untreated Patients with HCL

No. Pts. At Risk
Not Prev. Tx. 60 57 45 36 32 21 13 0
Prev. Tx 26 23 23 21 17 8 0

p=0.92
Figure 7. OS for Relapsed Patients with HCL

Dotted lines represent 95% confidence limits.
Figure 8. OS for Patients with HCL Achieving CR with 1 Cycle of 2-CdA

No. Pts.  At Risk
67  63  54  48  43  31  17  0

Dotted lines represent 95% confidence limits
Treatment of hairy cell leukemia with 2-chlorodeoxyadenosine (2-CdA): long-term follow-up of the Northwestern University experience

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