up to two decades ago the treatment of hairy cell leukemia (HCL) produced very disappointing results: median patient survival was only a few years. The introduction of the interferons (IFN) in 1984 and of the new purine analogues deoxycoformycin (DCF) and 2-chlorodeoxyadenosine (2CdA) in the early nineties dramatically improved the outcome of HCL patients, allowing a less complex and more optimistic approach to this disease.

Here we report a retrospective analysis of 34 patients with typical HCL, selected for treatment with IFN-α or 2CdA, observed between June 1985 and August 1996. The aim of the study was to evaluate outcome in relation to the different therapeutic regimens applied (IFN vs 2CdA).

Results
The patients' clinical and hematologic features before treatment are reported in Table 1. All patients were evaluable for response.

IFN. Twenty patients (77%) achieved a response, complete in 5 (19%) and partial in 15 (58%). Six patients (23%) were considered as non responders. No major hematological toxicity was observed during IFN treatment. In 4 patients with neutrophil counts lower than 1×10^9/L at the beginning of IFN treatment, filgrastim 300 µg s.c. was given every other day for 12 to 20 times. Extrahematological toxicity consisted of flu-like syndrome (14 cases), fever of unknown origin (FUO) (6 cases), 1°-2° WHO grade weakness (5 cases) and alopecia (3 cases), weight loss (2 cases), pruritus (2 cases), sweating (2 cases). After a median follow-up of 19 months and no statistical advantage was detected for those who achieved a CR vs those in PR. In the group treated with 2CdA, only 1 patient (4%) relapsed after a median follow-up of 14 months. At a median follow-up of 59 months (range 4-134), overall survival of all 34 patients was 97%, with only 1 patient having died of an acute leukemia. Our results confirm the favorable outcome currently expected for HCL and emphasize the therapeutic activity of 2CdA in the treatment of this disease.

©1997, Ferrata Storti Foundation
months (range 6-72), 6 of the 20 patients (30%) responsive to IFN still maintained their response, while 14 (70%) had relapsed. These included 3 of the 5 patients in CR (60%) and 11 of the 15 patients in PR (73%). Median PFS for these 20 patients was 19 months (Figure 1); no statistical differences were noted between the PFS of patients in CR and those in PR (p=0.3).

2CdA. All patients responded to 2CdA: overall, 18 (82%) obtained a CR and 4 (18%) a PR. No differences were observed between 2CdA used as first-line therapy (group A) or second-line therapy (group B) (Table 1). The median nadir of circulating neutrophils was $0.4 \times 10^9/L$ (0.1-1.4), and in eighteen patients (81.0%), 8/8 of group A and 10/14 of group B) filgrastim 300 µg s.c. was given a median of 7 times (3-17). The number of circulating CD4+ lymphocytes was $0.2 \times 10^9/L$ (0.04-0.3) and $0.2 \times 10^9/L$ (0.07-0.4×10^9/L) 2 and 12 months after therapy respectively. One patient in group A developed pneumonia 3 months after 2CdA but rapidly recovered with antibiotic therapy. Three patients (2 in group A and 1 in group B) experienced one episode of FUO. Hemoglobin and platelet reduction were mild and no extrahematological complications were observed. After a median follow-up of 14 months (range 4-37) only in 1 patient in group B showed disease progression 22 months after treatment (Figure 1).

In our series of 34 patients, with a median follow-up of 59 months (range 2-134), OS was 97% and only 1 person (a 48 year-old patient in complete remission) died of secondary acute non-lymphocytic leukemia 30 months after the end of 2 CdA and 44 months from diagnosis. No other secondary malignancies have been detected and, at present, all the other patients are alive.

**Discussion**

Our results underline the progress made in the treatment of HCL in these last two decades. Whether IFN or purine analogues (namely 2CdA and deoxycoformycin) should be considered the first-line therapy for HCL is still debated, even though, looking at the results of most investiga-
to be the treatment of choice. In fact, compared to IFN, purine analogues substantially improve the rate of response (up to 80% CR) and produce durable remissions. In our study DCF was excluded from the analysis due to the low number of patients treated with this drug.

The response rate observed in our cohort was similar to that reported in previous studies. In particular, treatment with 2CdA led to a higher CR rate and a statistical PFS advantage (p=0.0048) (Figure 1). Furthermore, the response was similar in both untreated and previously treated patients, confirming that 2CdA shows major activity even in patients resistant to IFN.

Since treatment with 2CdA is quite intensive and potentially more harmful than IFN, we also considered the toxic events associated with therapy. Both IFN and 2CdA proved to be safe. IFN caused mainly extrahematological toxicity, in particular a flu-like syndrome, as observed in other lymphoproliferative disorders, while 2CdA induced predominantly hematological toxicity, in particular an initial neutropenia and a long-lasting lymphocytopenia. Nevertheless, major infective complications were observed in only one patient (a pneumonia 3 months after treatment). It should also be considered that long-term treatment with IFN involves a certain risk of autoimmune disorders.

In conclusion, our experience confirms the high efficacy of 2CdA in the treatment of HCL. Since this agent also appears to be safe, especially if associated with growth factors, we believe that it should currently be preferred to IFN for the treatment of HCL. However, longer follow-up is required to establish the real impact of this drug on the OS of patients.

References