Low-Dose Cytosine Arabinoside in the Treatment of Acute Nonlymphocytic Leukemia

L. Luigi Cavanna
M. Michele Di Stasi
F. Fabio Fornari
G. Giuseppe Civardi
G. Giorgio Sbolli
G. Giuseppe Montanari
L. Luigi Buscarini

1. Divisione Medica, Ospedale Civile di Piacenza, Italia

We have read with interest the article of Jensen and Stentoft [1] about the treatment of relapsed and refractory acute nonlymphocytic leukemia (ANLL) with low-dose cytosine arabinoside (ARA-C). We would like to report our clinical experience of the treatment with low-dose ARA-C in 11 patients with ANLL.

The patients were classified according to the FAB criteria [2]; 2 cases had M↑ type, 5 M2 type, 1 M3, 2 M4, and 1 patient had chronic granulocytic leukemia (CGL) in myeloblastic transformation (table I). Three patients developed ANLL after myelodysplastic syndromes (MDS); 4 other patients were refractory to standard chemotherapy for remission induction, which was one course with daunorubicin 50 mg/m² day for 3 days, ARA-C 100 mg/m²/12 h and thioguanine 100 mg/m²/12 h on days 1–7, followed by one course with one day daunorubicin and 5 days ARA-C and thioguanine treatment. Also included were 3 elderly patients with de novo ANLL. The patient with CGL in the blast phase was unresponsive to the two courses of combination chemotherapy.

Treatment regimen. ARA-C was administrated 10 mg/m² s.c. every 12 h, usually for 21 days. To patients who had a response, ARA-C was given for 10 days every 4–6 weeks. Complete remission (CR) was defined as a reduction of bone marrow blasts to < 5% in the presence of peripheral granulocytes count > 2×10⁹/l, a platelet count > 100×10⁹/l and a hemoglobin level > 12 g/dl; partial response (PR) was defined as > 50% reduction in bone marrow blasts, an increase of the hemoglobin values > 10 g/dl, with an increase of > 50×10⁹/l platelets and > 1.5×10⁹/l granulocytes. Eight patients responded to therapy; there were 5 CR and 3 PR (table I).

Among the 5 patients with CR (2 with ANLL after MDS, 2 with refractory and 1 with de novo ANLL), 2 patients relapsed after 9 and 12 months, and 3 are in CR after 3,

Table I. Clinical data and response to low-dose ARA-C of 11 patients with ANLL

<table>
<thead>
<tr>
<th>Patients No.</th>
<th>Clinical Data and Response</th>
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</thead>
<tbody>
<tr>
<td>1–3</td>
<td>ANLL after MDS</td>
</tr>
<tr>
<td>4–8</td>
<td>Refractory disease</td>
</tr>
<tr>
<td>9–11</td>
<td>De novo ANLL</td>
</tr>
<tr>
<td>NR</td>
<td>No response</td>
</tr>
</tbody>
</table>

180
10 and 26 months, respectively. Among the 3 cases who showed PR, patient No. 5 previously refractory to conventional chemotherapy had improved bone marrow function, resumed his daily activities and was well for 18 months (table I). Patient No. 9 with de novo ANLL is still alive after 14 months from diagnosis. Patient No. 8 with CGL in blast crisis died 7 months after the start of low-dose ARA-C for infection and disease progression. The 3 patients who did not respond died within 3 months from diagnosis.

The therapy was well tolerated; none of the patients had gastrointestinal symptoms. The most severe toxic effect was myelosuppression: 4 patients showed serious trombocytopenia ( < 20×10^9/l) and 3 had granulocytopenia ( < 0.5×10^9/l). There were no deaths related to the treatment.

In conclusion, low-dose ARA-C induced responses in 8 of 11 patients with ANLL; it must be emphasized that 4 responses (2 CR and 2 PR) were obtained in 5 patients who were refractory to heavy combination chemotherapy and these data seem to confirm the results reported by Jensen and Stentoft [1].

References