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

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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 M₁ 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 administered 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 × 10⁷/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

Patients No. 1–3 had ANLL after MDS, No. 4–8 had refractory disease, and No. 9–11 de novo ANLL. NR = No response.

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 thrombocytopenia ($< 20 \times 10^9/l$) and 3 had granulocytopenia ($< 0.5 \times 10^9/l$). 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

- Jensen, M.K.; Stentoft, J.: Low-dose Cytosine Arabinoside in the treatment of relapsed and refractory acute non-lymphocytic leukemia. *Acta haemat.* 76: 127–129(1986).
- Bennet, J.M.; Catovsky, D.; Daniel, M.T.; Flandrin, G.; Galton, D.A.G.; Gralnick, H.R.; Sultan, C: The French-American-British (FAB) Co-operative Group: Proposal for the classification of the acute leukemia. *Br. J. Haemat.* 33: 451–458(1976).