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Crowther D, Powles R L, Bateman C J T, Beard M E J, Gauci C L, Wrigley P F M, Malpas J S, Fairley G H & Scott R B. Management of adult acute myelogenous leukaemia. *Brit. Med. J.* 1:131-7, 1973.
[Depts. Medicine and Haematology and I.C.R.F. Dept. Medical Oncology, St. Bartholomew's Hosp., London, and Inst. Cancer Research and Royal Marsden Hosp., Sutton, Surrey, England]

This paper described the use of combined cytosine arabinoside and daunorubicin for remission induction in patients with acute myelogenous leukaemia. Management policies were described that, together with the new chemotherapy, resulted in complete remissions in more than half the patients. [The *SCI*® indicates that this paper has been cited in over 200 publications.]

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In 1968 I started work at St. Bartholomew's Hospital as senior registrar to Sir Ronald Bodley Scott. During 1968 the few patients with acute myelogenous leukaemia (AML) with whom the team dealt were treated with single-agent cytosine arabinoside (AraC) or daunorubicin (DR). The results achieved by these agents were unsatisfactory, although it was recognised that they were the best single agents available for remission induction in AML.[1,2] For this reason, I suggested that a combination of these two agents be used intensively for induction therapy. The initial results of treating 37 patients with the AraC/DR combination were published in 1970.[3] Of these, 23 (or 62 percent) achieved a complete remission, the highest remission rate so far reported for AML.

In 1973 I updated these results (the *Classic* paper) and described the ground rules that we used for management. A treatment policy for "allcomers" was assessed, and there were no exclusions for early deaths; indeed, occasional deaths occurred during the supportive period before chemotherapy could be given. All patients were treated on an open general medical ward, but patients who became feverish were treated with broad-spectrum antibiotics within the first hour, before bacteriological results were available. This policy undoubtedly contributed to the high success rate. The chemotherapy was aggressive—5-day cycles were given every 10 days—and the treatment was individualised depending on bone-marrow aspiration results.

The anthracyclines were developed in Europe, and their use was slow to gain acceptance in the US. However, their delivery in combination with AraC is now accepted as first-line chemotherapy for AML in nearly all major treatment centres throughout the world. For example, a recent Medical Research Council (UK) study using a five-day cycle of AraC and two doses of DR produced remissions in more than 70 percent of a large number of patients with AML.[4] The optimal schedule for combining AraC and DR is still unknown, but seven-day cycles of AraC are often used.

Gordon Hamilton Fairley was one of the authors closely associated with this work and, at the time of its publication, had been made the first professor of medical oncology in the UK. He held this post until his untimely death by a terrorist bomb in London in 1975.

The reason this paper and the 1970 paper[3] have been so frequently cited is that they report the first description of the use of combination AraC and DR for remission induction in AML. The combination has stood the test of time, and this schedule and modifications of it remain the most commonly used induction chemotherapy for AML, achieving results as good as, if not better than, other combinations introduced later.[5]

1. **Ellison R R, Holland J F, Weil M, Jacquillat C, Boiron M, Bernard J, Sawitsky A, Rosner F, Gussoff B, Silver R T, Karanas A, Cuttner J, Spurr C L, Hayes D M, Blom J, Leone L A, Haurani F, Kyle R, Hutchison J L, Forcier R J & Moon J H.** Arabinosyl cytosine: a useful agent in the treatment of acute leukemia in adults. *Blood* 32:507-23, 1968. (Cited 340 times.)
2. **Boiron M, Jacquillat C, Weil M, Tanzer J, Levy D, Sultan C & Bernard J.** Daunorubicin in the treatment of acute myelocytic leukaemia. *Lancet* 1:330-3, 1969. (Cited 105 times.)
3. **Crowther D, Bateman C J T, Vartan C P, Whitehouse J M A, Malpas J S, Fairley G H & Scott R B.** Combination chemotherapy using L-asparaginase, daunorubicin, and cytosine arabinoside in adults with acute myelogenous leukaemia. *Brit. Med. J.* 4:513-7, 1970. (Cited 125 times.)
4. **Rees J K H, Hayhoe F G J & Gray R.** Treatment of acute myeloid leukaemia following remission. Results of a large collaborative study in U.K. *Proc. Amer. Soc. Clin. Oncol.* 3:190, 1984.
5. **Gale R P & Foon K A.** Therapy of acute myelogenous leukemia. *Semin. Hematol.* 24:40-54, 1987.

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