

The “7+3” regimen in acute myeloid leukemia

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**TITLE** Cytosine arabinoside (NSC-63878) and daunorubicin (NSC-83142) therapy in acute nonlymphocytic leukemia

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Nowadays, the majority of patients with acute myeloid leukemia (AML) achieve a complete remission and many are cured. This remarkable achievement takes place with a standardized induction regimen consisting of an anthracycline and cytarabine. The landmark paper in 1973 – from the prestigious USA group of James Holland at the Roswell Park Memorial Institute in Buffalo, New York – reported on an astounding complete remission rate of 63% among patients with both previously-treated and previously-untreated AML. The drugs used were the anthracycline, daunorubicin (formerly rubidomycin in France and daunomycin in the USA), and the pyrimidine antimetabolite, cytosine arabinoside. For a decade prior to this work, each of these drugs was shown to have potent anti-leukemic activity as single agents<sup>1,2</sup> and even combinations of these two drugs had been reported.<sup>3</sup> In all cases only a small number of remissions

were achieved and they were of very short duration. The ultimate breakthrough came, not with the addition of new drugs, but after longer exposure of the leukemic cells to the combination of daunorubicin and cytarabine, as cytosine arabinoside is now known. This breakthrough combination and schedule of drugs for AML, widely known as the “7 and 3” regimen, dramatically changed the prognosis of patients, has remained the backbone of standard therapy for close to five decades, and, amazingly, is still going strong. This remarkable development has been at the core of the current constantly improving outlook for newly-diagnosed patients with AML. From having an incurable disease in the early 1970s, approximately 35-40% of young adults can now expect to be long-term survivors – after starting with “7+3” induction therapy. Furthermore, and quite unthinkable even two decades ago, patients tolerate this combination well into their seventies.

The “7+3” Regimen

1973



| Drug   | Doses                 | Days          | Delivery            |
|--|-----------------------|---------------|---------------------|
| <b>Cytosine arabinoside (NSC-638678)</b><br><chem>NC1=NC=NC2=C1N=CN=C2C3=CC=CC=C3O</chem>          | 100 mg/m <sup>2</sup> | 1 2 3 4 5 6 7 | Continuous infusion |
| <b>Daunorubicin (NSC-83142)</b><br><chem>COc1ccc2c(c1)O[C@H]3[C@@H](O)[C@H](O)[C@@H](O)C3=O</chem> | 45 mg/m <sup>2</sup>  | 1 2 3 4 5 6 7 | Intravenous         |

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