

The International Symposium on the Clinical and Pharmacological Effects of the Daunorubicin-DNA Complex

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Introduction

Daunorubicin is the most widely used anthracycline in the treatment of acute leukemia. It is also the anthracycline that has been used for the longest time, its use dating back to the first clinical trials by Bernard et al. in the early 1960/s. Doxorubicin and rubidazone, which were developed later, also appear to have effects on acute leukemia and doxorubicin in particular appears to have a very wide application in the treatment of other malignancies.

Unfortunately, all the anthracycline derivatives have toxic effects on cardiac muscle and these effects are clearly related to the total amount of the drug administered. This limits their use to an induction period and early maintenance therapy, and precludes their use for long-term maintenance treatment and, in general, for the treatment of relapses. Based on de Duve's work on lysosomes, Trouet and his group have introduced the concept of lysosomotropic cancer chemotherapy. The principle is that by linking them to DNA, drugs such as daunorubicin and doxorubicin can be taken up into the lysosomes by endocytosis. Leukemic cells probably exhibit a higher endocytotic activity than the cardiac muscle

cells. Hopefully, therefore, the efficacy of the drugs should be increased and their cardiotoxicity reduced.

A few groups in Europe have been involved in research on the clinical and pharmacological effects of lysosomotropic substances, especially daunorubicin-DNA and doxorubicin-DNA. Our group (the Leukemia Group of Central Sweden) has been involved in this research for about one year and a half. Although it is as yet too early to draw firm conclusions, especially about the clinical effects of these substances, we felt it valuable to gather together people with experience in this field and to summarize the present state of knowledge. Many results presented during the symposium will certainly be preliminary. However, it is our hope that they will be of value not only for us who work in the field but also for others who will enter it in the future.

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