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Letter to the Editor

Daunorubicin-DNA Complex in Acute Nonlymphoblastic Leukemia

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With reference to the paper recently published by Paul et al. [6], we wish to make the following comments.

Firstly, we demonstrated in 1978 that in the rabbit the DNR-DNA complex was quickly and almost completely dissociated into the blood stream [1], this dissociation not being influenced by blockade of the R.E.S. system [3].

Secondly, we reported the first results on the plasma levels of the DNR-DNA complex in man in 1977 [2], a complete pharmacokinetic study being published in 1979 [5]. This last study demonstrated that the pharmacokinetic behaviour in man was similar to that in the rabbit.

Recently we reported that the tissue distribution of DNR whether as a free drug or as a complex with DNR did not differ [4]. Therefore, it is obvious that a very different cytostatic activity of this complex can not be expected when compared with the free drug infused under the same conditions.

In conclusion, all but one [5] of our references were omitted by Paul et al., who cited their own references as the first papers published in regard to the DNR-DNA complex. In fact, all of these works appeared after our publications.

Further experimental or clinical investigations on this DNR-DNA complex thus appear unwarranted.

References

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Response

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We are sorry that Dr. Hulhoven and Dr. Harvengt are not satisfied with our reference to their work in our paper "Comparison of Daunorubicin and Daunorubicin-DNA Complex in the Treatment of Acute Nonlymphoblastic Leukemia" [CCP 1981; 6: 65–73]. This work is a report of a clinical trial performed by the Leukemia Group of Central Sweden (LCS) 1976–1978.

There are no pharmacokinetic data in the paper. However, there are two sentences in the discussion concerning the pharmacokinetic properties of daunorubicin-DNA. On page 72, it is stated that "the major objection to this previous view is that the daunorubicin-DNA complex is dissociated to a relatively high degree in the plasma [5, 23, 24]. As these studies show, it is more likely that the daunorubicin-DNA complex may serve as a slow-release preparation of daunorubicin with pharmacokinetics different from those of the free drug [6, 14, 23]". In this part, which was introduced in order to explain the clinical results obtained, we referred to Dr. Hulhoven's main work [No. 5 in his letter] and to a work done by ourselves. We had no intention of making a comprehensive review of human and animal pharmacokinetic data obtained by us, Dr. Hulhoven and his coworkers, as well as by several other groups.

Dr. Hulhoven's work was presented in 1979, ours later (1980 and 1981), which is evident from the references [No. 14, 21, 23] in our paper. In these papers we reported interesting pharmacokinetic differences between free and DNA-linked drugs, although not as pronounced as reported in the early papers from Dr. Hulhoven's laboratory. It appears that Dr. Hulhoven came to other conclusions about the daunorubicin-DNA complex in a later work, published in 1982, long after the publication of our actual work. We may be excused for not having referred to this work [No. 4 in Dr. Hulhoven's letter]. However, we feel that neither Dr. Hulhoven's work nor our own justify the view of Dr. Hulhoven and Dr. Harvengt that further experimental and clinical investigations on the daunorubicin-DNA complex are unwarranted.

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