end of the infusion or approximately 4 hours after cessation of the infusion.

In accordance with Glantz et al. (1), we did not measure significant concentrations in the CSF of one patient in whom CSF was sampled. In another patient, we could examine a small sample of normal brain tissue, and we were not able to demonstrate paclitaxel. With respect to tumor tissue concentrations, however, our findings differed significantly from the findings of Glantz et al. (1), with tissue concentrations ranging from 464 to 2000 ng/g in all three patients. In two of our three patients, tumor tissue levels were significantly higher than plasma levels (tumor, 2000 ng/g; plasma, 160 ng/mL; tumor, 464 ng/g; and plasma, 211 ng/mL). Paclitaxel identity in tumor tissue was confirmed on the basis of the HPLC retention time and its ultraviolet spectroscopic properties as analyzed by photo-diode array detection in line with the HPLC system.

It is not quite clear how these different findings should be explained. Possibly, technical differences in the method of analysis might play a role, but also of importance may be the fact that Glantz et al. examined rat tumors and we examined human tumors. Lesser et al. (3) demonstrated that disruption of the blood-brain barrier in rats by the presence of tumor leads to relatively high intratumoral paclitaxel concentrations. Our three patients had been operated on and had received radiotherapy in the past, which probably disrupted the blood-brain barrier.

In a phase II protocol, Chamberlain et al. (4) recently demonstrated modest efficacy of paclitaxel in patients with recurrent primary brain tumors. On the basis of these results and on our data, we think that there still might be a rationale for paclitaxel, also in combination with radiotherapy, in the treatment of CNS malignancies.

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References


Note
Correspondence to: Jan J. Heimans, M.D., Department of Neurology, Free University Hospital, P.O. Box 7057, 1007 MB Amsterdam, The Netherlands.

Response

Thank you for forwarding us the letter by Heimans et al. We are well aware of their extensive pharmacologic studies related to paclitaxel (Taxol) but unfortunately were unaware of their publication in the Annals of Oncology when we submitted our manuscript to the Journal of the National Cancer Institute. We are pleased that our results concur with theirs concerning concentrations of paclitaxel in cerebrospinal fluid. We note with interest the high concentrations of paclitaxel in tumors compared with those in plasma; however, we cannot explain the differences between the concentrations in tumor tissue measured by them and by us. Although the assay employed by Heimans and colleagues is more sensitive than that used in our study, the concentrations of paclitaxel reported by them should have been detectable if present in the tumor tissue we studied. We also cannot comment on the differences between implanted rat tumors and primary, human neoplasms. It is a reasonable hypothesis that disruption of the blood-brain barrier in the patients from The Netherlands contributed to the higher intratumoral concentrations. We also agree with Heimans et al. that pharmacology data are not a substitute for a well-performed clinical trial and that their data, those of Lesser et al. (1), and ours are not substitutes for patient response data. While the data reported by Chamberlain et al. (2) are encouraging, the ultimate use of paclitaxel in central nervous system malignancies, and possibly even the most appropriate dose and schedule for its administration, will require more extensive clinical evaluation.

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References


Re: Long-Term Tamoxifen Treatment for Breast Cancer

Greenspan (1) points out that the review of my book (2) by Fabian (3) did not focus on the apparent association of tamoxifen with the detection of endometrial cancer. Greenspan quite rightly points out that there has been little balance in the reporting of concerns about tamoxifen. The reports of the association of tamoxifen with endometrial cancer (4,5) and its prognosis (6) are now known to be flawed or inappropriately reported. Obviously, a book review cannot cover all ground, but the answer to Dr. Greenspan's questions has been published elsewhere (7-10).

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Cooperative Research Sought by the Prof. N. N. Petrov Research Institute of Oncology, St. Petersburg

This letter is motivated by our deep concern regarding the situation in Russian cancer research and, specifically, in the oldest cancer research facility in Russia, the Prof. N. N. Petrov Research Institute of Oncology. The economic situation in Russia during recent years has led to heavy cuts in basic research, including cancer research. Federal budget funding for the institute for 1995 is only 547.9 million rubles, about $122,000. This money supports over 200 scientists and technicians. The average salary is $61 per month (the chief of laboratory is paid $105 per month), while the cost of living in Russia is now comparable to that in the United States. No funds are available for reagents, equipment, laboratory animals, etc. We at the institute are avoiding an inevitable decline in scientific potential through the enthusiasm of the dedicated staff.

N. N. Petrov, A. I. Serebrov, S. A. Kholidin, A. I. Rakov, L. F. Larionov, N. V. Lazarev, L. M. Shabad, V. M. Dilm, and many other scientists with worldwide reputations have worked at this institute. Today, a large group of scientists whose contributions to cancer research are well known to colleagues in other countries is working here. Many of these researchers have experience in cooperative studies with international institutions (the World Health Organization [WHO], the International Agency for Research on Cancer [IARC]) and with research institutions and universities of the United States, Europe, and Japan. Institute scientists have obtained international fellowships from IARC, the U.S. National Cancer Institute (NCI), WHO, the International Science Foundation (ISF), and other organizations. Many are members of the European Association for Cancer Research (EACR), the American Association for Cancer Research (AACR).

There is nothing in the priorities of the government and the Parliament that indicates increased funding for basic research in the foreseeable future. This funding situation will lead to a collapse of cancer research-related projects in Russia, with negative consequences for the international scientific community.

There already has been a “brain drain” from our institute, with many young scientists going to more profitable businesses or leaving for other countries. We want to stay and work in Russia. Therefore, we appeal to the international scientific community to consider the possibilities of grants for cooperative research with the N. N. Petrov Institute. This letter should not be seen as an appeal for humanitarian aid. Our qualifications and experience in collaboration with international research centers will allow us to respond to your proposals or to suggest new projects for cooperative work and to conduct them efficiently. We look forward to hearing from and working with the international cancer research community.

Note

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National Cancer Institute Response

Editor’s note: The above Correspondence by Alexandrov et al. was forwarded to the National Cancer Institute’s Office of International Affairs, which offers the following response:

We certainly appreciate the plight of our Russian colleagues and wish them the best under very trying circumstances. We would like to assure these authors, and readers in general, that the National Cancer Institute (NCI) is devoting significant resources for support of Russian biomedical scientists. Among the mechanisms of support are the following:

1) About 100 Russian scientists visit NCI-supported laboratories each year to receive specialized training and/or to conduct collaborative research with U.S. scientists. Support comes from either the Short-Term Scientist Exchange Program of NCI’s Office of International Affairs or from NCI intramural research funds under the National Institutes of Health (NIH) Visiting Program.

2) NCI also has made considerable resources available to cancer researchers in Russia and other countries of the former Soviet Union through its CDA-NIS Program (Career Development Awards for Young Cancer Researchers in the Newly Independent States of the United States).