LAN, K. K. G. and DEMETS, D. L. (1989). Changing frequency of interim analysis in sequential monitoring. *Biometrics* **45** 1017–1020.

LAURIE, J. A., MOERTEL, C. G., FLEMING, T. R., WIEAND, H. S., LEIGH, J. E., RUBIN, J., MCCORMACK, G. W., GERSTNER, J. B., KROOK, J. E., MALLIARD, J., TWITO, D. I., MORTON, R. F., TSCHETTER, L. K. and BARLOW, J. F., FOR THE NORTH CENTRAL CANCER TREATMENT GROUP AND THE MAYO CLINIC (1989). Surgical adjuvant therapy of large-bowel carcinoma: An evaluation of levamisole and the combination of levamisole and fluorouracil: The North Central Cancer Treatment Group and the Mayo Clinic. *Journal of Clinical Oncology* **7** 1447–1456.

LIN, D. Y. (1991). Nonparametric sequential testing in clinical trials with incomplete multivariate observations. *Biometrika* **78** 123–131.

LIN, D. Y., FISCHL, M. A. and SCHOENFELD, D. A. (1992). Evaluating the role of CD4-lymphocyte change as a surrogate endpoint in HIV clinical trials. *Statistics in Medicine*. To appear.

MACHADO, S. G., GAIL, M. H. and ELLENBERG, S. S. (1990). On the use of laboratory markers as surrogates for clinical endpoints in the evaluation of treatment for HIV infection. *Journal of AIDS* **3** 1065–1073.

MARX, J. L. (1989). Drug availability is an issue for cancer patients, too. *Science* **245** 346–347.

MEDICAL RESEARCH COUNCIL WORKING PARTY (1984). The evaluation of low-dose preoperative x-ray therapy in the management of operable rectal cancer: Results of a randomly controlled trial. *British Journal of Surgery* **71** 21–25.

MOERTEL, C. G., FLEMING, T. R., MACDONALD, J. S., HALLER, D. G., LAURIE, J. A., GOODMAN, P. J., UNGERLEIDER, J. S., EMERSON, W. A., TORMEY, D. C., GLICK, J. H., VEEDER, M. H. and MAILLIARD, J. A. (1990). Levamisole and fluorouracil for adjuvant therapy of resected colon carcinoma. *New England Journal of Medicine* **322** 352–358.

O'BRIEN, P. C. and FLEMING, T. R. (1979). A multiple testing procedure for clinical trials. *Biometrics* **35** 549–556.

PEPE, M. S. (1992). Inference using surrogate outcome data and a validation sample. *Biometrika* **79** 355–365.

PEPE, M. S. and FLEMING, T. R. (1991). A non-parametric method for dealing with mismeasured covariate data. *J. Amer. Statist. Assoc.* **86** 108–113.

POCOCK, S. J. (1977). Group sequential methods in the design and analysis of clinical trials. *Biometrika* **64** 191–199.

PRENTICE, R. L. (1989). Surrogate endpoints in clinical trials: Definition and operational criteria. *Statistics in Medicine* **8** 431–440.

RIDER, W. D., PALMER, J. A., MAHONEY, L. J. and ROBERTSON C. T. (1977). Preoperative irradiation in operable cancer of the rectum: Report of the Toronto Trial. *Canadian Journal of Surgery* **20** 335–338.

VOLBERDING, P. A., LAGAKOS, S. W., KOCH, M. A., PETTINELLI, C., MYERS, M. W., BOOTH, D. K., BALFOUR, H. H., REICHMAN, R. C., BARTLETT, J. A., HIRSCH, M. S., MURPHY, R. L., HARDY, D., SOEIRO, R., FISCHL, M. A., BARTLETT, J. G., MERIGAN, T. C., HYSLOP, N. E., RICHMAN, D. D., VALENTINE, F. T., COREY, L. and THE AIDS CLINICAL TRIALS GROUP OF THE NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (1990). Zidovudine in asymptomatic human immunodeficiency virus infection. *New England Journal of Medicine* **322** 941–949.

WHITEHEAD, J. (1986). Supplementary analysis at the conclusion of a sequential clinical trial. *Biometrics* **42** 461–471.

WITTES, J., LAKATOS, E. and PROBSTFIELD, J. (1989). Surrogate endpoints in clinical trials: Cardiovascular diseases. *Statistics in Medicine* **8** 415–425.

Comment

John Crowley and Stephanie Green

Dr. Fleming has been instrumental in implementing monitoring committees and stopping guidelines for randomized clinical trials in both cancer and AIDS. Through his research, educational activities and service on Government committees, he serves as a model of statistician involvement in important clinical research. We whole-heartedly agree with the general principles Tom has discussed in this article. We welcome the opportunity to expand on some of the specific issues he raises.

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DATA MONITORING COMMITTEES

Structure

The model of committees composed of independent investigators meeting every 6 months with open hearings beforehand is not practical in every setting, nor is it necessarily desirable. Funds are not available for committees of this sort for the 150 or so randomized trials being conducted in the cancer cooperative groups. Further, we believe that those who know the most about the trial are among those in the best position to judge it. In particular, it seems important to include some members who treat patients with the regimens being studied (and who thus face the ethical issues directly), as well as those who are most familiar with any problems with the data. Tom and we were involved in the development of the Southwest Oncology Group monitoring committee policy in 1985. Since then, the group has had good results using monitoring commit-