

Letter to the Editor

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VOEST *et al.* [1] have performed a meta-analysis of prognostic factors and treatment in advanced ovarian cancer. Their paper presents an interesting methodology to compare survival curves in individual trials with a 'mean survival curve', the latter being obtained by averaging the survival curves, across all studies. This methodology is of value to assess the importance of prognostic features based on the published results of several trials, but it does *not* allow one to compare the relative efficacy of various treatment approaches.

The authors have 'demonstrated a strong correlation between survival and cisplatin or doxorubicin containing regimens' (p. 717), and they suggest a causal basis for this correlation. They do not point out that the size of the residual tumor (more or less than 2 cm) exhibited about the same correlation with median survival as did the use of cisplatin, and that there was a very strong correlation between the use of cisplatin and the percentage of patients with a residual tumor of less than 2 cm. Hence the apparent benefit of cisplatin might be *entirely* due to the selection of patients entered in trials of cisplatin.

To make their case more convincing, the authors have performed a multiple regression analysis in which 'the use of cisplatin was found to be a factor that predicts independently of other variables a prolonged median survival ($P = 0.011$) and log relative risk ($P = 0.005$)' (p. 716). Even the skeptic might be overwhelmed by the statistical significance

of this finding, but the fact that cisplatin turned out to be a better predictor of survival than residual tumor may readily be explained by multi-collinearity, a well-known phenomenon which the authors have chosen not to discuss.

In fact, the two essential principles of comparing treatments via a meta-analysis are that:

- (i) in situations where *randomized* trials are available they should be the only studies employed in the meta-analysis, and
- (ii) patients in a treatment group of a given study should only be directly compared with patients of the other treatment groups *in that study*.

In undertaking this analysis of treatments for advanced ovarian cancer the authors have violated these two basic principles. Thus their claims for treatment efficacy are unfounded and misleading. However, if their paper is taken strictly and solely for what its title announces, a study of prognostic factors, then it is a worthwhile addition to both the medical and statistical literature.

REFERENCE

1. Voest EE, Van Houwelingen JC, Neijt JP. A meta-analysis of prognostic factors in advanced ovarian cancer with median survival and overall survival (measured with the log (relative risk)) as main objectives. *Eur J Cancer Clin Oncol* 1989, **25**, 711-720.