

Detection of disease change from a biological marker: using CA125 in ovarian cancer as an example

Wendi Qian¹, Marcia Hall², Gordon Rustin², Diana Kornbrot³

¹University of Cambridge, Cambridge, UK, ²Mount Cernon Cancer Centre, London, UK, ³University of Hertfordshire, Hertfordshire, UK

Objectives

In Oncology drug development, the great majority of phase 3 trials are negative. New strategies are required to rapidly identify novel agents prior to large randomised trials. The CA125 doubling trial successfully showed that an effective drug could be identified efficiently by testing whether the rate of increase in the tumour marker CA125 decreased after starting the novel agent, at a point identified by CA125 rising to four times its nadir level. However efficiency could be improved, if more patients could be included. This work explores identifying an earlier effective starting point by analysing the time course of CA125 rise.

Method/Models

Tumour growth is measured by the slope of the linear regression of $\ln(\text{CA125})$ level on time. This slope is estimated for time points: 1 to n , 2 to $n+1, \dots, C-n+1$ to C , where C is the time patient transfers to new drug or leaves trial. A new potential transfer point to novel drug is identified as both CA125 level $> \text{ULN}$ and slope $> .0121$ (estimated minimum slope before transfer). The number of additional patients available for trial of the novel agent within 9 months is the end point, explored using $n=3$ and $n=4$.

Results and Conclusions

The number of patients who did not receive drug, but would have received drug with the new method, and the number of patients who did transfer to drug, but might have transferred earlier depends on the exact combination of slope and absolute CA125 level chosen, hence boundary estimates are given. Between 12 and 28 patients who did not receive drug with the existing protocol would have received drug with the new method. Between 12 and 25 patients who received drugs within 6 months would have received drug earlier using the new method. In addition, 2 patients who were transferred to drug after 9 months could have been transferred within 9 months. These preliminary analyses show that the proposed new monitoring approach could be applied in the selecting novel active agents suitable for larger randomised trials. Simulation of statistical performance of the approach will be presented.