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Letter to the Editor

Molecular profiling of platinum resistant ovarian cancer: Use of the model in clinical practice

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Dear Sir,

With great interest we read the article by Helleman *et al*.,[1] investigating whether a gene set identified using microarrays could be used to predict platin resistance in ovarian cancer. The authors studied a training set obtained from 24 tumours that were analysed using cDNA microarrays. This set contained 5 women who were platin-resistant (the nonresponders) and 19 women who were platin-sensitive (the responders). The authors concluded that 69 genes were differentially expressed between the responders and the nonresponders. An algorithm based on clustering was used to identify the most predictive genes among these 69 genes in the training set. This resulted in 9 genes (the differential expression of these genes was later confirmed with qRT-PCR) that could significantly discriminate between the responders and the nonresponders in the training set. Subsequently, this 9-gene set was used to predict platin resistance in an independent test set of 72 tumours (9 nonresponders and 63 responders) using expression levels measured with qRT-PCR. This resulted in a sensitivity of 89% and a specificity of 59%.

However, when examining the independent test set performance, we are not convinced that the approach described by Helleman *et al*. is optimally tuned for implementation in clinical practice. For women that are platin-sensitive (the responders), the nonplatinum containing regimen strategies remain suboptimal.[2] Therefore, it is imperative to accurately identify patients that will respond to platin-based chemotherapy. Because the specificity of the model of Helleman *et al*. is only 59%, 41% of the responders will be predicted to have platin resistance and will therefore be wrongfully assigned to the group of patients where other management options are recommended. Although 89% (value of the sensitivity) of the women with platin-resistance are correctly classified by the model of Helleman *et al*. we believe that this is less critical in a clinical setting since these patients have worse prognosis, which can, at this moment, only be minimally improved by different treatment strategies. In conclusion, we feel that in clinical practice, a higher specificity—perhaps at the cost of a lower sensitivity—would have been more useful.

Yours sincerely,
Olivier Gevaert, Nathalie Pochet, Frank De Smet, Toon Van Gorp, Bart De Moor, Dirk Timmerman, Frédéric Amant and Ignace Vergote

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