Trial Watch

PREDICTING PROGNOSIS IN CASTRATION-RESISTANT PROSTATE CANCER

The inter-patient heterogeneity of castration-resistant prostate cancer (CRPC) leads to widely variable rates in overall survival, ranging from several months to several years. Various clinical parameters have been used to predict prognosis in CRPC with limited success, highlighting the need for better prognostic biomarkers that, ideally, can be assessed using minimally invasive procedures. Two prospective studies reported in *The Lancet Oncology* have shown that mRNA expression signatures from whole blood can be used to stratify patients with CRPC into high- and low-risk groups.

Both groups collected peripheral blood from an initial set of patients with CRPC as 'training' sets to derive potentially prognostic gene signatures. Ross *et al.* examined the gene expression profiles of 168 pre-selected genes in 62 patients with heterogeneous clinical characteristics and treatment regimens and derived a set of six genes, the expression levels of which were capable of stratifying patients into low- and high-risk groups. Strikingly, the median survival in the low-risk group was more than 34.9 months compared with only 7.8 months in the high-risk group ($P < 0.0001$). This was validated using a second set of 138 patients with CRPC. Although the difference in median survival was less striking in these patients (18.5 months for the low-risk group versus 9.2 months for the high-risk group), the prognostic power was still significant. Olmos *et al.* examined a training set of 94 patients with CRPC (cases, $n = 64$) or with clinically indolent prostate cancer and under active surveillance (controls, $n = 30$). Gene expression microarray data were analysed using latent process decomposition (LPD), which divided the patients into four groups. Patients with CRPC were evenly distributed throughout the groups, but those in group 1 (LPD1) had worse overall survival than those in other LPD groups (LPD1 overall survival 10.7 months versus 25.6 months in non-LPD1 groups, $P < 0.0001$). The authors found that a nine-gene signature was sufficient to classify these patients, and this was validated using a second cohort of 70 patients with CRPC. In this patient population, overall survival was 9.2 months in the LPD1 group versus 21.6 months in the non-LPD1 groups ($P = 0.001$).

Interestingly, the prognostic signatures identified in both studies included genes encoding proteins involved in immune function, suggesting that a dysfunctional immune system may be a key factor in determining poor prognosis in CRPC. However, more studies will be required to determine the functional roles of these genes. Furthermore, additional validation of the prognostic abilities of these signatures will be necessary before they can be incorporated into routine patient care.

ORIGINAL RESEARCH PAPERS Olmos, D. *et al.* Prognostic value of blood mRNA expression signatures in castration-resistant prostate cancer: a prospective, two-stage study. *Lancet Oncol.* 9 Oct 2012 (doi:10.1016/S1470-2045(12)70372-8) | Ross, R. W. *et al.* A whole-blood RNA transcript-based prognostic model in men with castration-resistant prostate cancer: a prospective study. *Lancet Oncol.* 9 Oct 2012 (doi:10.1016/S1470-2045(12)70263-2)