BIOMARKERS

Circulating tumor cells in prostate cancer

In prostate cancer, reliable markers of disease status are important for selecting and monitoring treatment. Two recent studies have shown that increased levels of circulating cells predict worse outcomes in patients with metastatic castration-resistant and clinically localized prostate cancer.

Howard Scher and colleagues used data from the IMMC38 trial, which previously evaluated whether a circulating tumor cell (CTC) cutoff of ≥5 cells per 7.5 ml predicted survival in patients with castration-resistant prostate cancer. In total, the reanalysis included 164 patients who were scheduled to receive first-line chemotherapy. CTC counts were performed using the validated CellSearch® and CellTracks® systems (Immunivest, Wilmington, DE). High baseline CTC counts were associated with increased risk of death, as was the magnitude of change in CTC count from baseline. By contrast, baseline PSA concentration and changes in PSA level were less-predictive of survival. Serum PSA did not offer any additional information on the risk for death, beyond that provided by CTC count and serum lactate dehydrogenase (LDH) concentration. The authors conclude that CTC count, as a continuous variable, might be useful for monitoring therapy in patients with metastatic castration-resistant prostate cancer. If properly validated, it might also have a role as a surrogate end point in clinical trials.

While CTC count might have potential as a biomarker in castration-resistant prostate cancer, these results will have to be confirmed and validated in well-designed prospective studies. In addition, even if CTC count is validated as a marker of survival, how this information is incorporated into clinical practice remains to be determined. "Survival in patients with low baseline CTC counts varied substantially," note the authors. "Low CTC counts at baseline do not ensure favorable prognosis for individual patients." Thus, at present, CTC counts can be used to inform clinical decision-making, but management should not be based on these alone.

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In a separate study, Pascal Eschwège and colleagues highlight that the presence of circulating prostate cells (CPCs) is associated with worse outcome in patients with clinically localized prostate cancer treated with radical prostatectomy (RP). The researchers assessed the presence of circulating prostate cells in 155 patients with clinically localized prostate cancer before RP using a dual real-time polymerase chain reaction (RT-PCR) assay to detect both PSA and PSMA (prostate-specific membrane antigen) transcripts. Patients with CPCs at baseline had significantly shorter recurrence-free survival when compared with those who were CPC-negative. "Our results unambiguously show the link between hematogenous spread of prostate cells, cancer recurrence and prognosis," says Sylvain Loric, corresponding author on the paper. "Thus, preoperative CPC detection could be added to initial patient staging to help identify the best treatment."

The researchers also examined the effect of intraoperative hematogenous cell seeding on patient survival. Interestingly, patients previously negative for CPCs who were CPC-positive after RP did not have worse progression-free survival when compared to those who remained CPC-negative after surgery. "This result seems to exclude tumor surgical management as a major cause of metastatic development," says Loric. The investigators intend to extend the duration of follow-up in order to determine the effects of CPCs on survival outcomes.

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Original articles Scher, H. I. *et al.* Circulating tumour cells as prognostic markers in progressive, castration-resistant prostate cancer: a reanalysis of IMMC38 trial data. *Lancet Oncol.* **10**, 233–239 (2009).
Eschwège, P. *et al.* Prognostic value of prostate circulating cells detection in prostate cancer patients: a prospective study. *Br. J. Cancer* **100**, 608–610 (2009).