

Tumour markers for prostate cancer

Prostate cancer is the third most common cancer in men world-wide. The number of patients diagnosed has greatly increased, in large part due to more accessible diagnostic techniques as exemplified by the tumour marker Prostate Specific Antigen [PSA]. PSA enables detection of even relatively small tumours, but does not provide any information on the aggressiveness of the tumour. Several publications have concluded that combining PSA with Tissue Polypeptide Specific antigen [TPS], a marker measuring disease activity, yields vital information for correct and efficient patient management, particularly in patients presenting with metastatic prostate cancer.

Depending on the stage of the disease, prostate cancer patients are offered various alternatives; e.g. so-called watchful waiting for low-risk patients, and combinations of adjuvant therapy for early stage patients with a high risk of metastatic development. For prostate cancer patients with an already developed metastatic spread, therapy is commonly focused on androgen suppression. The therapeutic effect is usually good for responding patients, but inevitably a hormone refractory condition develops resulting in tumour recurrence and uncontrolled disease. Once this happens secondary therapies are usually not satisfactory. Hormone refractory prostate cancer is a major problem in the management of patients with metastatic disease, and efficient ways of monitoring therapy are needed.

Tumour marker panels

Today tumour markers are an established part of cancer patient management. For prostate cancer, PSA is the main marker with proven use in screening, diagnosis, therapy monitoring and follow-up. However, limitations exist in certain clinical settings based on PSA's androgen-dependent expression. It is of vital importance to consider this, in particular during anti-androgen therapy, where the informative value of PSA may be reduced and the interpretation of a decreased serum PSA level becomes problematic. Here, PSA levels may have decreased because of cancer regression, or due to therapy-induced attenuation of the synthesis.



IDL Biotech assay for Tissue Polypeptide Specific antigen.

Thus, PSA serum levels may no longer correctly reflect tumour burden.

Use of tumour marker panels, i.e. well-defined combinations of two or more markers, is a common way to circumvent the biological impact described above, and to increase both sensitivity and the clinical information obtained. For prostate cancer, independent publications have presented data on the efficient use of the combination of PSA and TPS.

TPS identifies the serum concentration of cytokeratin fragments, which are intermediate filament proteins exclusively expressed in normal as well as in malignantly transformed epithelial cells. Increased levels of cytokeratins show an indirect correlation with the patient's tumour cell activity, and can be directly related to the effect of the applied therapy. A long lead-time compared to clinical manifestation is a main feature.

Combining PSA and TPS

The combined use of PSA and TPS in monitoring prostate cancer patients on hormonal therapy has been analysed in several independent trials. The added value of TPS was clearly demonstrated, not only because patients who responded to the applied therapy could be identified earlier, but also because later clinical progression could be predicted. In the latter case, patients who had lost

the ability to produce PSA could be identified.

In a recent European Organisation for Research and Treatment of Cancer (EORTC) side-study, these earlier findings were confirmed. Here the prognostic impact of TPS and PSA in metastatic prostate cancer patients treated with intermittent maximal androgen blockade (MAB) was evaluated. The study also found that patients who had attenuated PSA expression could be identified. The conclusions were that pre-treatment TPS levels could identify patients who would undergo rapid clinical progression, and that increased post-treatment levels following MAB signified clinical progression even when PSA remained normal (as seen in 28% of the patients with progressive disease). The recommendation was that TPS should be included as an adjunct marker to PSA in patients presenting with metastatic prostate carcinoma. Serial TPS measurements during MAB can identify patients with clinical progression, even when the PSA values in these patients remain in the normal range.

Conclusions

Based on published data it can be concluded that TPS provides new possibilities for monitoring and evaluating the efficacy of anti-androgen therapy. To obtain a better knowledge of the course of the disease during hormone manipulation, the combined use of the tumour markers PSA and TPS for serial testing was recommended.

References

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