Summary and Conclusion

• TPS® is the serum marker measuring cytokeratin 18
• TPS® is an effective indicator reflecting tumor cell activity
• TPS® testing is an aid in monitoring a patient’s response to therapy and clinical outcome in ovarian cancer
• The use of TPS® leads to better clinical decisions in ovarian cancer and more effective patient management
• TPS® contributes to a better surveillance of ovarian cancer patients
• The biomarker combination TPS® and CA 125 is the best choice for therapy monitoring in ovarian cancer

References:


The cytokeratin marker TPS® is of additive value during follow-up of ovarian cancer to obtain better clinical decisions and more effective patient management.

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Ovarian cancer
Ovarian cancer is the fifth leading cause of death from cancer in women and the leading cause of death from gynecological cancer. Ovarian cancer has been called the silent killer because it frequently causes non-specific symptoms, which contribute to diagnostic delay and poor prognosis. Symptoms of ovarian cancer are: abdominal pressure, fullness, swelling/bloating, urinary urgency and pelvic discomfort or pain. An abnormal physical examination, a blood test or medical imaging can provide evidence leading to ovarian cancer diagnosis. Treatment usually involves surgery and chemotherapy and sometimes also radiotherapy.

Tumor markers in ovarian cancer
Tumor markers have been shown to be useful in ovarian cancer for prediction of prognosis, monitoring therapy response and for early detection of recurrences. Many studies have been designed to identify prognostic factors for determination of suitable treatment and also when to change treatment. CA125 is the most documented and best performing single marker for ovarian cancer and is the only marker approved for monitoring of ovarian cancer progression and for treatment response. The prognostic information derived from CA125 measurements has failed to make a major impact on patient management, as the majority of patients with epithelial ovarian cancer will relapse. Different biomarkers have been proposed to be of additive value to CA125 during follow-up of ovarian cancer to obtain better patient management eg various mucin markers, CEA and LDH. However, none of these marker combinations have proved to be generally useful in the monitoring of disease progression or regression. Published reports, describes the use of the cytokeratin marker TPS in the follow-up of ovarian cancer patients. The prognostic significance of the combination CA125 and TPS in ovarian cancer patients (all FIGO stages) after three chemotherapy courses and elevated CA125 levels had a poor prognosis. More importantly the prognostic accuracy could be even further increased by the addition of TPS and the use of TPS leads to better clinical decisions and patient management.

Cytokeratin Filaments
All eucaryotic cells have cytoplasmic cytoskeletal structures known as intermediate filaments. The cytoskeletal network is responsible for the mechanical integrity of the cell and it is critical during cellular processes like cell division, motility and cell to cell contacts. At present more than 20 different cytokeratins have been identified, of which cytokeratin 8, 18 and 19 are the most abundant in simple epithelial cells. The cytokeratins are epithelial cell specific and the cytokeratin pattern is usually preserved during the transformation of normal cells into malignant cells.

Tissue Polypeptide Specific Antigen (TPS)
TPS is the only test that specifically measures cytokeratin 18. It is a monoclonal assay measuring the reactivity against a well defined epitope structure on cytokeratin 18, the M3 epitope. TPS is a marker of tumor cell activity and it is not related to tumor burden.

TPS in the follow up of ovarian cancer
A multicentre evaluation of predictive factors of 10 year overall survival in ovarian cancer patients was performed using the tumor markers CA125 and TPS after 3 combined chemotherapy courses. CA125 levels >25 kU/L and TPS >100 U/L were adverse predictive factors of outcome. In a multivariate analysis these factors were both independent.
In FIGO stage III and IV ovarian cancer patients (patients with advanced and spread disease) with CA125 and TPS marker levels below the discrimination level (cut off point) after 3 chemotherapy courses, indicated a favourable prognosis for the patients. Patients with an elevated serum marker level of CA125 or TPS or both markers, demonstrated unfavourable prognosis.
In ovarian cancer patients, with FIGO stage III+IV and optimal debulking, CA125 and TPS serum marker levels after three chemotherapy courses are highly predictive factors of 10-year overall survival. Therefore, as early as after three chemotherapy courses, both short and long-term prognosis can be obtained using the serum marker combination CA125 and TPS.

Conclusions
1. In patients with radical surgery (FIGO Stage I and Stage II) no difference in 10-year overall survival was observed.
2. In FIGO Stage III+IV patients, CA125 >25 kU/L and TPS >100 U/L were adverse predictive factors of clinical outcome and these factors were also independent in multivariate analysis.
3. Ovarian cancer patients (Stage III+IV) with optimal debulking (n=60), showed a 10 year overall survival of 23% and if both CA125 and TPS were elevated, the survival was 0%.
4. If one of the markers CA125 or TPS were elevated in the combined patient group (Stage III+IV) the 10-year overall survival was 10%.
5. When both CA125 and TPS were below the cut off levels the survival was 35%.