S100

Introduction

The incidence of malignant melanoma is increasing with an annual rate of about 5%. Despite all efforts being made in the early detection of melanoma, 20% of the affected people will die as a result of tumour metastases. Immune modulating treatment with interleukin-2 induces long-term survival in 5-10% of patients with metastatic malignant melanoma, but at the expense of significant toxicity for the patients. Thus, a serum marker that reflects tumour load and can predict response and prolonged survival would greatly improve the clinical management.

Protein S100 with focus on S100B

S100B is a neuronal protein present in high concentrations in glial and Schwann cells. It is also found in significant amounts in malignant melanocytes.

Protein S100 has since long been known for its value in immunohistochemistry for detection of malignant tumours of melanocytic origin.

The S100 family consists of twenty members. The first member was isolated 1965 from bovine brain tissue and it was named S100 due to its solubility in 100% saturated ammonium sulphate.

S100B in Malignant Melanoma

Serum S100B has been shown to give valuable information regarding many aspects of the clinical management of malignant melanoma:

Staging - gives additional information to clinical staging.

Prognosis - the expression of S100B is directly related to the degree of malignancy.

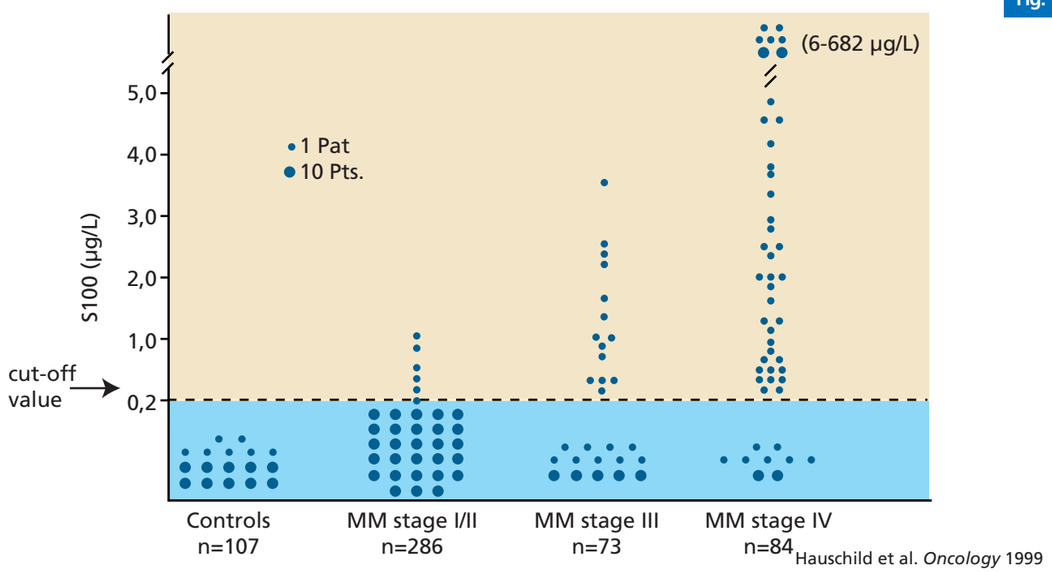
Treatment monitoring - studies have indicated that treatment outcome can be predicted in approximately 95% of all cases already after 4 weeks of treatment without additional clinical investigations.

Follow up - for early detection of recurrences

Staging

Several studies have demonstrated that S100B concentrations are significantly related to clinical stage as well as survival (Fig. 1).
A review of multiple clinical studies indicated increasing sensitivity of serum S100B with clinical stage up to 70-80% in stage IV. Combining a positive serum S100B value and Breslow thickness > 4 mm resulted in sensitivity for the presence of secondary spread of 91% and specificity of 95%.

Fig. 1



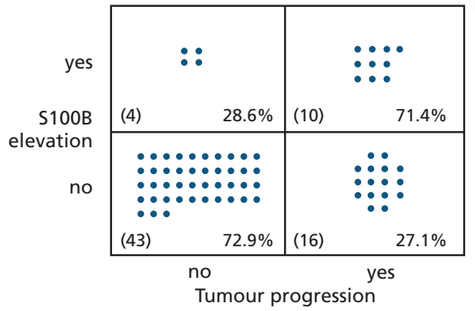
Hauschild et al. *Oncology* 1999

S100B serum levels in melanoma (stages I-IV) and control patients

Prognosis

S100B is an independent prognostic factor. Pre-treatment levels of serum S100B predict survival time in melanoma patients. Survival is significantly longer in melanoma patients with normal S100B levels compared to those with elevated levels (Fig. 2, Table 1). Even within the same clinical stage survival is significantly influenced by the S100B level (Fig. 3). S100B is the only significant prognostic factor in a multivariate test for advanced-stage melanoma patients. In conclusion a large number of papers have shown that S100B is the most reliable prognostic marker for patients with stage III and IV melanoma.

Fig. 2



Hauschild et al. *Oncology* 1999

Correlation of tumour progression with initial serum S100B values (stage III patients)

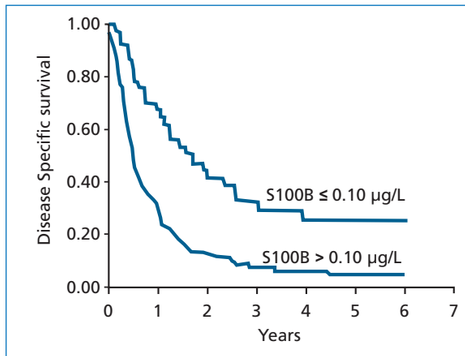
Table 1

Serum Level	Median Survival
< 0.2 µg/L	14 months
0.2 - 0.6 µg/L	10 months
0.6 - 3.0 µg/L	6 months
> 3.0 µg/L	3 months

Hauschild et al. *Oncology* 1999

Medium Survival in Stage IV patients

Fig. 3



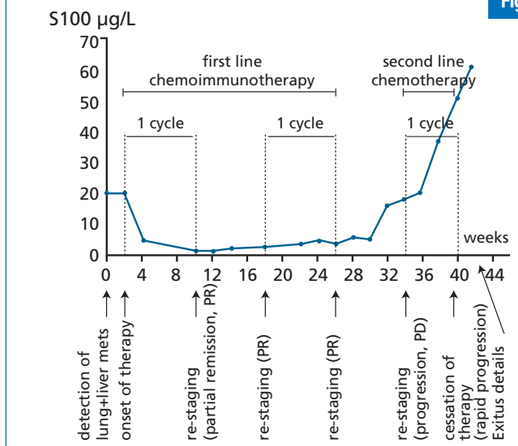
Djureen-Mårtensson et al. *J Clin Oncol* 2001

Melanoma-specific survival in patients (stages II and III) in relation to serum S100B levels

Treatment monitoring

Several studies indicate that serum S100B concentrations may be useful in treatment monitoring. Rising or falling serial serum S100B protein values correlate with disease progression or response to therapy (Fig. 4). The most interesting results are based on an interim analysis after 4 weeks of treatment. At this time the rate of adequate identification of responders was 95%. These studies imply that unsuccessful treatment can be terminated or altered early if serum S100B concentrations are increased.

Fig. 4



Hauschild et al. *Br J Dermatol* 1999

Serial measurements of S100B in a 26-year old man during the first line chemoimmunotherapy and second line polychemotherapy

Follow-up and early detection of recurrences

Rising levels of serum S100B protein have been shown to be a specific and sensitive marker of tumour progression, which precedes other evidence of melanoma recurrence. A rise in serum S100B may indicate melanoma progression 5-23 weeks before other evidence of metastatic spread. Repeatedly increasing serum S100B levels during follow-up should lead to further evaluation of the patient by chest X-ray, CT scan and clinical examination. Early detection of relapse could lead to earlier treatment and an overall better outcome of the disease. A recent paper has demonstrated that LIAISON® S100 has superior clinical sensitivity.

Summary

- Clinical evaluations of serum S100B protein have proved that S100B is an excellent marker for clinical management of malignant melanoma patients.
- LIAISON® S100 has demonstrated superior clinical sensitivity.