COMMENTARY

A fresh perspective on an established marker: S100B-dynamics for early detection of melanoma recurrence

There are a number of biomarkers that are currently investigated for their potential in aiding melanoma diagnosis, predicting the course of the disease and response to treatment, however, most remain limited to research projects and highly specialized settings.[1] To date, only S100B and lactate dehydrogenase are recommended for supporting prognosis and monitoring of melanoma by most national guidelines. S100B protein is considered a measure of tumour burden with several studies highlighting worse outcome in patients with elevated serum levels.[2] The marker has also been investigated for its potential to indicate disease relapse during follow-up of melanoma patients. For this purpose, cut-off values have been established that vary depending on the test at use. S100B serum levels exceeding the cut-off can be an early sign of recurrence of the disease, however high false-negative rates have been reported requiring additional follow-up measures, mainly realized by imaging.[3] This "black and white" approach of how S100B serum levels are used today is certainly easy for the daily routine, but may not be most effective in gaining insights into the disease status of a patient.

In this issue of JEADV, Ertekin *et al.*[4] analysed retrospective data from a tightly monitored cohort of 289 stage IIB, IIC and III melanoma patients including their respective monthly S100B measures. In this cohort, only 35.7% of relapses manifested with elevated S100B levels (sensitivity 35.7%; specificity 92.5%). In patients with disease progression but normal S100B reads, the authors looked into the dynamic changes of this biomarker prior to the timepoint of confirmed progression. They conclude that the dynamic changes of S100B reads were able to predict recurrence of the disease in 41.2% of patients, while the specificity of the test remained high (92.4%) – certainly an appealing approach, but one must be cautious.

This model was tailored to the timepoint of confirmed disease progression, and only S100B reads at the time of true progression and values immediately preceding progression were considered for analysis. Any previous (slight) changes in S100B serum levels were not accounted for. Additionally, it remains an open question if small changes of serum S100B levels, particularly for low numerical reads, are a true representation of the disease's biology. Several studies have confirmed that serum S100B cannot be used for diagnosis of early stages of the disease or melanoma screening, since the value of S100B-levels in patients with low tumour burden appears to be small.[5] Further, there are a number of known cofactors that could contribute to changes in serum S100B levels including cardiovascular and neurological disease that probably need to be taken into account to increase the robustness of dynamic S100B biomarker models.[3,5]

These are certainly tasks that are beyond a retrospective analysis and require a large number of patients ideally in a prospective (multicenter) trial.

While the authors should be commended both for their efforts in diving into an exciting and understudied field, and for providing a freely available webpage where physicians can plug in data to run analyses of S100B-dynamics in their own patients, the limitations outlined in this commentary should be kept in mind.

Conflicts of interest

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C. Posch[1,2,*]

[1]Department for Dermatology and Allergy, Klinikum rechts der Isar – Technical University of Munich,German Cancer Consortium (DKTK), Munich, Germany, [2]Faculty of Medicine, Sigmund Freud University, Vienna, Austria

*Correspondence: C. Posch. E-mail: christian.posch@tum.de

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