

Advanced melanoma: Antibodies in the blood indicate side effects of immunotherapy

Immunotherapies have greatly improved the treatment of metastatic melanoma, but they can cause serious side effects. A study led by researchers from Heidelberg University's Medical Faculty, the Dermato-Oncology Section of the Dermatology Clinic at Heidelberg University Hospital, and the National Center for Tumor Diseases (NCT) in Heidelberg now shows that autoantibodies detected in the blood before the start of therapy could help to better assess the individual risk of side effects in patients. The National Center for Tumor Diseases (NCT) Heidelberg is a joint institution of the German Cancer Research Center (DKFZ), the Heidelberg University Hospital (UKHD), the Heidelberg Medical Faculty of the Heidelberg University and the Thoraxklinik Heidelberg.

Immunotherapies have fundamentally changed the treatment of advanced black skin cancer (metastatic melanoma) in recent years. They can activate the body's own defense system in such a way that it specifically recognizes and fights tumor cells. But this effect also has a downside: during treatment, many patients develop so-called autoantibodies that target the body's own healthy tissue. This can result in serious side effects, such as inflammation of the intestines, skin, or other organs. Until now, there have been few reliable ways to predict who is particularly at risk before treatment begins.

A new multicenter study now provides evidence that certain autoantibodies were already present before treatment and were later associated with the occurrence of side effects. The researchers examined blood samples from 331 patients with metastatic melanoma who received various forms of immunotherapy.

In doing so, the researchers found a number of autoantibodies that coincided with an increased risk of immune-related side effects. Of particular interest was that the amounts of autoantibodies formed differed in their composition depending on the type of immunotherapy used. This suggests that side effects do not always arise according to the same principle, but that different biological mechanisms play a role depending on the therapy.

One focus of the study was on intestinal inflammation, which can be one of the most stressful complications and occurred significantly more frequently with combination immunotherapy than with monotherapy. Here, too, the team identified autoantibodies that reliably reflected the risk across different forms of treatment.

Some antibodies were associated with a higher risk, while others appeared to have a protective effect. Jessica Hassel, head of the Dermato-Oncology Section at the Dermatology Clinic of Heidelberg University Hospital (UKHD), NCT Heidelberg, is leading the study.

She says of the work: "In the future, an autoantibody profile from a blood sample could help to better assess the personal risk of severe side effects under different immunotherapies even before the start of immunotherapy. This would allow us to make more informed decisions about which therapy is best suited for a patient—for example, whether combined immunotherapy is safe. If we know who is particularly at risk before starting therapy, we can better support patients and take early countermeasures." This would make treatments safer and support the right therapy decision for each individual. Since it is a highly scalable test, it could in principle be used widely. However, before it can be used in routine clinical practice, the results must be confirmed in further studies.

Robin Reschke, Max Eder Junior Research Group Leader at Heidelberg University's Medical Faculty and dermatological oncologist at the UKHD Dermatology Clinic, NCT Heidelberg, adds: "Another study on autoantibody-based prediction of response to immunotherapies is in the planning stage. The focus is on better understanding the relationship between autoantibody profiles and the immune response to the tumour."

Publication

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