

## **Tracking melanoma: circulating melanoma cells (cmcs) and immune changes during immunotherapy**

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### **Abstract**

**Background:** Melanoma remains a challenging malignancy with limited prognostic and predictive biomarkers. Circulating melanoma cells (CMCs) and the immune response, particularly cytotoxic T cells, hold promise for improving melanoma diagnosis, prognosis, and treatment monitoring.

**Objective:** This study investigates the relationship between CMCs, T-cell exhaustion markers, and clinical parameters in melanoma patients, with a particular focus on how these factors change in response to immunotherapy.

**Materials and Methods:** Blood samples were collected from 38 melanoma patients and 19 healthy controls at baseline. A subset of patients (n=25) also provided blood samples after immunotherapy. CMCs were enumerated using the CellSearch® system. Flow cytometry was employed to assess T-cell profiles, focusing on CD8+ T cells expressing exhaustion markers TIGIT and TIM-3. Clinical data, including disease stage, LDH levels, BRAF mutation status, and metastasis formation, were correlated with CMC and T-cell findings.

**Results:** CMCs were detected in approximately 50% of patients at baseline, but not in healthy controls. While CMC positivity tended to decrease after immunotherapy, this change was not statistically significant. Baseline CMC counts showed limited correlation with standard clinical parameters. However, a significant negative correlation was observed between CMC counts post-immunotherapy and lymphocyte counts. Notably, CMC presence correlated with increased expression of T-cell exhaustion markers. Serum S100B levels were elevated in melanoma patients compared to controls and correlated with disease burden. Additionally, lower PMEL expression in melanoma tissue correlated with improved treatment response.

**Conclusion:** Integrating CMC analysis with immunological and tissue-based biomarkers may enhance melanoma management and risk stratification. The dynamics of CMCs post-treatment, particularly in relation to lymphocyte counts and T-cell exhaustion, warrant further investigation. This multifaceted approach holds potential for optimizing melanoma treatment strategies and improving patient outcomes.

### **Do you have any conflicts of interest?**

No, I do not have a conflict of interest.