Background  
Checkpoint inhibitor (CPI)-induced CNS inflammation is a severe neurological adverse event.  
1-2 CPI-induced CNS inflammation can be difficult to diagnose because symptoms indicate more common conditions such as tumor progression or infection.  
3-5 There is a clinical need for blood tests to facilitate diagnosis of CPI-induced CNS inflammation.

Our objective was to evaluate if increased concentrations of brain damage markers S-calcium-binding protein B (S100B) and neurofilament light chain (NfL) in serum indicate CPI-induced CNS inflammation.

Methods  
Medical records and laboratory data were examined in patients with metastatic melanoma or metastatic renal cell carcinoma. The patients were treated with double checkpoint inhibition (nivolumab and ipilimumab) or monotherapy (nivolumab) between March 2018 and April 2022 (n=197) at Sahlgrenska University Hospital, Sweden. In patients with suspected CNS-inflammation, brain MRI and analysis of cerebrospinal fluid were performed and brain damage markers S100B and NfL in serum were analyzed repeatedly. S-100B has a dual function as it is secreted by some melanoma metastases as well as damaged astrocytes.  
6-7 S-100B concentrations in patients with melanoma metastases that do not secrete S-100B (n=29) and renal cell carcinoma patients (n=10) were used as double checkpoint inhibitor treated controls. As controls for NfL, we analyzed frozen plasma from melanoma patients treated with double checkpoint inhibition (ipilimumab + nivolumab) or monotherapy nivolumab (n=49).

Results  
Nine out of 197 patients had a verified CPI-induced CNS inflammation (4.6%) within 200 days from the first double checkpoint inhibitor treatment (table 1). S100B and NfL in serum increased during CNS inflammation (figure 1A-D and F) and normalized when patients were treated with immunosuppression (figure 1A-C, E and G). S100B concentration in serum increased early in patients with CPI-induced CNS inflammation (figure 1A-C), whereas NfL increased later (figure 1A-C). The sensitivity of an increased S100B and NfL to detect a CPI-induced CNS inflammation was 100% for S100B and 79% for NfL and the specificity was 89% for S100B and 74% for NfL (figure 2).

Conclusions  
The combined analysis of S100B and NfL in serum is a tool for early detection and monitoring of CPI-induced CNS inflammation. Early diagnosis of CPI-induced CNS inflammation may save lives, prevent long-term hospitalization, and reduce neurological complications.

REFERENCES  