

1 Intracranial metastases are common in non-small-cell lung cancer (NSCLC) patients,  
2 whose prognosis is very poor. In addition, intracranial progression is common during  
3 systemic treatments due to the inability to penetrate central nervous system (CNS)  
4 barriers, whereas the intracranial effects of cancer immunotherapies remain unclear. We  
5 analyzed clinical data to evaluate the frequency of intracranial progression in advanced  
6 NSCLC patients treated with PD-1 blockade therapies compared with those treated  
7 without PD-1 blockade therapies, and found that the frequency of intracranial progression  
8 in advanced NSCLC patients treated with PD-1 blockade therapies was significantly  
9 lower than that in patients treated with cytotoxic chemotherapies. In murine models,  
10 intracranial rechallenged tumors after initial rejection by PD-1 blockade were suppressed.  
11 Accordingly, long-lived memory precursor effector T cells and antigen-specific T cells  
12 were increased by PD-1 blockade in intracranial lesions. However, intracranial  
13 rechallenged different tumors are not suppressed. Our results indicate that cancer  
14 immunotherapies can prevent intracranial progression, maintaining long-term effects  
15 intracranially as well as systemically. If intracranial recurrence occurs during the  
16 treatment with PD-1 blockade therapies, aggressive local therapies could be worthwhile.