



**Figure S1** Two representative cases with significant responses to the combination of temozolomide and pembrolizumab as first-line therapy. (A,B) The first patient was found to have multiple liver and pulmonary metastases after 19 months since diagnosed with acral melanoma, then received temozolomide plus pembrolizumab as first-line therapy. After 19 courses of chemotherapy and 22 courses of pembrolizumab, she showed nearly complete remission of all metastatic deposits, which has been maintained for 16 months since the beginning of her combination therapy (C,D). The second case was also diagnosed with acral melanoma and developed multiple liver and pulmonary metastases 25 months after surgery. He received combined therapy of temozolomide plus pembrolizumab as shown in the first patient and at data cutoff, after five courses of chemotherapy and seven courses of pembrolizumab, the lungs and liver lesions had shrunk continuously with a remission rate of 90% approximately.