



Supplementary Figure S4. Early FDG PET/CT guides patient management. a, 89 year-old male with lung, mediastinal, adrenal, and osseous metastases (patient 1) imaged with FDG PET/CT at baseline and 3 days after starting pembrolizumab. The patient was classified as having stable metabolism (SM) based on a 24.4% increase in tumor SUV_{MAX} on the day 3 scan (PET1). However, axial PET (top) and fused PET/CT (bottom) images of the brain demonstrated a new FDG avid lesion in the left precentral gyrus (white arrow, $SUV_{MAX} = 9.46$) on the day 3 scan which was not visible on the baseline scan. An axial post-contrast T1-weighted image of the brain (right) on a follow-up brain MRI performed 3 weeks later showed a corresponding enhancing lesion (white arrow) consistent with a metastasis, which in retrospect was likely present on the baseline MRI, and was subsequently treated with radiation therapy. The patient went on to have a durable partial response to therapy. **b**, 67 year-old male with lung, nodal, subcutaneous, and mesenteric metastases (patient 9) imaged with FDG PET/CT at baseline and at the times specified after starting pembrolizumab. The patient was classified as having a metabolic flare (MF) based on a 78.4% increase in tumor SUV_{MAX} on the day 12 scan (PET1). Axial PET (top) and fused PET/CT (bottom) images of the upper abdomen demonstrated a new FDG avid lesion in the spleen (white arrow, $SUV_{MAX} = 4.93$) on the day 12 scan which increased in FDG activity at 3 months (white arrow, $SUV_{MAX} = 7.04$) and correlated with an enhancing lesion on abdominal MRI (images not shown). The splenic lesion subsequently resolved on the 6 month FDG PET/CT, and no splenic lesions were seen on additional follow-up scans. The patient went on to have a durable complete response to therapy.