

1 Supplemental Materials

2 Supplemental Table 1 Definition of immune-related adverse events

Immune-related adverse events were defined as adverse events with no clear alternate etiology and requiring systemic corticosteroid or immunosuppressant treatment within 30 days of onset or that required the use of systemic hormonal supplementation. Specific events included:
• Pneumonitis
• Colitis
• Hepatitis (including aspartate aminotransferase or alanine aminotransferase elevations $>3 \times$ ULN or bilirubin $>1.5 \times$ ULN)
• Nephritis (including serum creatinine $> 1.5 \times$ ULN)
• Pancreatitis
• Motor and sensory neuropathy
• Myocarditis
• Encephalitis
• Endocrinopathies (including but not limited to hypothyroidism, hyperthyroidism, hypophysitis, diabetes mellitus, and adrenal insufficiency)
• Ocular toxicities (uveitis)
• Skin reactions including Stevens–Johnson syndrome or toxic epidermal necrolysis
• Diarrhea

3 ULN, upper limit of normal.

4 **Supplemental Methods**

5 Measurement of ipilimumab concentrations

6 An immunoaffinity approach with magnetic beads coated with Protein G was used to
7 enrich ipilimumab from human plasma. Because ipilimumab is too large for practical
8 direct quantitative analysis using LC/MS/MS technology, it was subjected to proteolysis
9 with trypsin, following standard protein denaturation, reduction, and alkylation
10 processing steps. As a result of the trypsin digestion, characteristic peptide fragments
11 originating from the antibody are produced. The characteristic peptides were quantified
12 as surrogates for determining ipilimumab concentrations. The validated assay has a
13 quantifiable range of 1 – 100 µg/mL.

14 Definition of a DLT

15 A DLT was defined as grade 2 pneumonitis or ocular toxicity necessitating
16 discontinuation of pacmilimab, treatment-related grade ≥3 AEs (except grade 4
17 lymphopenia, non-febrile neutropenia lasting ≤48 hours; grade 3 nausea, vomiting,
18 diarrhea, asthenia, constipation, pyrexia lasting ≤48 hours; correctable, asymptomatic
19 electrolyte imbalance; clinically manageable endocrinopathy; or tumor flare)