Supplemental Table 1. Diagnostic Criteria for Subspecialist Review of irAE Admissions

Specialty / Toxicity Type	Confirmed Toxicity	Suspected Toxicity	Not Toxicity
ALLERGY			
Infusion Reaction	Timing and symptoms of the reaction were consistent with a grade I-IV hypersensitivity reaction and treatment intervention (e.g. epinephrine) provided definitive symptomatic relief.	Timing and symptoms of the reaction were consistent with a grade I-IV hypersensitivity reaction.	Timing and symptoms of the reaction were not consistent with a grade I-IV hypersensitivity reaction and/or an alternative diagnosis was more likely.
DERMATOLOGY			
Skin Eruption	New skin eruption within 6 months of ICI initiation or dose increase with either A) biopsy consistent with known pattern of ICI toxicity, or B) clinical exam consistent with known pattern of ICI toxicity.	Same as confirmed toxicity; however not meeting all 3 criteria (time course, pathology, or clinical exam).	Alternative trigger more likely, or eruption/pathology unrelated to hypersensitivity reaction from drug (eg: folliculitis or focal skin cancer).
GASTROENTEROLOGY / HEPATOLOGY			
Colitis	Biopsy-proven disease.	Clinical symptoms consistent with gastroenteritis (new onset diarrhea, urgency, abdominal pain, nausea, and/or vomiting) and/or colitis (new onset diarrhea, urgency, and/or abdominal pain) without another identifiable cause (such as infection, obstruction, ischemic injury, or other drug-induced enterocolitis) and a positive clinical response to systemic steroids; or atypical symptoms (isolated abdominal pain and/or cramping) in the context of suggestive imaging and positive clinical response to steroids.	GI symptoms with another identifiable cause and response to appropriate treatment; spontaneous resolution of symptoms with conservative management; biopsy negative.
Hepatitis	Elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT), or alkaline phosphatase (ALP) with or without elevated bilirubin where other etiologies (including infectious hepatitis, ischemic hepatitis, local or metastatic disease progression, or other drug-induced liver injury) are deemed unlikely and a liver biopsy is consistent with immune-mediated hepatotoxicity.	Elevated AST, ALT, or ALP with or without elevated bilirubin where other etiologies (including infectious hepatitis, ischemic hepatitis, local or metastatic disease progression, or other drug-induced liver injury) are deemed unlikely and a liver biopsy was not performed or resulted in inconclusive findings.	Elevated AST, ALT, or ALP with or without elevated bilirubin where an alternative explanation was deemed a more likely cause of hepatotoxicity.
ENDOCRINOLOGY			
Diabetes	New insulin-sensitive diabetes at least 2 weeks following ICI treatment in a patient without prior diabetes or pre-diabetes, presenting with diabetic ketoacidosis (DKA), or with other evidence of new insulin deficiency (including low or undetectable C-peptide, new insulin requirement, relatively low insulin-requirement) and autoimmune etiology (positive anti-GAD or anti-IA2 antibodies).	New diabetes at least 2 weeks following ICI treatment with insulin-sensitive phenotype but lacking one or more features of confirmed toxicity (e.g. negative antibodies or normal C-peptide with other features to suggest insulin-sensitivity) and without features to suggest insulin-resistance. Existing diabetes with new insulin requirement with a clear insulin-sensitive phenotype (including low or undetectable C-peptide, new insulin requirement, relatively low insulin-requirement).	Diabetes without DKA and with an insulin-resistant phenotype, including: high insulin requirements, concurrent high dose steroids or pre-existing insulin resistance or multiple features of metabolic syndrome preceding the diagnosis of diabetes. New or worsening diabetes with altered pancreatic mass, including partial or total pancreatectomy, history of recurrent or chronic pancreatitis.

Supplemental Table 1. Diagnostic Criteria for Subspecialist Review of irAE Admissions

Specialty / Toxicity Type	Confirmed Toxicity	Suspected Toxicity	Not Toxicity
ENDOCRINOLOGY (cont.)			
Thyroiditis	Transient hyperthyroid phase (low TSH, high free T4) followed by apparently permanent hypothyroidism (high TSH, low free T4) starting at least 2 weeks after the initiation of ICI without other confounding medications, with hypothyroid phase persisting in the outpatient setting. Isolated apparently permanent hypothyroidism starting at least 2 weeks after the initiation of ICI without other confounding medications.	Isolated transient hyperthyroidism occurring at least 2 weeks after initiation of ICI without evidence of Graves (including negative thyroid stimulating antibodies, absent uptake of radioactive iodine scan), or confounding medications. Transient isolated hypothyroidism occurring in the outpatient setting (to distinguish from non-thyroidal illness) at least 2 weeks following initiation of ICI. Pre-existing autoimmune hypothyroidism with significant increase in levothyroxine dose following initiation of ICI therapy without other confounding factors.	Transient or permanent abnormal TSH or free T4 for which an alternative explanation was deemed more likely (including non-thyroidal illness, iodinated contrast, confounding medications). Pre-existing hypothyroidism without changes on ICI.
Hypophysitis	The presence of new hypopituitarism and/or new reversible radiographic pituitary enlargement following treatment with ICI in the absence of an alternative etiology.	New hypopituitarism of uncertain etiology (for example, exogenous glucocorticoids potentially impacting cortisol assessment) after treatment with ICI without radiographic changes in the pituitary gland.	Absence of hypopituitarism and radiographic changes in the pituitary gland or the existence of an alternative etiology for such findings.
CARDIOLOGY			
Myocarditis	Biopsy-proven disease or clinical syndrome with elevated troponin and a cardiac MRI with features consistent with myocarditis.	One of the following: • Suggestive cardiac MRI with either clinical syndrome or elevated troponin • New onset reduced EF occurring concomitantly with clinical syndrome/elevated troponin • Cardiac arrest in the setting of recent ICI and no pathology/imaging.	Alternative explanation for the syndrome.
NEUROLOGY			
Neuro Toxicity	Clinical syndrome with symptoms and signs of autoimmunity affecting the central and/or peripheral systems; consistent findings on imaging of the central nervous system, electrodiagnostic studies and/or serum and/or cerebrospinal fluid testing; absence of another identifiable cause.	Clinical syndrome with symptoms and signs of autoimmunity affecting the central and/or peripheral systems; inability to reasonably completely exclude another potential cause which would present with a similar neurologic syndrome due to incomplete or inconclusive diagnostic testing.	Neurologic symptoms with an alternative explanation objectively identified.
NEPHROLOGY			
Renal Toxicity	Biopsy-proven disease (evidence of acute interstitial nephritis -AIN-).	Unexplained rise in creatinine (≥1.5 fold rise in creatinine from baseline) with a minimum duration of 72 hours concurrent with another extra-renal immune related adverse event, or resolving with corticosteroid treatment or cessation of ICI. Acute kidney injury (AKI) identified or with resolution with corticosteroid treatment.	An alternative explanation for AKI • Hemodynamic AKI (prerenal azotemia or acute tubular necrosis) • Obstruction • AKI of undetermined cause if insufficient diagnostic workup was pursued

Supplemental Table 1. Diagnostic Criteria for Subspecialist Review of irAE Admissions

Specialty / Toxicity Type	Confirmed Toxicity	Suspected Toxicity	Not Toxicity
PULMONOLOGY			
Pulmonary Toxicity	New hypoxemia and/or ground glass opacities or consolidation on CT scan with documented absence of alternative explanatory etiologies (e.g. infection confidently ruled out by bronchoscopy, cardiogenic pulmonary edema, or known alternative autoimmune etiology of DAH) that improves/resolves with steroids or immunosuppressants.	Same as confirmed without ability to clearly exclude alternative etiology or co-treatment with steroids/ immunosuppressants and other drugs targeting an alternative etiology (e.g. steroids + antibiotics).	Alternative etiology of findings.
RHEUMATOLOGY			
Musculoskeletal (MSK)	MSK pathology unequivocally correlating with ICI therapy and alternative etiology excluded based on history/exam/imaging/labs.	MSK pathology potentially though not unequivocally correlating with ICI therapy. Inability to reasonably completely exclude another potential cause.	Alternative explanation for syndrome.
HEMATOLOGY[a]			
Autoimmune Hemolytic Anemia (AIHA) White blood cell count and platelets are usually preserved in AIHA. Pancytopenia suggests a second process is present	ICI-AIHA can be suspected but never definitively confirmed.	All must be met: • 2g decrease in the patient's hemoglobin concentration from its baseline value defined as the patient's hemoglobin in the prior 4-6 months • At least two laboratory features of hemolysis: serum lactate dehydrogenase > 1.5x upper limit of normal; indirect bilirubin > 1.5x upper limit of normal; elevated reticulocyte percentage or absolute count; low or undetectable serum haptoglobin; and presence of spherocytes on peripheral blood smear • AIHA occurrence after initiation of ICI • ICI therapy is considered the most likely etiology of AIHA by the treating hematologist or oncologist • Direct antiglobulin test (DAT or Coombs) positive	• Anemia without evidence of autoimmune-mediated hemolysis • Hemolytic anemia due to inherited red cell disorders, drug-dependent hemolysis, infection, thrombotic microangiopathy, enzymopathy, acquired complementopathy, valvular pathology, or other identifiable cause.
Immune Thrombocytopenia (ITP) • The red and white blood cell counts are usually preserved in ITP. Pancytopenia suggests a second process is present • Positive anti-platelet antibodies are supportive but not required for the diagnosis • A low or normal thrombopoietin level is supportive but not required for the diagnosis	ICPi-ITP is a diagnosis of exclusion and can be suspected but not definitively confirmed.	All must be met: • Decrease in platelet count to <100 x103/mcL and a > 25% decrease from pre-ICI baseline value defined as the patient's platelet count in the prior 4-6 months • Thrombocytopenia after initiation of ICI • Exclusion of other causes of thrombocytopenia, including review of the peripheral blood smear to rule out a microangiopathic process • ICI therapy is considered the most likely etiology of ITP by the treating hematologist or oncologist	Thrombocytopenia clearly due to drug-dependent thrombocytopenia, cytotoxic medication, infection, splenomegaly, microangiopathic processes, infiltration of the bone marrow, post-transfusion purpura, or other causes.

Supplemental Table 1. Diagnostic Criteria for Subspecialist Review of irAE Admissions

Specialty / Toxicity Type	Confirmed Toxicity	Suspected Toxicity	Not Toxicity
HEMATOLOGY[a] (cont.)			
Autoimmune Neutropenia (ICPI-N) • Anti-granulocyte antibodies are usually not helpful in making a diagnosis and are not routinely tested • The red cells and platelets are usually preserved in autoimmune neutropenia (ICPI-N) • Pancytopenia suggests a second process is present	ICPI-N is a diagnosis of exclusion and can be suspected but not definitively confirmed.	All must be met: • Decrease in ANC to < 1500 microL • ICPI-N occurrence after initiation of ICI • Exclusion of other causes of neutropenia, which includes review of the peripheral blood smear • ICI therapy is considered the most likely etiology of neutropenia by the treating hematologist or oncologist	Isolated neutropenia due to medication, cytotoxic chemotherapy, splenomegaly, infection (especially tick borne and viral illnesses), infiltration of the bone marrow, or other causes.
Aplastic Anemia	All must be met: • Pancytopenia due to bone marrow failure with low or absent reticulocyte count • Hypocellular bone marrow biopsy consistent with Aplastic Anemia (AA) as determined by an expert hematopathologist • AA occurrence after initiation of ICI • ICI therapy is considered the most likely etiology of AA by the treating hematologist or oncologist	Pancytopenia after initiation of ICI with low or absent reticulocyte count, exclusion of other causes of AA but without bone marrow biopsy	Pancytopenia due to medications, radiotherapy, infection, bone marrow infiltration/fibrosis, myelodysplastic syndrome, hematologic malignancy, inherited/acquired genetic disorders, or other identifiable cause.

a Bone marry biopsy is recommended when bone marrow infiltration is suspected.

b If the suspicion for AIHA is high but the DAT/Coombs is negative, one must consider that the DAT is a "false negative" due to technical reasons. This can occur in the setting of low concentration of IgG molecules or complement deposited on the RBC surface; removal of low-affinity IgG molecules by washing; or IgA or IgM on the red cell surface (standard DAT techniques only detect IgG and complement).

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TABLE S2. Patients with autoimmune conditions at baseline.

Patient ID	**Previous autoimmune disease**	**On systemic immunosuppressive treatment at the start of ICI**	**Autoimmune flare**	**Sex**	**Age**
1	Crohn Disease	No	Yes	Male	74
2	Cutaneous Discoid Lupus	No	No	Male	72
3	Immune thrombocytopenia purpura (ITP)	No	No	Female	81
4	Polymyalgia Rheumatica	Yes (5 mg pred and hydroxychloroquine)	No	Male	69
5	Vasculitis	No	No	Male	74
6	Psoriasis	No	No	Female	65
7	Rheumatoid Arthritis	Yes (5 mg prednisone)	No	Female	75
8	Rheumatoid Arthritis	No	No	Male	69
9	Rheumatoid Arthritis	No	Yes	Male	62
10	Rheumatoid Arthritis	No	No	Female	79
11	Rheumatoid Arthritis	No	Yes	Female	74
12	Rheumatoid Arthritis	Yes (leflunomide)	No	Male	78
13	Ulcerative Colitis	Yes (low dose azathioprine)	No	Male	64
14	Ulcerative Colitis	Yes (sulfasalazine)	Yes	Female	49

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14	Ulcerative Colitis	No	No	Female	49