Supplementary Table 1: Results of Item Generation from First Iteration of The 2019 ACR/EULAR Classification Criteria for IgG4-RD

Preliminary Exclusion Criteria
Clinical / Serologic
Active cancer in the affected organ
A positive ANCA with a specificity for proteinase 3 or myeloperoxidase
Positive SSA, SSB, anti-RNP, anti-Smith, anti-dsDNA, anti-mitochondrial antibody
Diffuse alveolar hemorrhage
Sensorimotor polyneuropathy
Long bone involvement
Lack of objective response of mass lesion to steroids
Elevated C-reactive protein
Age less than 20 years old
High-titer anti-mitochondrial antibody
Cytopenia of >1 lineage without another explanation
Severe pain requiring analgesia (except for retroperitoneal fibrosis)
Temperature >39°C without another cause
Temperature >38°C without another cause
HHV8+ in the blood
Radiologic
Necrosis, cavitation, hemorrhage, hypervascular mass
Salivary /Lacrimal glands: Duct dilation, peri-glandular invasion
Pancreas: arterial encasement, diffuse duct dilatation
Bile Ducts: web-like stenosis/pseudo-diverticulum ERCP/MRCP
Kidney: exophytic (>50% capsulated mass), hypervascular lesion, urothelial mass, dilation, diffuse atrophy
Aorta/Large Vessels: Severe stenosis
Rapid progression within 4-6 weeks
Lesion crossing tissue planes
Focal mass or focal mass with duct dilation in the pancreas
Ascites, pelvic/local fluid collection
Splenomegaly > 14 cm
Matted lymph nodes
Mesenteric lymph nodes >1cm
Lung: Pneumonia, >5 cysts, cavity, calcified mass
Salivary, lacrimal gland: Unilateral enlargement
Kidney: unilateral, parenchyma like abnormality
Kidney: renal medullary without cortical
PET negative
Focal brain, bone, joint, gastrointestinal tract, liver, uterus, ovaries, ureter, bladder, or prostate lesions
Pathologic
Neoplasia
Monotypic inflammatory infiltrates
Neutrophilic abscess
Extensive necrosis
Primarily granulomatous inflammation
Necrotizing vasculitis
Pathologic evidence of infectious etiology
Pathologic features of Rosai-Dorfman disease
Granuloma
Keloidal fibrosis
Xanthogranulomatous inflammation
Neutrophils (>5/hpf)
Injury of duct epithelium

Lymphoepithelial lesion
Giant cells
Predominant (myo)fibroblast if proliferation
Primary glomerular disease without TIN
Preliminary Inclusion Criteria
Clinical/Serologic
Serum IgG4 (normal, up to 2x ULN, 2-5x ULN, >5x ULN) OR serum IgG4/IgG ratio
Renal dysfunction and hypocomplementemia (C3 and/or C4 and/or CH50)
Serum IgE concentration and/or serum absolute eosinophil elevation
“Typical” or “classic” single organ involvement (e.g., autoimmune pancreatitis)
Multi-organ involvement (>2 typical organs) - current or historic
H/o atopic disease (nasal polyps, allergic rhinitis/conjunctivitis, asthma, eczema)
Sub-acute/insidious onset
Radiologic
Salivary Glands
Either submandibular or lacrimal gland enlargement
Bilateral submandibular and lacrimal enlargement
Infraorbital/supra orbital nerve enlargement
Thorax
Paravertebral band-like soft tissue in thorax
Peribronchovascular and septal thickening
Pancreas
Diffuse Pancreas enlargement (loss of lobulations) +/- capsule like rim decreased enhancement +/- intra pancreatic biliary duct enhancement
Diffuse or multi-focal pancreatic duct narrowing
Diffuse smooth wall thickening or stricture of extra pancreatic biliary tree
Segmental or multi-focal pancreatic low-attenuation masses without duct dilatation
Renal and Retroperitoneum
Bilateral renal cortex low density areas
Renal pelvis thickening/soft tissue
Retroperitoneal plaque-like soft tissue
Circumferential or anterolateral peri-aortic soft tissue
Pathological
Dense lymphoplasmacytic infiltration
Lymphoplasmacytic infiltrate with IgG4+ plasma cells Excluding lymph node, skin or thyroid
IgG4/IgG plasma cell ratio
Fibrosis
Obliterative phlebitis
Eosinophilic infiltrate
Tubular basement membrane electron-dense deposits

Supplementary Table 2: Results of Item Reduction for The 2019 ACR/EULAR Classification Criteria for IgG4-RD

Exclusion Criteria
Broad
Clinical or pathologic evidence of active cancer in the affected organ (e.g., carcinoma, inflammatory myofibroblastic tumor, lymphoma, sarcoma, Erdheim-Chester disease, or other)
Clinical or pathologic evidence of infection in the affected organ
Clinical
Untreated Graves' disease in the setting of orbital swelling
Sensorimotor axonal polyneuropathy
Long bone abnormalities without alternative explanation
Diffuse alveolar hemorrhage
Polymyalgia rheumatica symptoms
Serologic
ANCA with specificity for proteinase 3 or myeloperoxidase
Positive SS-A (Ro) or SS-B (La) antibody
Positive dsDNA, ribonucleoprotein (RNP), or Smith (Sm) antibody
Positive anti-mitochondrial antibody (AMA)
Another auto-antibody associated with high specificity for another immune-mediated condition
Positive serological test for syphilis in a pattern consistent with active infection
Cryoglobulinemia of > 3% in the setting of active hepatitis C infection
Serological evidence of HHV8 infection
Severe peripheral blood eosinophilia ($\geq$ 1500/mm^3)
Radiologic:
Findings in any organ indicative of: Necrosis, cavitation, hemorrhage; Hypervascular mass (excluding hemangioma); Rapid radiologic progression of lesion in < 4-6 weeks; Lesion crossing tissue planes
Focal lesions of the brain, bone, joint, gastrointestinal tract, liver, uterus, ovaries, ureter, bladder, or prostate, without evidence of IgG4-RD in other organs
Loculated abdominopelvic fluid collection
Conglomerated/matted lymph nodes
Salivary/Lacrimal glands: Ductal dilatation; Peri-glandular invasion; Solitary/dominant mass in a unilateral lacrimal, submandibular, parotid, or sublingual gland
Pancreas: Focal mass with preserved acinar pattern in remainder of pancreas; Diffuse ductal dilatation; Vascular encasement of greater than 180 degrees of SMA or SMV by a pancreatic lesion
Splenomegaly > 14 cm in the absence of alternative explanation (e.g., portal hypertension)
Kidney: exophytic (> 50%/capsulated) mass or urothelial mass
Aorta and its branches: Severe arterial stenosis (excluding the coronary arteries)
Pathological
Monotypic inflammatory infiltrates
Neutrophilic abscess
Necrotizing vasculitis
Extensive necrosis
Primarily granulomatous inflammation
Pathologic features of Rosai-Dorfman disease (S100-positive macrophages demonstrating emperipolesis)
Preliminary Inclusion Criteria with Positive Weights
Clinical/Serologic
Serum IgG4 > 5X upper limit of normal
Serum IgG4 between 2X & 5X upper limit of normal
General Pathologic
Dense lymphoplasmacytic infiltrate
IgG4+ Plasma Cell Staining (excluding lymph node, GI tract, skin, and thyroid)
IgG4+ plasma cells: $\geq$50/hpf
IgG4+ plasma cells: between 10/hpf & 50/hpf
IgG4+/IgG plasma cell ratio: > 0.70

IgG4+/IgG plasma cell ratio: > 0.40 but < 0.70
Storiform pattern of fibrosis
Obliterative phlebitis
Lacrimal and Salivary Glands
Simultaneous enlargement of three or four of the following glands – lacrimal, parotid, sublingual, and submandibular glands – occurring in a bilateral distribution (can be asymmetric)
Enlargement of any two of the following glands: lacrimal, parotid, submandibular, or sublingual, in a bilateral distribution (can be asymmetric)
Enlargement of any of the following glands, in a bilateral distribution: lacrimal, parotid, submandibular, or sublingual (can be asymmetric)
Orbit
Orbital mass not involving lacrimal glands or extra-ocular muscles
Infraorbital/supra orbital nerve enlargement
Diffuse thickening of an extra-ocular muscle
Chest and Thoracic Aorta
Paravertebral band-like soft tissue in thorax
Peribronchovascular and septal thickening
Obliterative arteritis
Pancreato-Biliary Tree
Diffuse pancreas enlargement (loss of lobulations) + capsule-like rim decreased enhancement + intra-pancreatic biliary duct enhancement
Diffuse pancreas enlargement (loss of lobulations) + capsule-like rim decreased enhancement
Diffuse pancreas enlargement (loss of lobulations)
Diffuse or multi-focal pancreatic/biliary duct narrowing.
Smooth wall thickening of biliary tree >2.5mm with visible lumen
Retroperitoneum
Circumferential or anterolateral peri-aortic soft tissue
Diffuse thickening of the aortic wall
Retroperitoneal plaque-like soft tissue
Preliminary Inclusion Criteria with Negative Weights
Broad
Age <20
Lack of objective response of mass lesion to glucocorticoids. *Glucocorticoid response is defined as unequivocal improvement in the clinical lesions, serologic abnormalities, or radiology findings within one month of beginning ≥40 mg/day of prednisone.*
Fever: Temperature >38°C without another cause
Clinical/Serologic
Serum C-reactive protein > 5X upper limit of normal
Cytopenia of >1 cell line without another explanation
General Pathologic
Xanthogranulomatous Inflammation
Neutrophils > 5cells/HPF
Injury of duct epithelium
Lymphoepithelial lesion
Chest and Thoracic Aorta
Calcified lung mass
History or family history of Marfan syndrome (for aortopathy)
Pancreato-biliary tree
Presence of beading of the biliary tree
Presence of pseudo-diverticula of the biliary tree
Renal
Tubular basement membrane deposits

Supplementary Table 3: Inclusion Criteria Met by Cases and Mimickers in the First Validation Cohort

Inclusion Criteria	Classified as IgG4-RD (N=366)	Submitted as a Mimicker (N=324)
Serum IgG4 Concentration		
IgG4 Not Checked	13 (4%)	147 (45%)
IgG4 Normal	49 (13%)	104 (32%)
IgG4 > Normal < 2x ULN	49 (13%)	33 (10%)
IgG4 ≥ 2x ULN < 5x ULN	120 (33%)	34 (10%)
IgG4 ≥ 5x ULN	135 (37%)	6 (2%)
Histopathology		
Biopsy Not Performed	34 (9%)	51 (16%)
Dense Lymphoplasmacytic Infiltrate	136 (37%)	59 (18%)
Dense Lymphoplasmacytic Infiltrate and Storiform Fibrosis	97 (27%)	0 (0%)
Dense Lymphoplasmacytic Infiltrate and Obliterative Phlebitis	12 (27%)	2 (1%)
Dense Lymphoplasmacytic Infiltrate, Storiform Fibrosis, and Obliterative Phlebitis	67 (18%)	1 (0.3%)
Immunostaining (See Supplementary Table 3b)		
Not Performed	71 (19%)	234 (72%)
Group A	10 (3%)	42 (13%)
Group B	65 (18%)	27 (8%)
Group C	166 (45%)	17 (5%)
Group D	54 (15%)	4 (1%)
Symmetric Salivary Gland Involvement		
No Glands Affected	161 (44%)	246 (76%)
One Set of Glands	100 (27%)	46 (14%)
Two or More Sets of Glands	105 (29%)	32 (10%)
Thoracic Findings		
Septal and/or Bronchovascular Thickening	35 (10%)	16 (5%)
Paravertebral Mass	11 (3%)	4 (1%)
Pancreatic Findings (Mutually Exclusive, Highest Category Reported)		
Diffuse pancreatic enlargement with loss of lobulations	29 (8%)	7 (2%)
Diffuse pancreatic enlargement AND capsule-like rim with decreased enhancement	30 (8%)	0 (0%)
Diffuse pancreatic enlargement AND biliary tract involvement (diffuse or multifocal narrowing OR smooth wall thickening)	76 (21%)	5 (2%)
Renal Involvement		
Hypocomplementemia	36 (10%)	25 (8%)
Renal pelvis thickening/soft tissue	19 (5%)	2 (1%)
Bilateral renal cortex low-density areas	40 (11%)	0 (0%)
Retroperitoneum		
Diffuse thickening of the abdominal aortic wall	16 (4%)	22 (7%)
Circumferential or antero-lateral soft tissue around the infra-renal aorta or iliac arteries	52 (14%)	14 (4%)

Supplementary Table 4: Inclusion Criteria Met by Cases and Mimickers in the Second Validation Cohort

Inclusion Criteria	Classified as IgG4-RD (N=219)	Submitted as a Mimicker (N=164)
Serum IgG4 Concentration		
IgG4 Not Checked	2 (1%)	28 (17%)
IgG4 Normal	23 (11%)	84 (51%)
IgG4 > Normal < 2x ULN	54 (25%)	31 (19%)
IgG4 ≥ 2x ULN < 5x ULN	66 (30%)	15 (9%)
IgG4 ≥ 5x ULN	74 (34%)	6 (4%)
Histopathology		
Biopsy Not Performed	26 (12%)	21 (13%)
Dense Lymphoplasmacytic Infiltrate	103 (47%)	49 (30%)
Dense Lymphoplasmacytic Infiltrate and Storiform Fibrosis	61 (28%)	8 (5%)
Dense Lymphoplasmacytic Infiltrate and Obliterative Phlebitis	2 (1%)	1 (1%)
Dense Lymphoplasmacytic Infiltrate, Storiform Fibrosis, and Obliterative Phlebitis	13 (6%)	2 (1%)
Immunostaining (See Table 8b)		
Not Performed	47 (22%)	87 (53%)
Group A	9 (4%)	44 (27%)
Group B	30 (14%)	15 (9%)
Group C	99 (45%)	14 (9%)
Group D	34 (16%)	4 (2%)
Symmetric Salivary Gland Involvement		
No Glands Affected	85 (39%)	136 (83%)
One Set of Glands	68 (31%)	17 (10%)
Two or More Sets of Glands	66 (30%)	11 (7%)
Thoracic Findings		
Septal and/or Bronchovascular Thickening	25 (11%)	8 (5%)
Paravertebral Mass	4 (2%)	5 (3%)
Pancreatic Findings (Mutually Exclusive, Highest Category Reported)		
Diffuse pancreatic enlargement with loss of lobulations	19 (9%)	9 (6%)
Diffuse pancreatic enlargement AND capsule-like rim with decreased enhancement	17 (8%)	0 (0%)
Diffuse pancreatic enlargement AND biliary tract involvement (diffuse or multifocal narrowing OR smooth wall thickening)	50 (23%)	1 (1%)
Renal Involvement		
Hypocomplementemia	34 (16%)	6 (2%)
Renal pelvis thickening/soft tissue	11 (5%)	1 (1%)
Bilateral renal cortex low-density areas	25 (11%)	5 (3%)
Retroperitoneum		
Diffuse thickening of the abdominal aortic wall	12 (6%)	4 (2%)
Circumferential or antero-lateral soft tissue around the infra-renal aorta or iliac arteries	21 (10%)	11 (7%)

Supplementary Table 5: Mimicker Conditions in the Derivation and Validation Cohorts

The mimickers from the Derivation Cohort included: Adenocarcinoma; Adult-onset Asthma with Periocular Xanthogranulomas; Allergies; Aortic atherosclerosis; Autoimmune hepatitis; Autoimmune hepatitis plus pancreatitis due to Azathioprine therapy; Autoimmune pancreatitis type 2; Cholangiocarcinoma; Chronic pancreatitis (non-specific); Chronic rhino-sinusitis; Chronic sialoadenitis; Dacryoadenitis; Eosinophilic granulomatosis with polyangiitis; Erdheim-Chester disease; Fibroinflammatory mass (pseudotumor); Fibromyalgia; Giant cell arteritis; Granulomatosis with polyangiitis; Hashimoto's thyroiditis; Hypereosinophil syndrome; Idiopathic aortitis; Idiopathic orbital pseudotumor; Idiopathic pachymeningitis; Idiopathic retroperitoneal fibrosis; Idiopathic sclerosing sialoadenitis; Idiopathic supraglottic inflammation; Inflammatory bowel disease; Inflammatory myofibroblastic tumor; Intraductal papillary-mucinous neoplasm of pancreas; Large-vessel giant cell arteritis; Liposarcoma; Lymphoma (Follicular); Lymphoma (large B cell); Lymphoma (MALT); Lymphoma (Mantle cell); Lymphoma (Marginal zone lymphoma); Lymphoma (unspecified); Microscopic polyangiitis; Mixed cryoglobulinemia; Multi-centric Castleman's disease; Non-specific dacryoadenitis; Pancreatic cancer; Plasmacytoma; Primary sclerosing cholangitis; Primary sclerosing cholangitis & Crohn's disease; Rheumatoid arthritis; Rosai-Dorfman disease; Sarcoidosis; Sarcoma; Sjögren's syndrome; Systemic lupus erythematosus; T cell lymphoma; Tubulo-interstitial nephritis (non-IgG4-related); Tubulointerstitial nephritis/uveitis (TINU) syndrome

The mimickers from the Validation Cohort included: Adenocarcinoma; Adenocarcinoma (poorly-differentiated intestinal); Adenocarcinoma (probably pancreatic origin); Adult-onset Asthma with Periocular Xanthogranulomas; Allergies and Fibromyalgia; ANCA-associated vasculitis; ANCA-associated vasculitis & fibrosing mediastinitis; Aortic atherosclerosis; Autoimmune hepatitis; Autoimmune hepatitis plus pancreatitis due to Azathioprine therapy; Autoimmune pancreatitis type 2; Cholangiocarcinoma; Cholangiocarcinoma & pancreatic cancer; Cholangitis due to *Echinococcus multilocularis* infection; Chronic idiopathic appendicitis; Chronic pancreatitis; Chronic rhino-sinusitis; Chronic sialoadenitis; CREST/Sjögren overlap syndrome with cryoglobulinemic vasculitis; Dacryoadenitis; Diffuse lymphoid hyperplasia; Eosinophilic granulomatosis with polyangiitis; Epstein-Barr virus infection; Erdheim-Chester disease; Fibroinflammatory mass (pseudotumor); Fibroinflammatory mass (pseudotumor) - Esophageal polyp with prominent IgG4+ cells; Fibrosing Hashimoto thyroiditis; Giant cell arteritis; Granulomatosis with polyangiitis; Hashimoto's thyroiditis; Hypereosinophil syndrome; Hypophysitis (indeterminate type) and enlarged salivary gland; Idiopathic aortitis ; idiopathic fibrosing mediastinitis and non-specific cholestatic liver disease; Idiopathic orbital pseudotumor; Idiopathic pachymeningitis; Idiopathic retroperitoneal fibrosis; Idiopathic sclerosing sialoadenitis; idiopathic supraglottic inflammation; Infectious mediastinitis (tuberculosis); Inflammatory bowel disease; Inflammatory fibroid polyps associated with multiple GISTs in patient with neurofibromatosis; Inflammatory myofibroblastic tumor; Inflammatory myofibroblastic tumor with ROS1 rearrangement; Inflammatory myopathy with bronchiolitis with organizing pneumonia and eczema; Intraductal papillary-mucinous neoplasm of pancreas; Langerhans histocytosis; Large-vessel giant cell arteritis ; Liposarcoma associated with retroperitoneal fibrosis; Liposarcoma in retroperitoneum; Lymphoma (follicular; grade 3A); Lymphoma (Follicular); Lymphoma (large B cell); Lymphoma (MALT); Lymphoma (Mantle cell); Lymphoma (Marginal zone lymphoma); Lymphoma (NHL); Lymphoma (unspecified); Lymphoproliferative disease; Metastatic cancer (carcinoma of the breast); Microscopic polyangiitis; Microscopic polyangiitis (MPO-ANCA vasculitis)/aortitis/Graves' disease; Microscopic polyangiitis and interstitial lung disease; Mixed cryoglobulinemia and psoriatic arthropathy; Mucinous neoplasm of appendix with metastasis in peritoneum; Multi-centric Castleman's disease; Multicentric Castleman's disease plus sarcoidosis; Necrobiotic xanthogranuloma; Necrotizing vasculitis; Neuroendocrine tumor; Non-specific pleurisy; Non-specific dacryoadenitis; Optic neuropathy; Orofacial granulomatosis with Crohn's disease; Palpebral conjunctival mass; Pancreatic cancer; Pancreatic divisum; Parotidomegaly related to alcoholism; PFAPA syndrome; Plasmacytic laryngitis (polyclonal) and autoimmune hepatitis; Plasmacytoma; Primary sclerosing cholangitis; Primary sclerosing cholangitis & Crohn's disease; Primary sclerosing cholangitis; Crohn's disease; and autoimmune hemolytic anemia; Probable transitional cell carcinoma; Pulmonary hyalinizing granuloma; Pulmonary hyalinizing granuloma (probable); Refractory gastric ulceration; Rheumatoid arthritis; Rosai-Dorfman disease; Sarcoidosis; Sarcoidosis + systemic lupus erythematosus; Sarcoma; Sclerosing pancreatitis; Seronegative rheumatoid arthritis plus chronic pancreatitis; drug-induced; Sicca syndrome; Sicca syndrome plus asthma; Sjögren's syndrome; Sjögren's syndrome plus primary biliary cirrhosis; Superinfected orbital pseudotumor; T cell lymphoma; Tubulo-interstitial nephritis; (non-IgG4-related); Tubulointerstitial nephritis (query autoimmune cause); Tubulointerstitial nephritis/uveitis (TINU) syndrome; Tumor of mediastinum (sternum); Uncertain - Multicentric Castleman's disease versus bone marrow process; Unicentric Castleman's Disease; Unknown