Cell Reports Medicine, Volume *1*

Supplemental Information

ACCELERATE: A Patient-Powered Natural History Study Design Enabling Clinical and Therapeutic Discoveries in a Rare Disorder

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Supplemental Information

Table S1. Data processing metrics in the patient-powered arm, related to Figure 1

Data requests and receipt	
Days from enrollment to receipt of requested pathology reports	
Median [IQR]	25 [3, 67]
Range	0-466
Number of medical institutions data requested per patient	
Median [IQR]	3.0 [2.0, 4.0]
Range	1, 11
Total medical data requests sent	
N	1228
Days from receipt of pathology report to receipt of comprehensive medical data	
Median [IQR]	145 [44, 282]
Range	11, 787
Data entry	
Days from start of data entry until completion of PI review	
Median [IQR]	44 [16.5, 92.0]
Range	1, 485
Medical record length per patient (pages)	
Median [IQR]	531 [274, 1041]
Range	11, 8450
Pages entered per week per data analyst	
Median [IQR]	321 [243, 437]
Total aggregate pages received, as of data cut off	216,851
CAS review	
Days from PI review until CAS review	
Median [IQR]	158 [119.0, 245.0]
CAS Grades, N (%)	
1, Other diagnosis	42 (28.8)
2, Insufficient data for diagnosis	9 (6.2)
3, Sufficient data: Possible diagnosis	32 (21.9)
4, Sufficient data: Probable diagnosis	51 (34.9)
5, Sufficient data: Affirmative diagnosis	12 (8.2)

Table S2. Data collection elements, related to STAR Methods

Category	Data Element
Clinical features	Fatigue
	Malaise
	Night sweats
	Fever
	Unintentional weight loss
	Tumor pain/ lymph node pain
	Dyspnea
	Pruritus
	Fluid retention
	Peripheral neuropathy
	Violaceous lymphocytic papules/ cherry hemangiomata
	Skin disorders
	Interstitial lymphocytic pneumonitis
	Enlarged liver
	Enlarged spleen
	Lymphadenopathy
	Joint pain
Lymph node features	Atrophic/ regressed germinal centers
	Onion skinning
	Follicular dendritic cell prominence
	Vascular proliferation
	Dysplastic follicular dendritic cells
	Budding germinal centers
	Hyperplastic germinal centers
	Interfollicular plasmacytosis
	Lollipop sign
	Architectural alteration
	Expanded mantle zone
	EBV-encoded RNA positive staining
	HHV-8 positive staining
Bone marrow features	Atrophic/ regressed germinal centers
	Myelofibrosis
	Atypical megakaryocytes
	Megakaryocyte hyperplasia
	Plasmacytosis
	Plasmacytosis clonality
	Hemophagocytosis
	Cellularity
	Emperipolesis
	Myeloid to erythroid ratio
Laboratory tests (ordered by frequency of collection)	Hemoglobin
	Platelets
	White blood cells
	Creatinine
	Blood urea nitrogen
	Absolute neutrophil count
	Absolute lymphocyte count
	Absolute monocyte counts
	Absolute eosinophil count

	Albumin Absolute basophil count Alanine aminotransferase Total bilirubin Alkaline phosphatase Aspartate aminotransferase Estimated glomerular filtration rate Lactate dehydrogenase Red blood cell distribution C-reactive protein Calcium (266 additional lab test have been collected with option to add others)
Co-morbidities	All diagnosed comorbid disorders collected
Surgeries	Lymph node biopsy Autologous peripheral blood stem cell transplant Allogeneic stem cell transplant Plasmapheresis/ plasma exchange Radiation therapy Bone marrow biopsy Splenectomy (40 additional procedures with option to add others)
Castleman-treating medications (ordered by frequency of collection)	Prednisone Rituximab Siltuximab Dexamethasone Methylprednisolone Tocilizumab Cyclophosphamide Immunoglobulin human normal Etoposide Prednisolone (52 additional medications with option to add others)
Flares	Defined as period from symptom start to at least partial response
Adverse drug reactions	All adverse drug reactions associated with a Castleman treating product
Hospitalizations	All hospitalizations and reason for hospitalization during period from diagnosis to present

Table S3. Best clinical response as assessed by the site physicians (PDA), related to STAR Methods

Response	Definition
Complete response	Physician-determined complete improvement in all Castleman disease-associated symptoms and laboratory values after initiation of the regimen.
Partial response	Physician-determined complete improvement in at least 50% of Castleman disease-associated symptoms and laboratory values, but not a complete response after initiation of the regimen
Stable disease	Physician-determined stable symptoms or a response after initiation of the regimen that does not meet the definition for PR or PD
Progressive disease	Physician-determined worsening in at least 50% of Castleman disease-associated symptoms or laboratory values after initiation of the regimen

Table S4. Best clinical response as assessed by the ACCELERATE Registry Team (PPA), related to STAR Methods

Response	Definition
Complete response	100% normalization of all assessed response criteria* after initiation of the regimen
Partial response	At least 50% normalization of all assessed response criteria* after initiation of the regimen, but does not meet a complete response
Stable disease	Does not meet the definition for partial response or progressive disease
Progressive disease	At least 50% worsening in the number of assessed response criteria* after initiation of the regimen

*Constitutional symptoms, organomegaly, lymphocytic interstitial pneumonitis, cherry hemangiomas/ violaceous papules, C reactive protein/ estimated sedimentation rate, hemoglobin, platelet count, albumin, creatinine/ estimated glomerular filtration rate, immunoglobulin g/ gammaglobulin