CONTENTS

I. Supplementary Methods

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1. Task force meetings proceedings:

Per European Alliance of Rheumatology Associations (EULAR) and American College of Rheumatology (ACR) standard operating procedures (SOPs) the following steps were followed.

- August 2019 (NIH Bethesda): A face-to-face meeting was convened to define the focus of the task force and identify the target population.
- A EULAR task force was established and consisted of: nine pediatric rheumatologists (including one delegate of the EULAR young rheumatologists' network EMEUNET), seven neurologists, a neurologist and geneticist (double board certified), two geneticists, an immunologist, a health care professional, three fellows, three patient representatives (one for each disease) from the autoinflammatory alliance (n=2) and the Aicardi Goutières Syndrome Americas Association (AGSAA) (n=1) and three methodologists .
- Systematic literature review (SLR): A systemic literature review was conducted by three research fellows (KCG, MR, LL), with support from a librarian and epidemiologist (DH and DP), and a senior methodologist (ED) to identify relevant literature published before September 2020. The search was performed using PubMed, Embase and the Cochrane Library up to and including August 2020. Overall, 2961 references pertaining to the 3 diseases were identified, 71 of which were finally included (or for SAVI, 13/875 references, for CANDLE/PRAAS 12/801 references and for AGS 55/1297).
- Based on the SLR results, statements were drafted by the expert group. Two rounds of pre-consensus meeting Delphi questionnaires were sent using REDCap (https://projectredcap.org/software/), a secure Web-based system with the technical help of the University of Toronto. The purpose was to develop draft statements regarding the diagnosis, treatment, and long-term management of CANDLE/PRAAS, SAVI and AGS that

were circulated to be considered as potential points to consider. The task force members were asked to indicate their agreement with each statement (in the first round) and with draft statements that were circulated in the second survey with yes/no and, were given a free text option and suggestions to capture all relevant items. Responses were anonymous. Draft statements with 80% or higher agreement were retained for voting at the consensus meeting, and draft statements, that did not achieve 80% agreement, were marked for further discussion and refinement at the two consensus meetings.

- Delphi questionnaires: The Delphi technique, which uses a series of well-defined mail questionnaires, with the first one laid out broadly to avoid any biases, and the subsequent ones based on the results of the prior ones, was used to generate draft statements. Two surveys have been conducted through RedCap, a secure Web-based system, with the technical help of the University of Toronto. The first semi-structured, anonymous Delphi questionnaire was sent to 28 Task Force members, 22 were also voting members, (KU was a voting member but was not sent the questionnaire). The task force was asked to indicate "yes/no" to proposed questions and members were also given a free text option and asked to provide comments to existing questions and to add additional questions that they considered important to be addressed. If a statement reached ≥80% agreement in the first Delphi survey, the statement was included for discussion to the consensus meetings. The second Delphi questionnaire/survey was sent to the same 28 Task Force members who participated in the first Delphi survey. Similarly, participants were asked to indicate their agreement by answering "yes or no" to questions and were given to possibility to add comments in a free text option. After the second Delphi questionnaire, draft statements for all questions that had achieved a higher than 80% agreement were generated by the steering committee members.

Draft statements were also written for questions that had achieved between 20% to 80% agreement. All draft statements were distributed to the Task Force members prior to the consensus meeting. The lower percentage of consensus/agreement was indicated for draft statements that achieved less than 80% agreement. The draft statements with >80% agreement were discussed and voted on first at the consensus meetings, and those with a lower level of agreement were discussed next and generated longer discussions, more refinements and some draft statements ended up being ultimately excluded.

- Most Task Force members responded to the Delphi surveys within one week. Those who had not responded were sent daily reminders individually. For both rounds of Delphi questionnaires, a 100% response rate was achieved. The questionnaire data and the results from the SLR were used to generate draft statements that were discussed in two consensus meetings.
- Due to the coronavirus pandemic 2019 (COVID-19) travel restrictions prohibited face-to-face meetings. The two consensus meetings were thus held virtually online. One consensus meeting included voting members with expertise in CANDLE and SAVI and was held on October 8, 2020, and one with members with expertise in AGS on October 19, 2020.
    - The SLR results were presented by the fellows for each disease and discussed during the consensus meetings.
    - The draft statements that were distributed to the task force members prior to each consensus meeting were discussed, refined, and voted on.
    - Overarching statements and statements pertaining to both groups were voted on in both consensus meetings while statements pertaining to only CANDLE or SAVI and AGS were voted on in the respective meetings only.

- Statements with between 20% and 80% agreement were chosen for ongoing discussion and possible major revision during the second part of the consensus meeting, while the rest (<20% agreement) were dropped and were not included as points to consider statements. A methodologist (BMF) trained in nominal group technique, and a EULAR methodologist (ED) led the voting members attending the virtual consensus meeting through the consensus process. The voting members included, the two conveners (RGM, PB), 1 allied health professional (KU) and 3 experts (MLK, BN, DE) attended both meetings, and the rest of the expert panel (CP, SO[1], GAMS, EPH, TA, LAA, AV, MG, RCD, YJC, DT, FG, SO[2], EF) and patient advocates (DRC, KB, ES) attended one meeting based on their disease specific experience/expertise.
- The voting panel consisted of 23 people (19 experts, one allied health professional and three patient representatives [one for each disease]). During the consensus meetings, the joint statements were voted on by all members of the voting panel. However, CANDLE/SAVI specific statements were voted on by ten experts, one allied health professional, one SAVI and one CANDLE patient representative. The AGS specific statements were voted on by 14 experts, one allied health professional and one AGS patient representative.

- Reaching consensus: All statements included in the tables that reached the minimum 80% consensus were retained in the final formulation of the recommendations. If one of the sub-statements did not reach that threshold in the pre-consensus Delphi or at the consensus meetings, it was discussed and reworded or modified with the aim of achieving a secondary 80% consensus. If the 80% level was not achieved in any way, the statement was eliminated.

Eliminated statements were listed in the procedural materials that are available upon request. The proportion of agreement (80-100%) among the task force at the end of the second conference was recorded.

- A post-consensus meeting questionnaire with the finalized statements was distributed among all voting members of both consensus meetings and a level of agreement was obtained based on marking on a scale from 0 to 10, with 0 indicating no agreement and 10 indicating full agreement. Using those data, the mean and standard deviation (SD) of level of agreement for each statement was calculated.
- The manuscript was reviewed and approved by all task force members and the EULAR executive committee before submission.

2. Search Terms

a) *Search Terms for SAVI*

(((((SAVI syndrome) OR STING associated vasculopathy) OR stimulator of IFN genes-associated vasculopathy) OR severe pulmonary fibrosis [Title/Abstract]) OR TMEM173[Title/Abstract])

b) *Search Terms for CANDLE/PRAAS*

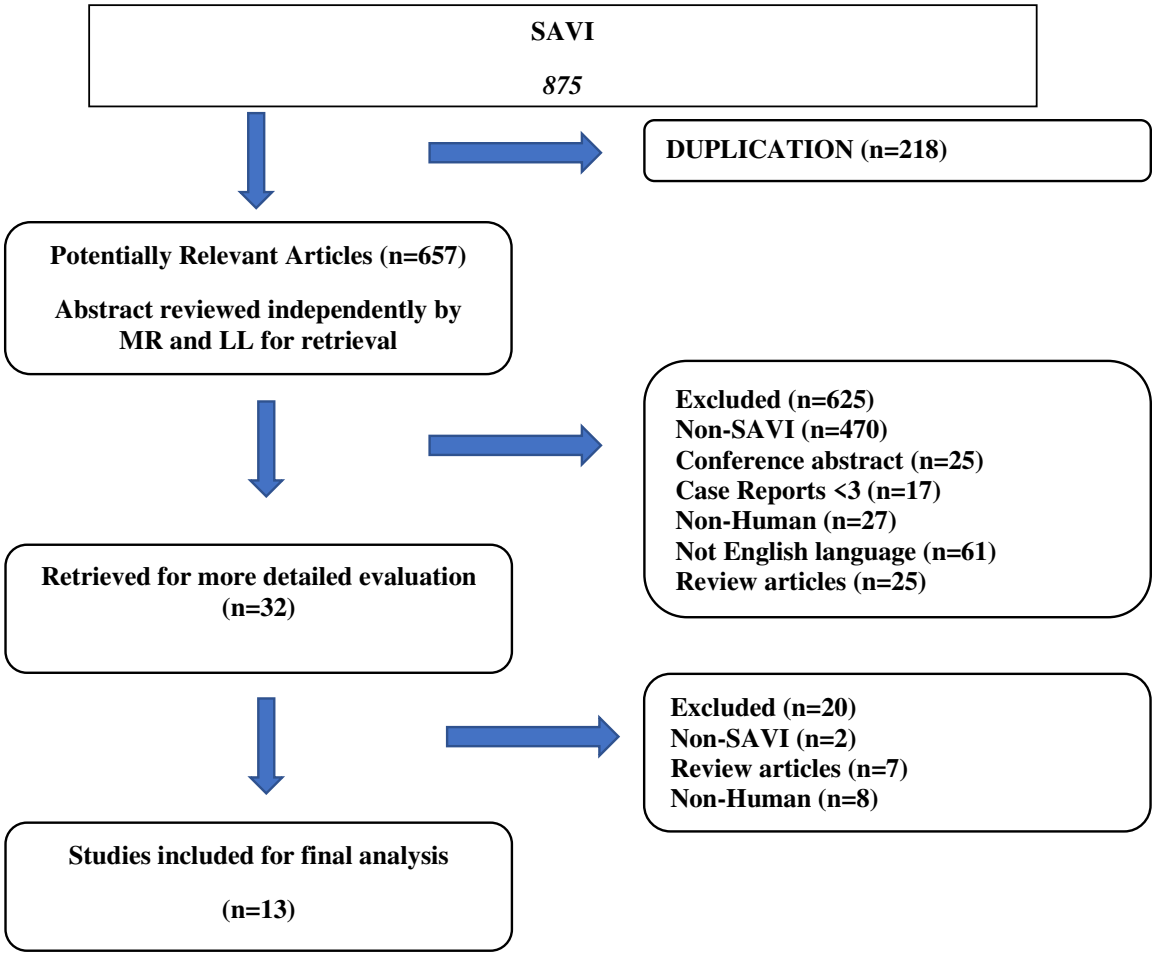
(((((((CANDLE syndrome) OR (Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated temperature)) OR proteasome associated autoinflammatory syndrome) OR PRAAS) OR CANDLE/PRAAS) OR PSMB8 gene) OR (Joint contractures Muscular atrophy microcytic anemia and Panniculitis Associated lipodystrophy)) OR Nakajo-Nishimura syndrome) OR Japanese autoinflammatory syndrome [Title/Abstract])

c) ***Search Terms for AGS***

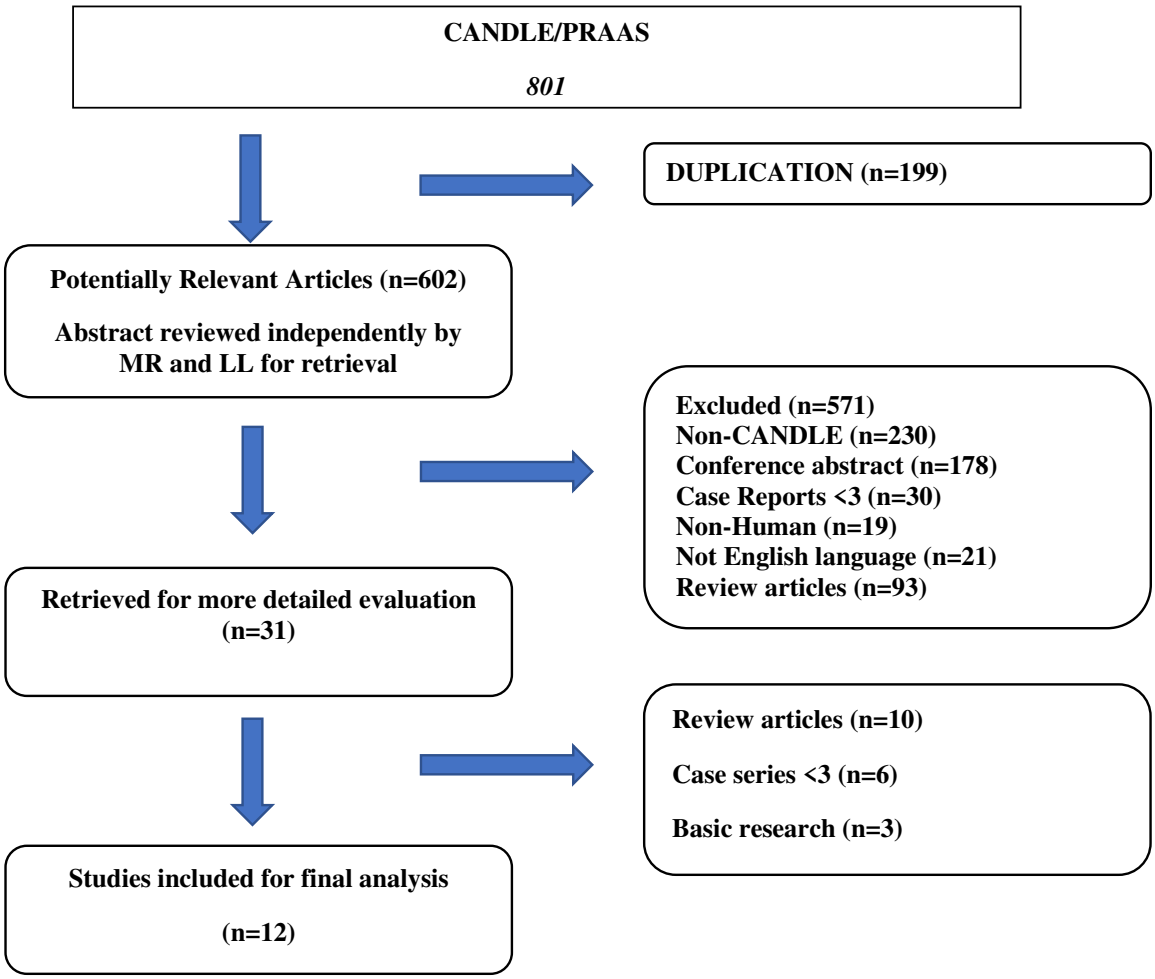
(Familial Infantile Encephalopathy with Intracranial Calcification and Chronic Cerebrospinal Fluid Lymphocytosis OR Cree Encephalitis OR Encephalopathy with Basal Ganglia Calcification OR Aicardi Goutières syndrome OR Pseudotoxoplasmosis syndrome OR Pseudo-TORCH syndrome OR Aicardi-Goutières Syndrome 1 OR Aicardi-Goutières Syndrome 2 [Title/Abstract])

3. Flowcharts

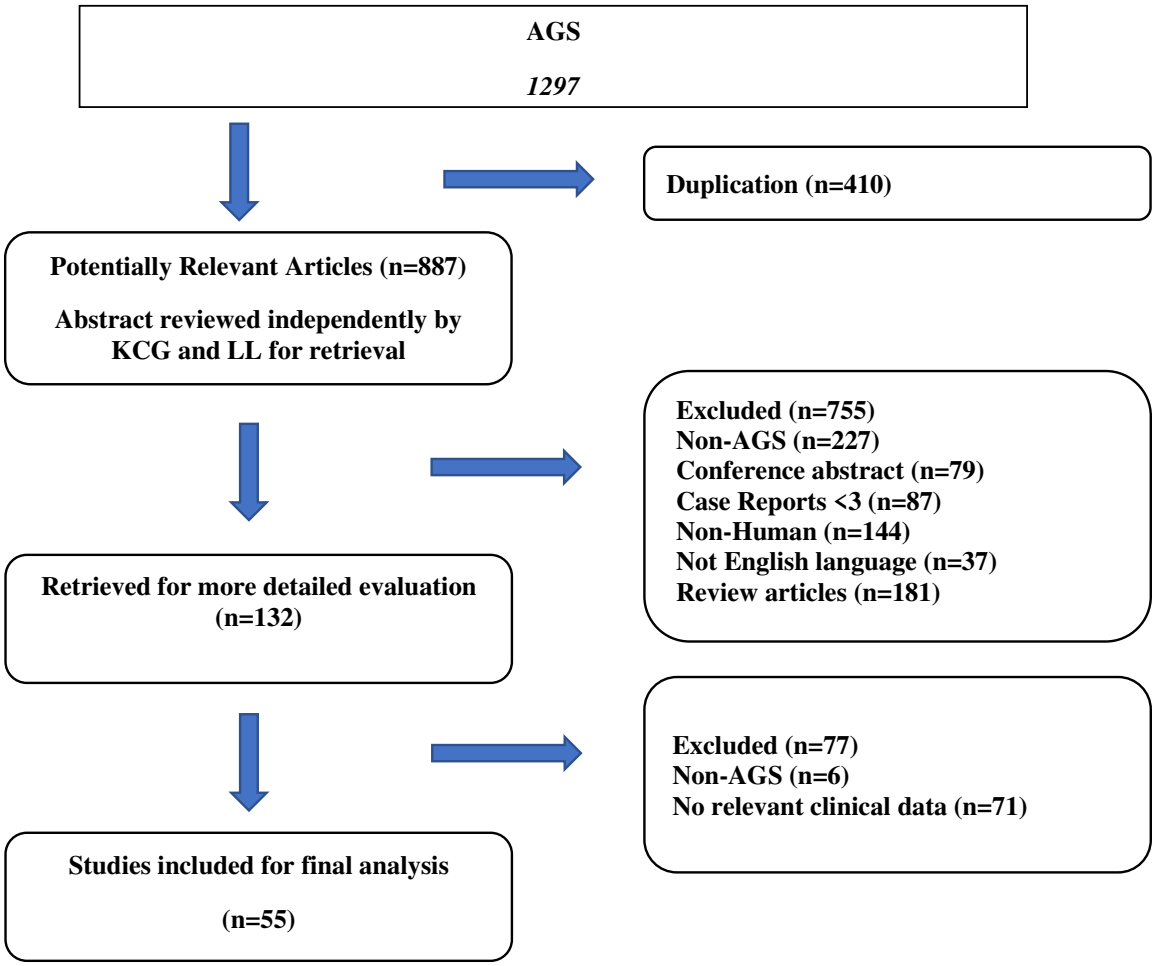
a. ***Flowchart for SAVI***



b) ***Flowchart for CANDLE/PRAAS***



c) ***Flowchart for AGS***



II. Supplementary Tables

Supplementary table 1. Included articles for SAVI for final analysis

1	**Frémond ML et al**. Efficacy of the Janus kinase 1/2 inhibitor ruxolitinib in the treatment of vasculopathy associated with *TMEM173*-activating mutations in 3 children. ***J Allergy Clin Immunol. 2016.***
2	**Jeremiah N et al.** Inherited STING-activating mutation underlies a familial inflammatory syndrome with lupus-like manifestations. ***J Clin Invest, 2014.***
3 A	**Kim H et al.** Pharmacokinetics, Pharmacodynamics, and Proposed Dosing of the Oral JAK1 and JAK2 Inhibitor Baricitinib in Pediatric and Young Adult CANDLE and SAVI Patients. ***Clin Pharmacol Ther, 2018.***
3 B	**Sanchez GA et al.** JAK1/2 inhibition with baricitinib in the treatment of autoinflammatory interferonopathies. ***J Clin Invest, 2018.***
4	**Liu Y et al.** Activated STING in a vascular and pulmonary syndrome. ***N Engl J Med, 2014.***
5	**Melki I et al.** Disease-associated mutations identify a novel region in human STING necessary for the control of type I interferon signaling. ***J Allergy Clin Immunol, 2017.***
6	**Picard C et al.** Severe Pulmonary Fibrosis as the First Manifestation of Interferonopathy (*TMEM173* Mutation). ***Chest, 2016.***
7	**Volpi S et al.** Efficacy and Adverse Events During Janus Kinase Inhibitor Treatment of SAVI Syndrome. ***J Clin Immunol, 2019.***
8	**Konig N et al.** Familial chilblain lupus due to a gain-of-function mutation in STING. ***Ann Rheum Dis, 2018.***
9	**Tang Xiaolei, et al.** "STING-Associated Vasculopathy with Onset in Infancy in Three Children with New Clinical Aspect and Unsatisfactory Therapeutic Responses to Tofacitinib." **Journal of Clinical Immunology (2019): 1-9**
10	**Clarke S. L. N., et al.** "Type 1 interferonopathy presenting as juvenile idiopathic arthritis with interstitial lung disease: report of a new phenotype." **Pediatric Rheumatology 18 (2020): 1-5.**
11	**Keskitalo Salla, et al.** "Novel *TMEM173* mutation and the role of disease modifying alleles." ***Frontiers in immunology*** **10 (2019): 2770.**
12	**Lin Bin, et al.** "A novel *STING1* variant causes a recessive form of STING-associated vasculopathy with onset in infancy (SAVI)." ***Journal of Allergy and Clinical Immunology*** **(2020).**

SAVI, STING-associated vasculopathy with onset in infancy.

Supplementary table 2. Included articles for CANDLE/PRAAS for final analysis

1 A	**Argarwal AK et al.** *PSMB8* encoding the beta5i proteasome subunit is mutated in joint contractures, muscle atrophy, microcytic anemia, and panniculitis-induced lipodystrophy syndrome. ***Am J Hum Genet, 2010.***
1 B	**Garg A et al.** An autosomal recessive syndrome of joint contractures, muscular atrophy, microcytic anemia, and panniculitis-associated lipodystrophy. ***JCEM, 2010.***
2	**Al-Mayouf SM et al.** Monogenic interferonopathies: Phenotypic and genotypic findings of CANDLE syndrome and its overlap with C1q deficient SLE. ***International Journal of Rheumatic Diseases, 2018.***
3	**Arima K et al.** Proteasome assembly defect due to a proteasome subunit beta type 8 (*PSMB8*) mutation causes the autoinflammatory disorder, Nakajo-Nishimura syndrome. ***Proc Natl Acad Sci U S A, 2011.***
4	**Brehm A et al.** Additive loss-of-function proteasome subunit mutations in CANDLE/PRAAS patients promote type I IFN production. ***J Clin Invest, 2015.***
5 A	**Kim H et al.** Pharmacokinetics, Pharmacodynamics, and Proposed Dosing of the Oral JAK1 and JAK2 Inhibitor Baricitinib in Pediatric and Young Adult CANDLE and SAVI Patients. ***Clin Pharmacol Ther, 2018.***
5 B	**Sanchez GA et al.** JAK1/2 inhibition with baricitinib in the treatment of autoinflammatory interferonopathies. ***J Clin Invest, 2018.***
6	**Kitamura A et al.** A mutation in the immunoproteasome subunit *PSMB8* causes autoinflammation and lipodystrophy in humans. ***J Clin Invest, 2011.***
7	**Liu Y et al.** Mutations in proteasome subunit beta type 8 cause chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature with evidence of genetic and phenotypic heterogeneity. ***Arthritis Rheum, 2012.***
8	**Torrelo A et al.** Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) syndrome. ***J Am Acad Dermatol, 2010.***
9	**de Jesus Adriana A., et al.** "Distinct interferon signatures and cytokine patterns define additional systemic autoinflammatory diseases." ***The Journal of Clinical Investigation*** **130.4 (2020).**
10	**Ayaki Takashi, et al.** "Myositis with sarcoplasmic inclusions in Nakajo–Nishimura syndrome: a genetic inflammatory myopathy." ***Neuropathology and Applied Neurobiology*** **(2020).**

CANDLE/PRAAS, chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature/ proteasome-associated autoinflammatory syndrome.

Supplementary table 3. Included articles for AGS for final analysis

1	**Adang LA, et al.** Developmental Outcomes of Aicardi Goutières Syndrome. ***Journal of Child Neurology, 2020.***
2	**Adang LA, et al.** Development of a neurologic severity scale for Aicardi Goutières Syndrome. ***Mol Genet Metab, 2020.***
3	**de Jesus AA et al.** Distinct interferon signatures and cytokine patterns define additional systemic autoinflammatory diseases. ***The Journal of Clinical Investigation, 2020.***
4	**Lhamtsho D et al.** Novel RNASEH2C mutation in multiple members of a large family: insights into phenotypic spectrum of Aicardi-Goutières Syndrome. ***BMJ Neurology Open, 2020.***
5	**Rice GI et al.** Genetic and phenotypic spectrum associated with *IFIH1* gain-of-function. ***Hum Mutat. 2020.***
6	**Vanderver A, et al.** Janus Kinase Inhibition in the Aicardi-Goutières Syndrome. ***N Engl J Med, 2020.***
7	**Videira G et al.** Diagnosis of Aicardi-Goutières syndrome in adults: a case series. ***Movement Disorders Clinical Practice, 2020*.**
8	**Garau J et al.** Molecular Genetics and Interferon Signature in the Italian Aicardi Goutières Syndrome Cohort: Report of 12 New Cases and Literature Review. ***J Clin Med, 2019.***
9	**Moreno Medinilla EE et al.** Aicardi-Goutières syndrome: Phenotypic and genetic spectrum in a series of three cases. ***An Pediatr (Barc), 2019.***
10	**Meesilpavikkai K et al**. Efficacy of Baricitinib in the Treatment of Chilblains Associated with Aicardi-Goutières Syndrome, a Type I Interferonopathy. ***Arthritis & rheumatology, 2019.***
11	**Samanta D et al.** Multiple Autoimmune Disorders in Aicardi-Goutières Syndrome. ***Pediatric neurology, 2019.***
12	**Tonduti D et al.** Spontaneous MRI improvement and absence of cerebral calcification in Aicardi-Goutières syndrome: Diagnostic and disease-monitoring implications. ***Molecular Genetics and Metabolism, 2019.***
13	**Zimmermann N et al.** Assessment of Clinical Response to Janus Kinase Inhibition in Patients with Familial Chilblain Lupus and *TREX1* Mutation. ***JAMA Dermatol, 2019.***
14	**Adang LA et al.** Aicardi Goutières syndrome is associated with pulmonary hypertension. ***Molecular Genetics and Metabolism, 2018.***
15	**Al Mutairi F et al.** Phenotypic and Molecular Spectrum of Aicardi-Goutières Syndrome: A Study of 24 Patients. ***Pediatric Neurology, 2018.***
16	**Hebbar M et al.** p.Arg69Trp in *RNASEH2C* is a founder variant in three Indian families with Aicardi–Goutières syndrome. ***American Journal of Medical Genetics, 2018.***
17	**Rice GI et al.** Reverse-Transcriptase Inhibitors in the Aicardi–Goutières Syndrome. ***NEJM, 2018.***
18	**Armangue T et al.** Neonatal detection of Aicardi Goutières Syndrome by increased C26:0 lysophosphatidylcholine and interferon signature on newborn screening blood spots. ***Mol Genet Metab, 2017.***
19	**Rice GI, et al.** Genetic, Phenotypic, and Interferon Biomarker Status in ADAR1-Related Neurological Disease. ***Neuropediatrics, 2017.***

20	**Wang BX et al.** Interferon-Stimulated Gene Expression as a Preferred Biomarker for Disease Activity in Aicardi–Goutières Syndrome. ***Interferon & Cytokine Research, 2017.***
21	**Cattalini M et al.** Exploring Autoimmunity in a Cohort of Children with Genetically Confirmed Aicardi–Goutières Syndrome. ***J Clin Immunol, 2016.***
22	**La Piana R et al.** Neuroradiologic patterns and novel imaging findings in Aicardi-Goutières syndrome. ***Neurology, 2016***
23	**Stellitano LA et al.** Leukodystrophies and genetic leukoencephalopathies in childhood: a national epidemiological study. ***Neurology, 2016.***
24	**Yarbrough K et al.** The Importance of Chilblains as a Diagnostic Clue for Mild Aicardi–Goutieres Syndrome. ***American Journal of Medical Genetics, 2016.***
25	**Bursztejn AC et al.** Unusual cutaneous features associated with a heterozygous gain-of-function mutation in *IFIH1*: overlap between Aicardi– Goutières and Singleton–Merten syndromes. ***Br J Dermatol, 2015.***
26	**Crow YJ et al.** Characterization of Human Disease Phenotypes Associated with Mutations in *TREX1, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, ADAR*, and *IFIH1*. ***American Journal of Medical Genetics, 2015.***
27	**Uyur-Yalçın E et al.** Clinical and neuroradiologic variability of Aicardi-Goutiéres syndrome: Two siblings with *RNASEH2C* mutation and a boy with *TREX1* mutation. ***The Turkish Journal of Pediatrics, 2015.***
28	**Vanderver A et al.** Early onset Aicardi Goutières syndrome: MRI pattern Recognition. ***J Child Neurol, 2015.***
29	**Abe J et al.** A nationwide survey of Aicardi-Goutières syndrome patients identifies a strong association between dominant *TREX1* mutations and chilblain lesions: Japanese cohort study. ***Rheumatology, 2014.***
30	**Crow YJ et al**. Mutations in *ADAR1, IFIH1*, and *RNASEH2B* Presenting as Spastic Paraplegia. ***Neuropediatrics, 2014.***
31	**Livingston JH, et al.** A type I interferon signature identifies bilateral striatal necrosis due to mutations in *ADAR1*. ***J Med Genet, 2014.***
32	**Oda H, et al.** Aicardi-Goutières syndrome is caused by *IFIH1* mutations. ***Am J Hum Genet, 2014***.
33	**Ramantani G et al.** Epilepsy in Aicardi Goutières syndrome. ***European Journal of Pediatric Neurology, 2014.***
34	**Rice GI, et al.** Gain-of-function mutations in *IFIH1* cause a spectrum of human disease phenotypes associated with upregulated type I interferon signaling. ***Nat Genet, 2014.***
35	**Abe J et al.** Heterozygous *TREX1* p.Asp18Asn mutation can cause variable neurological symptoms in a family with Aicardi-Goutières syndrome/familial chilblain lupus. ***Rheumatology, 2013.***
36	**Livingston JH et al.** Recognizable phenotypes associated with intracranial calcification. ***Developmental Medicine & Child Neurology, 2013.***

37	**Izzotti A et al.** Different Mutations in Three Prime Repair Exonuclease 1 and Ribonuclease H2 Genes Affect Clinical Features in Aicardi-Goutières Syndrome. J ***Child Neurol, 2012.***
38	**Ostergaard E et al.** A novel RNASEH2B splice site mutation responsible for Aicardi–Goutières syndrome in the Faroe Islands. ***Acta Pædiatrica, 2012.***
39	**Rossler L et al.** Aicardi-Goutières syndrome with emphasis on sonographic features in infancy. ***Pediatric Radiology, 2012.***
40	**Xin B et al.** Homozygous mutation in *SAMHD1* gene causes cerebral vasculopathy and early onset stroke. ***Proc Natl Acad Sci U S A, 2011.***
41	**Ramesh VA et al.** Intracerebral large artery disease in Aicardi–Goutières syndrome implicates *SAMHD1* in vascular homeostasis. ***Developmental Medicine & Child Neurology, 2010.***
42	**Ramantani G el al.** Expanding the Phenotypic Spectrum of Lupus Erythematosus in Aicardi-Goutières Syndrome. ***Arthritis & Rheumatism, 2010.***
43	**Thiele H et al.** Cerebral Arterial Stenoses and Stroke: Novel Features of Aicardi-Goutières Syndrome Caused by the Arg164X Mutation in SAMHD1 Are Associated with Altered Cytokine Expression. ***Human Mutation, 2010.***
44	**Izzotti A et al.** Interferon-Related Transcriptome Alterations in the Cerebrospinal Fluid Cells of Aicardi-Goutières Patients. ***Brain Pathology, 2009.***
45	**Izzotti A et al.** Brain damage as detected by cDNA-microarray in the spinal fluid of patients with Aicardi-Goutières syndrome. ***Neurology, 2009.***
46	**Uggetti C et al.** Aicardi-Goutières Syndrome: Neuroradiologic Findings and Follow-Up. ***American Journal of Neuroradiology, 2009.***
47	**Rice G et al.** Heterozygous mutations in TREX1 cause familial chilblain lupus and dominant Aicardi-Goutières syndrome. ***American Journal of Human Genetics, 2007.***
48	**Rice G et al.** Clinical and Molecular Phenotype of Aicardi-Goutières Syndrome. ***The American Journal of Human Genetics, 2007.***
49	**Lanzi G et al.** The natural history of Aicardi–Goutières syndrome: Follow-up of 11 Italian patients. ***Neurology, 2005.***
50	**Abdel-Salam GMH et al.** Aicardi-Goutières syndrome: clinical and neuroradiological findings of 10 new cases. ***Acta Paediatrica, 2004.***
51	**Crow YJ et al.** Congenital Glaucoma and Brain Stem Atrophy as Features of Aicardi–Goutières Syndrome. ***American Journal of Medical Genetics, 2004.***
52	**Blau N et al.** Cerebrospinal fluid pterins and folates in Aicardi-Goutières syndrome: a new phenotype. ***Neurology, 2003.***
53	**Lanzi G et al.** Aicardi-Goutières Syndrome: a description of 21 new cases and a comparison with the literature. ***European Journal of Pediatric Neurology*****, 2002.**
54	**Crow YJ et al.** Aicardi-Goutières Syndrome Displays Genetic Heterogeneity with One Locus (AGS1) on Chromosome 3p21. ***American Journal of Human Genetics, 2000.***

55	**Goutières F et al.** Aicardi-Goutières Syndrome: An Update and Results of Interferon-a Studies. ***Annals of Neurology, 1998.***

AGS, Aicardi-Goutières syndrome.

Supplementary Table 4. Summary of janus kinase inhibitor (JAKI) dosing regimens published in the literature

	Weight class (kg)	**Minimum/maximum doses based on published literature (mg/kg/day)***	**References**
Baricitinib			
CANDLE/PRAAS	10-20	0.3/0.8	Sanchez et al.,[1] Kim et al.,[2] Boyadzhiev et al.[3]
	20-40	0.15/0.4	Sanchez et al.,[1] Kim et al.[2]
	>40	NA/0.25	Sanchez et al.,[1] Kim et al.[2]
SAVI	10-20	0.3/0.8	Kim et al.[2]
	20-40	0.15/0.4	Sanchez et al.,[1] Kim et al.[2]
	>40	NA/0.25	Sanchez et al.,[1] Kim et al.[2]
AGS	4.5-8.5	0.12/0.44, age < 6 months 0.24/0.89, age ≥ 6 months	Vanderver et al[4]
	8.5-20	0.3/0.8	Vanderver et al.[4], Kim et al.[2]
	20-40	0.15/0.4	Vanderver et al.[4], Kim et al.[2]
	>40	NA/0.25	Vanderver et al.[4], Kim et al.[2]
Ruxolitinib			
CANDLE/PRAAS	10-20	no data available	NA
	20-40	0.5 /0.75	de Jesus et al.[5]
	>40	no data available	NA
SAVI	10-20	0.5/1	Raffaele et al.[6], Frémond et al.[7]
	20-40	0.25/1.25	Volpi et al.[8], Frémond et al.[7]
	>40	no data available	NA
AGS	10-20	0.2/0.8	Tungler et al.[9], Mura et al.[10]
	20-40	no data available	NA

	>40	no data available	NA
Tofacitinib**		No dosing data per weight were reported	NA

*Dosing regimens proposed here are based on normal renal function. Most of them are based on eGFR calculations using bedside Schwartz formula for children <18 years and Cockcroft-Gault equation for adults (≥18 years)
https://www.kidney.org/professionals/KDOQI/gfr_calculatorPed
https://www.kidney.org/professionals/kdoqi/gfr_calculatorCoc
**Published data for tofacitinib is incomplete. No published dosing data for CANDLE and AGS are available and one paper reports on tofacitinib in two SAVI patients. Both patients (13 months and 64 months) received 2.5 mg BID and both were reported have failure to thrive[11]
AGS, Aicardi-Goutières Syndrome; CANDLE/PRAAS, Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated temperature/Proteasome-Associated Autoinflammatory Syndrome; kg, kilogram; mg, milligram; NA, not available; SAVI, STING-associated vasculopathy with onset in infancy.

The dosing listed in the table is based on published data; the respective articles are listed. Only reports that included the patient's weight and dosing regimen were included. For baricitinib, a formal pharmacokinetic (PK) analysis in patients with CANDLE, SAVI and AGS allowed for estimation of the exposure and PK profile at the doses listed. Dose adjustment for reduced renal function were also provided.[2] None of the treatments are approved by FDA or EMA for the treatment of CANDLE, SAVI or AGS.

The dosing regimens summarized in this supplementary table were reviewed by all members in the task force and reflective current practice by the expert physicians who are treating these patients.

Long-term safety assessments for treatment with JAKIs have not firmly been established. Follow outcomes and safety data have been published for baricitinib.[1 4] For the other janus kinase inhibitors (JAKI) long-term safety data on the doses published and summarized in the table has not been established yet. Until further safety data are available, all the patients should be monitored for BK viral load in urine and blood.

Close safety monitoring is required and includes the following labs in most research studies:

Safety labs every 3 months for JAK inhibitors (see also table 3):

- Complete blood count (CBC) with differential with reticulocyte count
- Renal function (serum creatinine, blood urea nitrogen (BUN), estimated glomerular filtration rate (eGFR) (bedside Schwartz calculation for patients < 18 years of age), creatinine clearance, standard urinalysis, beta 2 microglobulin
- Liver function tests (alkaline phosphatase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, direct bilirubin, gamma glutamyl transferase (GGT))
- BK virus test (blood and urine)
    - Every 3-6 months
    - Additional follow-up is recommended for patients with suspected renal impairment
- Other: Electrolytes and glucose and Chemistry profile (creatinine kinase, uric acid) and Lipid panel (cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides)
- Tuberculosis (purified protein derivative (PPD) skin test or QuantiFERON) test yearly.

Supplementary Table 5. Summary of the autoantibodies and related clinical features of autoimmune disease in CANDLE/PRAAS, SAVI and AGS that has been published in the literature

a. Antibodies that were elevated but not associated with clinical disease in CANDLE/PRAAS, SAVI and AGS	
c-ANCA (low titer) p-ANCA (low titer) dsDNA (low titer)	Transient elevations of dsDNA or c-ANCA or p-ANCA positive antibodies have been reported in patients with SAVI but were not associated with disease severity and patients did not develop immune complex-mediated glomerulonephritis nor vasculitis.[1 12]

	Anti-dsDNA antibodies have not yet been reported in the context of hypocomplementemia.
ANA (low titer) Anti-phospholipid antibodies (low titer)	Up to 62.5% of patients with SAVI[12], up to 42% of patients with CANDLE/PRAAS[1 13-19] and up to 23% of patients with AGS[20] have positive ANA. Antiphospholipid antibodies are present in patients with CANDLE/PRAAS (up to 43%), SAVI and AGS.[1 20 21]
b. Antibodies that were elevated and associated with autoimmune disease in CANDLE/PRAAS, SAVI and AGS	
RF and anti-CCP	Rheumatoid factor (RF) positivity was reported in 57% of SAVI patients with joint symptoms[12] while anti-cyclic citrullinated peptide (anti-CCP) was present in some patients but systematic testing has not been performed.[21 22]
p-ANCA (high titer)	Necrotizing pauci-immune crescentic glomerulonephritis has recently been described in three patients with confirmed SAVI, in two with measured antibodies with high titer p-ANCA.[23 24]
Coomb's test (antiglobulin test) anti-platelet antibodies	One CANDLE patient with Evans Syndrome[25] and two CANDLE patients with autoimmune hemolytic anemia have been reported.[5 17]
anti-thyroid peroxidase	Hypothyroidism is present in AGS, one study reporting aggregate data describes that as much as 4% of affected patients can infrequently develop antibodies directed against the thyroid gland with (sub)clinical thyroiditis[26]. In SAVI, the positivity of anti-thyroid peroxidase (TPO) antibodies can be associated either with hypo- or hyperthyroidism.[27]
Liver-specific antibodies	Autoimmune hepatitis and the presence of liver-specific antibodies (that can include anti-nuclear, anti F-actin, and anti-smooth muscle antibodies) have been described in AGS.[26 28]

ANA, antinuclear antibodies; AGS, Aicardi-Goutières syndrome; ANCA, anti-neutrophil cytoplasmic antibodies; anti-CCP, anti- cyclic citrullinated peptide; CANDLE/PRAAS, chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature / proteasome-associated autoinflammatory syndrome; dsDNA, double stranded DNA, RF, rheumatoid factor; SAVI, STING-associated vasculopathy with onset in infancy.

There is insufficient data on the value of monitoring autoantibody titers for assessing response to treatment.

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