RIIP

RENCONTRES EN IMMUNOLOGIE & IMMUNOTHERAPIE PRATIQUES

29 et 30 SEPTEMBRE 2022

UIC-P - Espaces Congrès
16, rue Jean Rey - 75015 Paris

IMAGE FREEPIK

Sous l'égide de :

AI2R Filière · aviesan alliance nationale pour les sciences de la vie et de la santé · CeRéMAIA · GRI · European Reference Network for rare or low prevalence complex diseases · Fédération Immunologie · Imidiate · RITA Rare Immunodeficiency AutoInflammatory AutoImmune · Société Française de Dermatologie et de Pathologie Sexuellement Transmissible · Société Française d'Immunologie · SFR société française de rhumatologie · SOFREMIP Rhumatologie & maladies inflammatoires pédiatriques · SNFEM

RENCONTRES EN IMMUNOLOGIE & IMMUNOTHERAPIE PRATIQUES

PIMS, MIS-C ou Maladie Kasawaki ?

Alexandre Belot, MD, PhD
HFME, Hospices Civils de Lyon
CIRI
Alexandre.belot@chu-lyon.fr

29 et 30 SEPTEMBRE 2022
UIC-P - Espaces Congrès
16, rue Jean Rey - 75015 Paris

Sous l'égide de :

May 2020:
A new emergent disease highlighted in the media

le dauphiné libéré | Définir ma page d'accueil | ABONNEZ-VOUS | Le journal

Ain | Alpes-de-Haute-Provence | Hautes-Alpes | Ardèche | Drôme | Haute-Savoie | Isère | Savoie | Vaucluse | Plus

› Santé › Coronavirus

Santé

Une mystérieuse maladie peut-être liée au coronavirus frappe les enfants

LE PROGRÈS | Ain | Jura | Rhône | Loire | Haute-Loire

› Santé › Coronavirus

Auvergne-Rhône-Alpes

Kawasaki atypique: quatre ou cinq enfants touchés dans la région

Pédiatre à l'hôpital Femme mère enfant de Bron et chercheur à l'Institut national de la santé et de la recherche médicale (Inserm), le Pr Alexandre Belot s'interroge, comme ses collègues, sur l'influence du coronavirus sur cette maladie rare inflammatoire qui ne touche que quelques enfants en Europe à la fin de l'hiver et au début du printemps.

Newsletters | L'EXPRESS | S'abonner : 1€ le 1e

ACTUALITÉS | LE CORONAVIRUS | ÉCONOMIE | L'HEBDO | LIFESTYLE | SERVICES

BANQUE des TERRITOIRES
Proche c'est bien,
Disponible, c'est mieux !

A VOIR • L'hôpital public face au coronavirus | Olivier Véran, ministre de la Santé | Le professeur Didier Raoult | "Covid-19", le nouveau

Actualité | Société | Santé

"PHÉNOMÈNE RÉEL"

Le lien entre la maladie de Kawasaki et le Covid-19 est "confirmé" selon un pédiatre

Par LEXPRESS.fr ,
publié le 15/05/2020 à 20:57

Le Monde | Consulter le journal | Se connecter

ACTUALITÉS | ÉCONOMIE | VIDÉOS | OPINIONS | CULTURE | M LE MAG | SERVICES

SANTÉ • CORONAVIRUS ET PANDÉMIE DE COVID-19

Partage

Un lien entre des syndromes inflammatoires chez les enfants et le Covid-19

Depuis le 1er mars, 135 cas de formes atypiques du syndrome de Kawasaki ont été recensés en France. Les enfants touchés avaient pour la plupart été infectés par le SARS-CoV-2 et sont en majorité d'origine africaine ou antillaise

Definitions

Syndrome de Kawasaki-Like…

Syndrome inflammatoire multisystémique de l'enfant
Multisystem Inflammatory syndrome occuring in Children (MIS-C)
Pediatric Inflammatory Multisystem Syndrome (PIMS)

Myocarditis epidemics/ Inflammatory syndrome in children

- In France **National effort of pediatricians** thanks to
  - Santé publique France
  - GPIP, GFRUP, SOFREMIP, Société cardiologie filiale cardiologie pédiatrique, FAI2R & SFP.
- New case notification-> national surveillance

Results of the national Surveillance

Eurosurveillance Europe's journal on infectious disease surveillance, epidemiology, prevention and control

RAPID COMMUNICATION

SARS-CoV-2-related paediatric inflammatory multisystem syndrome, an epidemiological study, France, 1 March to 17 May 2020

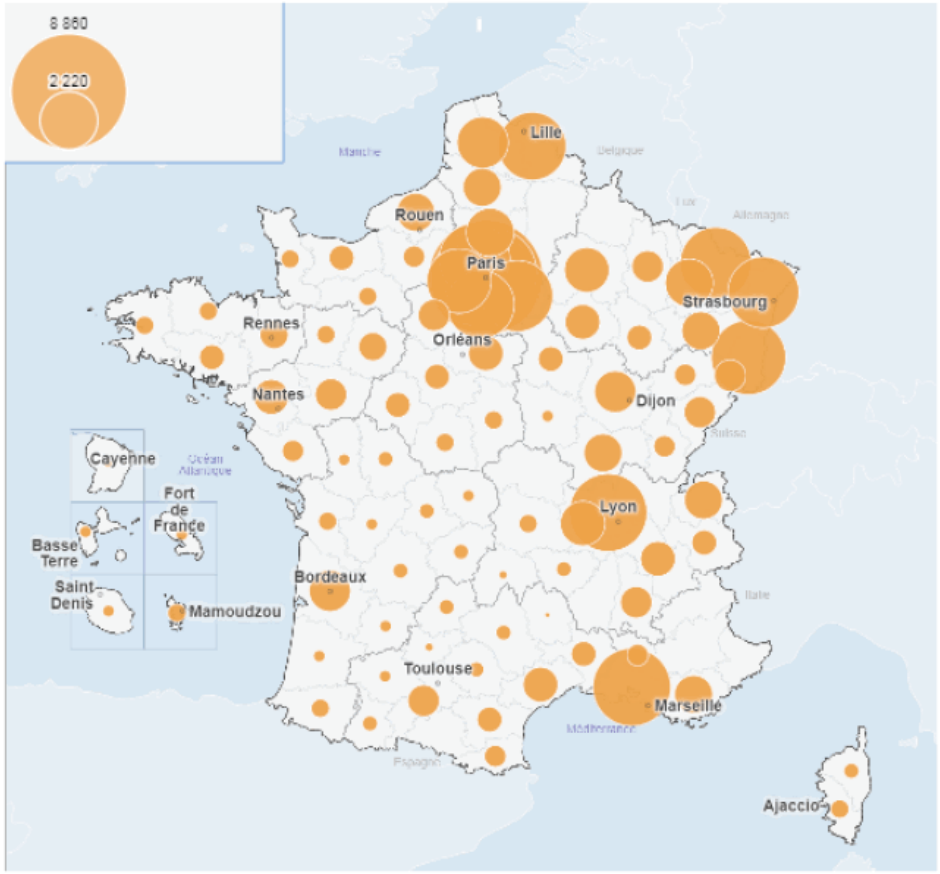
Alexandre Belot[1], Denise Antona[2], Sylvain Renolleau[3], Etienne Javouhey[3], Véronique Hentgen[4], François Angoulvant[4], Christophe Delacourt[5], Xavier Iriart[6], Caroline Ovaert[6], Brigitte Bader-Meunier[7], Isabelle Kone-Paut[7], Daniel Levy-Bruhl[2]

1. Filière de santé des maladies auto-immunes et auto-inflammatoires rares (FAI2R), Lyon, France
2. Santé Publique France, Agence nationale de Santé publique, Saint-Maurice cedex, France
3. Groupe francophone de réanimation et d'urgences pédiatriques (GFRUP), Paris, France
4. Groupe de pathologies infectieuses pédiatriques (GPIP), Nice, France
5. Société Française de Pédiatrie (SFP), Paris, France
6. Société Française de Cardiologie, filiale de Cardiologie pédiatrique et congénitale (FCPC), Paris, France
7. Société francophone dédiée à l'étude des maladies inflammatoires pédiatriques (SOFREMIP), Paris, France

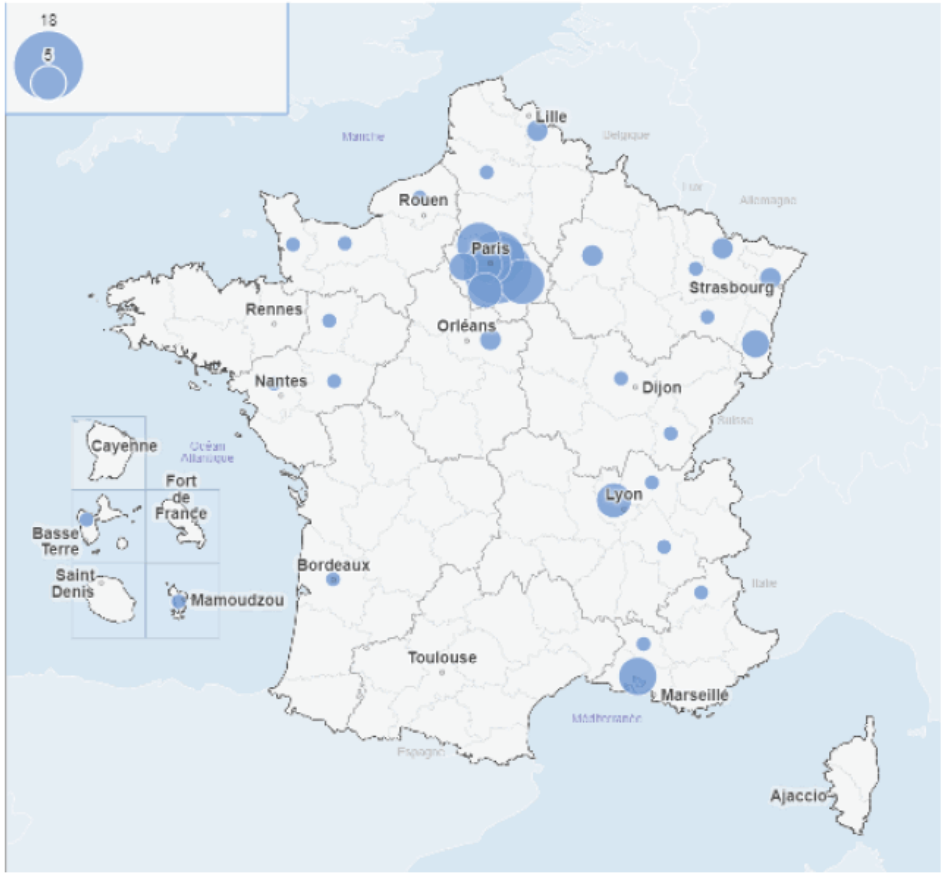
Correspondence: Alexandre Belot (alexandre.belot@chu-lyon.fr)

Spatial link to COVID-19 Pandemy

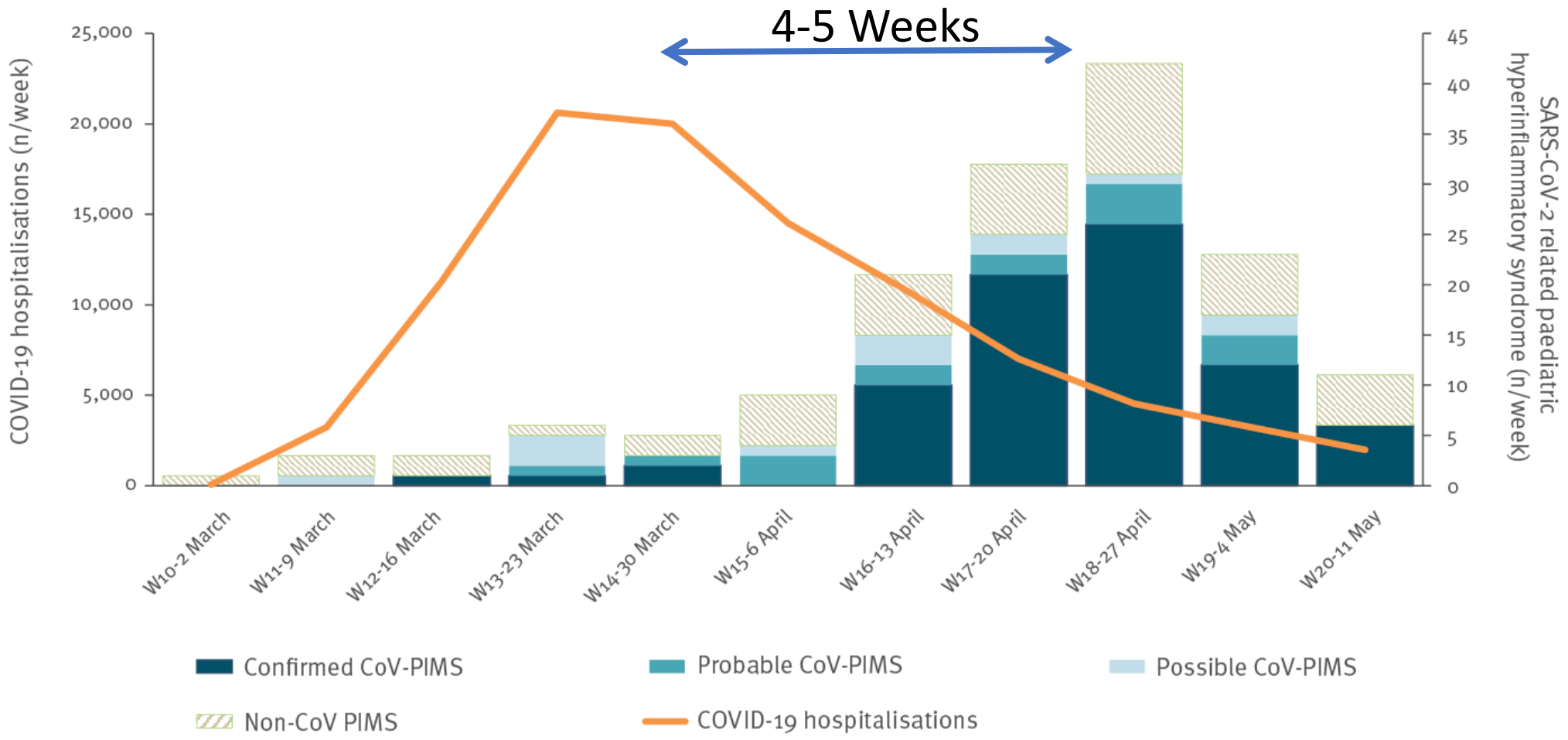
A. COVID-19 hospitalisations (n = 106,500)



B. CoV-PIMS cases (n = 108)



Temporal link to COVID-19 Pandemic



N=108

Temporal link to COVID-19 Pandemic

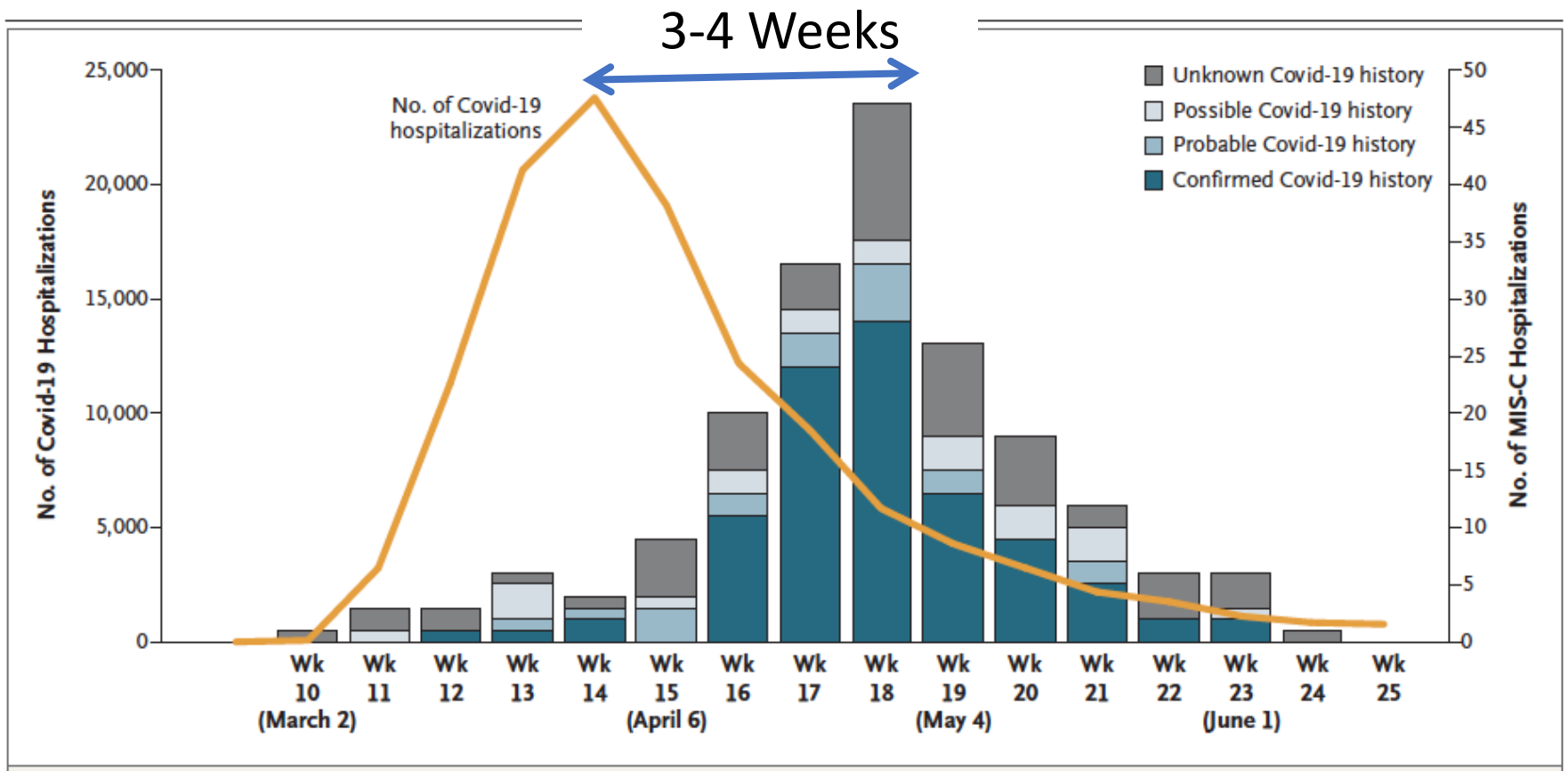
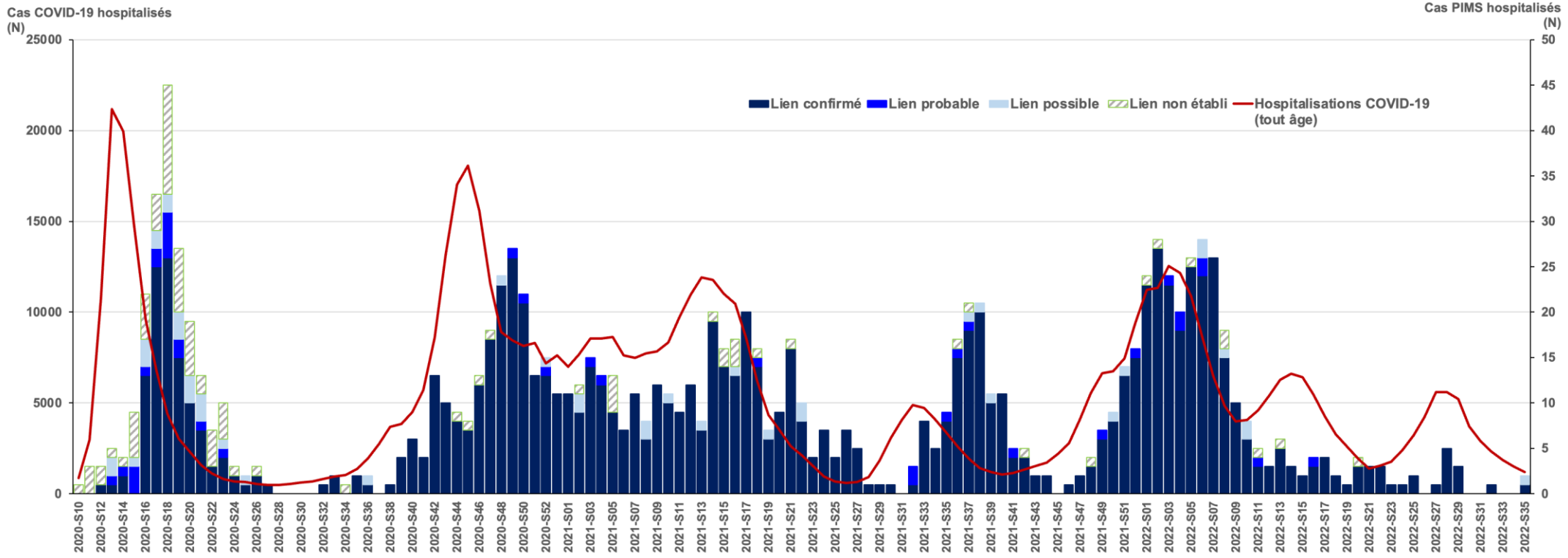


Figure 1. Temporal Distribution of Hospitalizations for Covid-19 and MIS-C in France.

Between March 2 and June 21, 2020, a total of 195 hospitalizations for the multisystem inflammatory syndrome in children (MIS-C) were reported in France, of which 138 cases were classified as being associated (possible, probable, or confirmed history) with SARS-CoV-2, the virus that causes coronavirus disease 2019 (Covid-19). Also shown is the number of hospitalizations for Covid-19 in the general population in France.

N=195

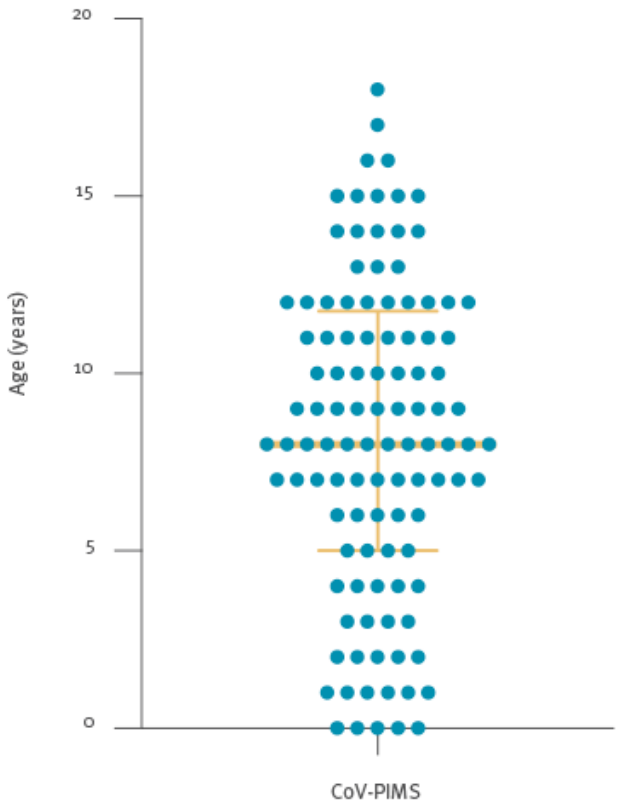
MIS-C case distribution / COVID_19 (all age) per week, France, 02/03/2020- 04/09/2022, n=1160

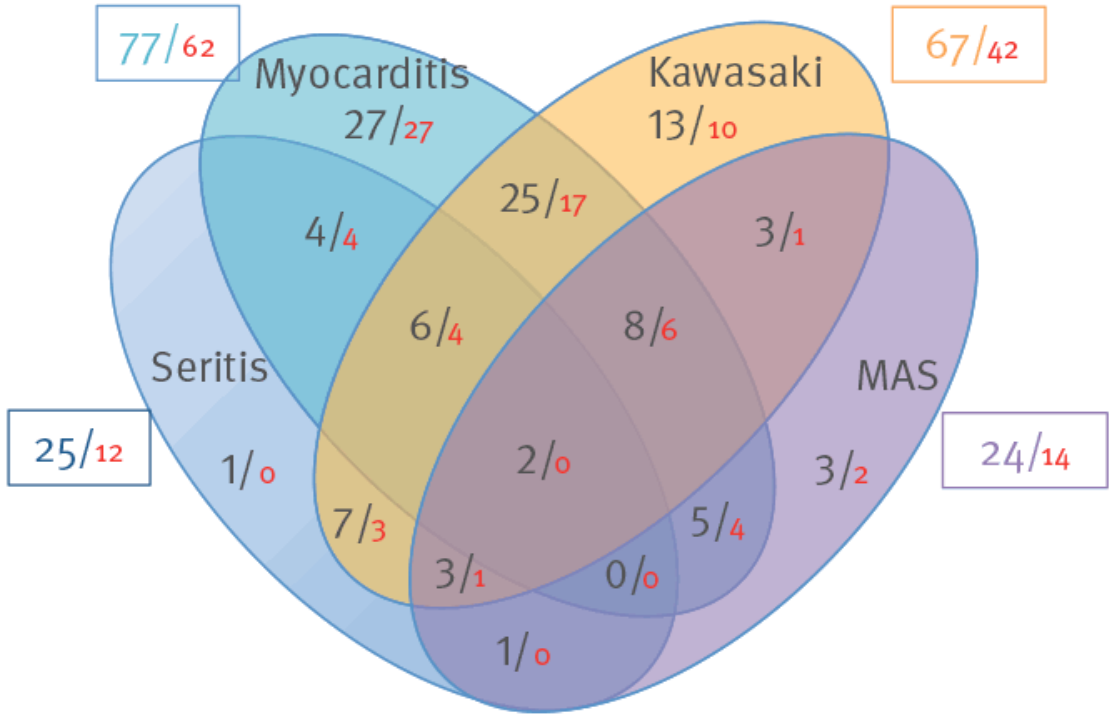


Santé publique France

* Données provisoires à la date de l'analyse

A broad spectrum of symptoms
“Kawa-like disease”

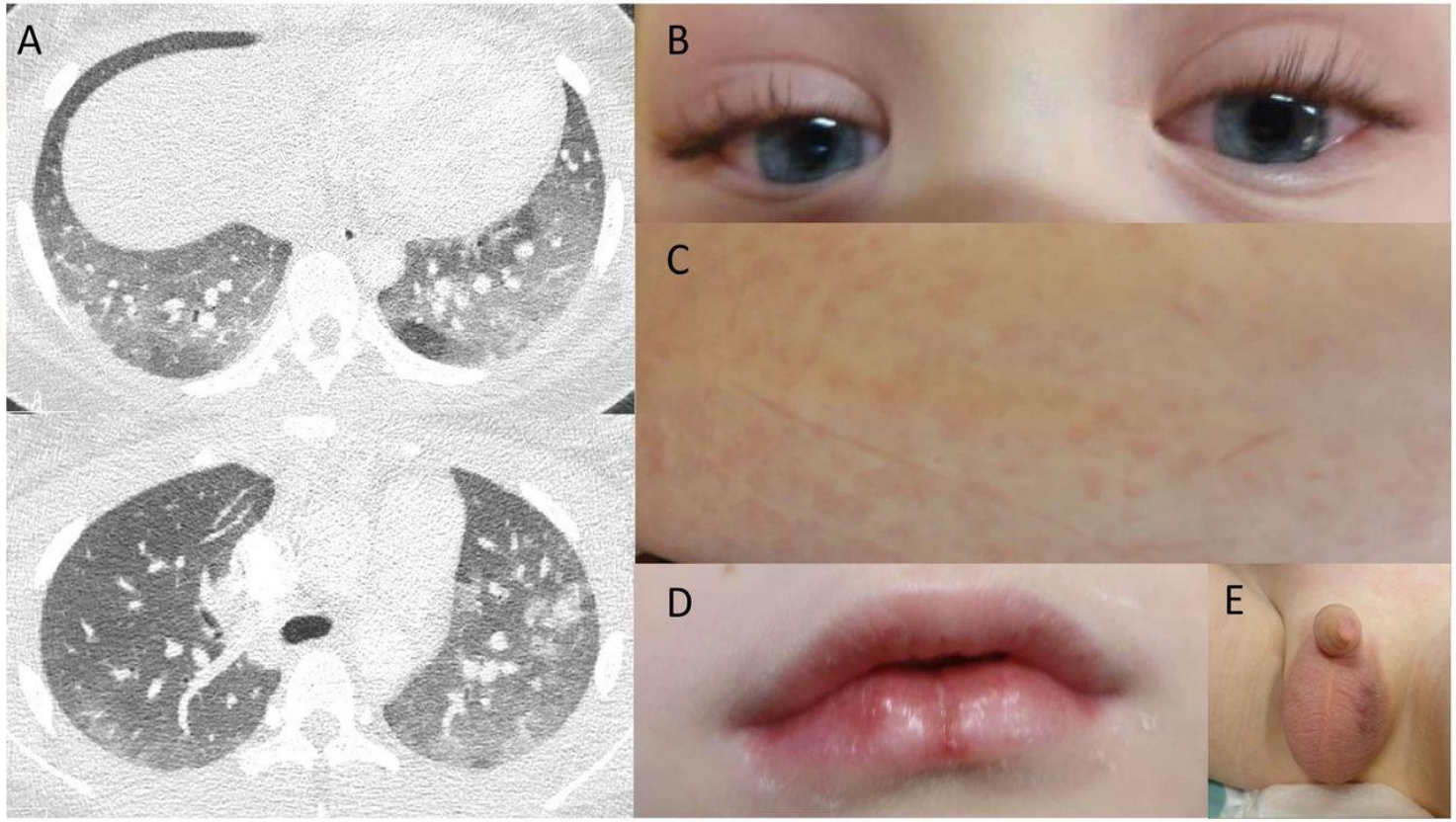


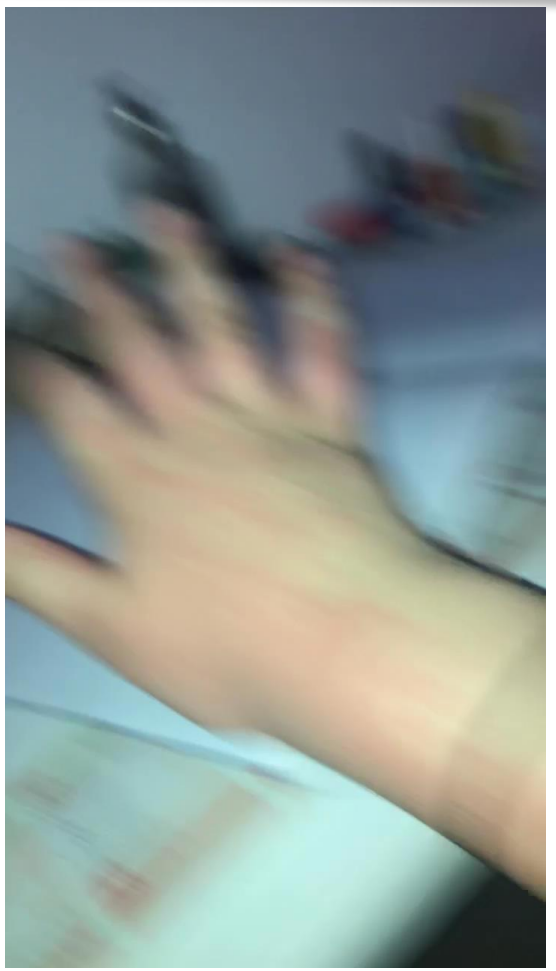


2/3
in
intensive
care unit

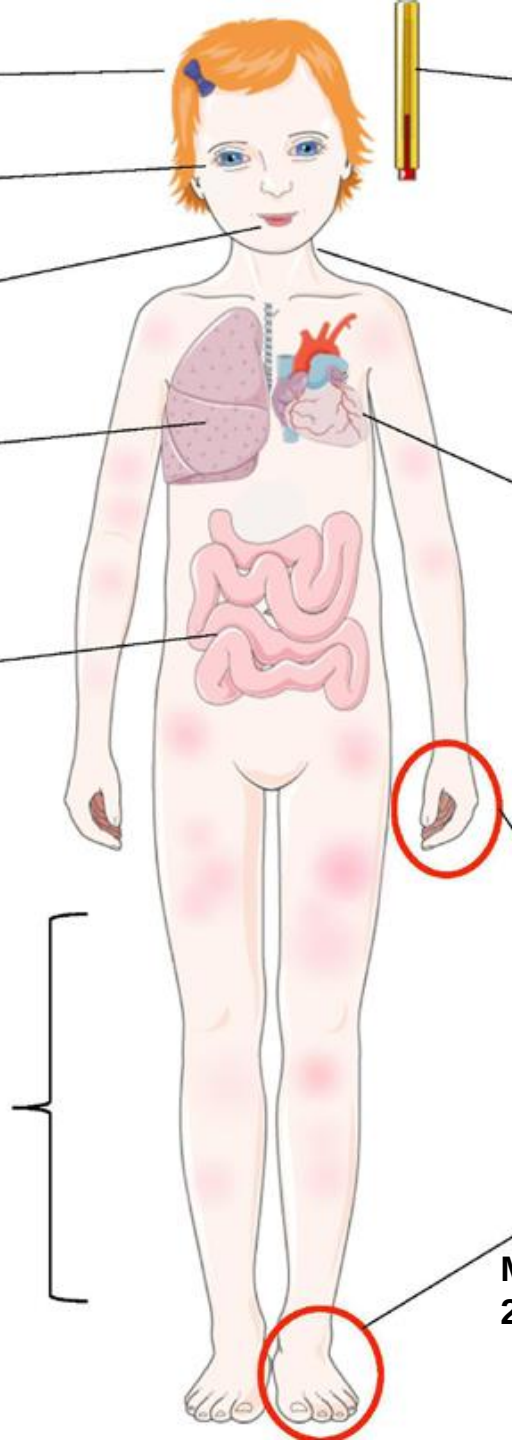
ALL COV-PIMS (n = 108)
Confirmed CoV-PIMS (n = 79)

Clinical characteristics





Marie Pouletty et al. Ann Rheum Dis doi:10.1136/annrheumdis-



Neurological signs 56%

Conjunctivitis 94%

Red and cracked lips 87%

Respiratory signs 12%

Gastrointestinal signs 81%

Diffuse skin rash 81%

Fever> 4 days 100%

Cervical adenopathy >1.5cm 37%

Coronary dilations 19%
14% in severe forms
Pericarditis 25%
14% in severe forms
Myocarditis 44%
86% in severe forms

Hands and feet oedema,
Redness at palms and soles
68%

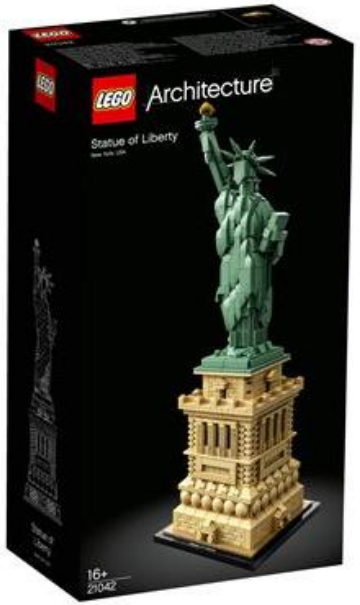
Kawa-COVID-19
Children 10 years [4.7-12.5]
M/F: 1

Marie Pouletty et al. Ann Rheum Dis doi:10.1136/annrheumdis-2020-217960

treatment

NOT the same
BUT Looks Like the same

NOT the same at all



Kawasaki Disease

MIS-C

Think to
another diagnosis

treatment

AHA SCIENTIFIC STATEMENT

Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease

A Scientific Statement for Health Professionals From the American Heart Association

Mc Crindle BW, Circulation 2017

Empiric therapies based on Kawasaki disease guidelines, mainly:

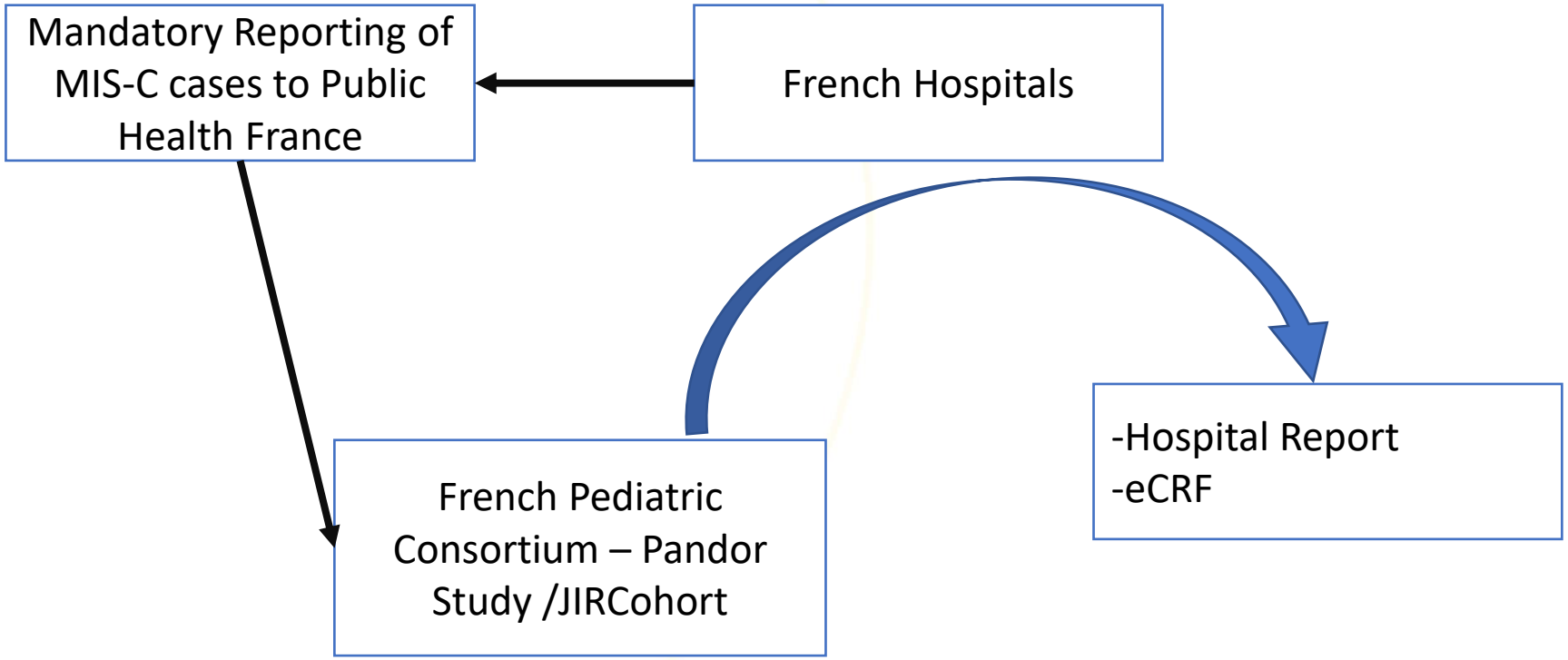
- IVIG alone
- IVIG+steroids

- IVIG-Resistant Kawasaki Diseases
- Kawasaki diseases with shock

treatment

- IV IG 2g/kg (as for Kawasaki Disease)

Data Source


Mandatory Reporting of MIS-C cases to Public Health France
French Hospitals
French Pediatric Consortium – Pandor Study /JIRCohort
-Hospital Report
-eCRF

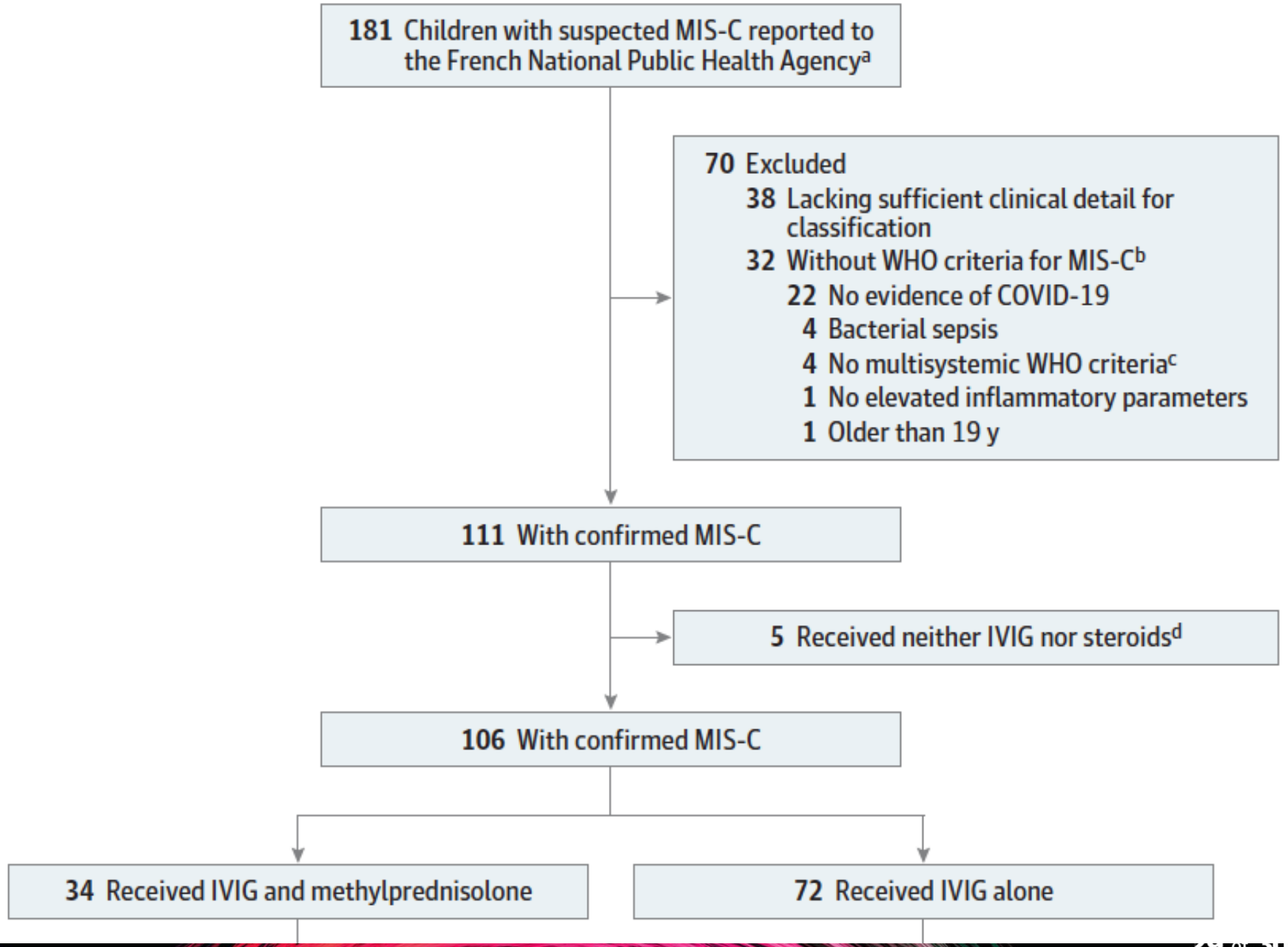
Research

JAMA | Original Investigation

Association of Intravenous Immunoglobulins Plus Methylprednisolone vs Immunoglobulins Alone With Course of Fever in Multisystem Inflammatory Syndrome in Children

Naïm Ouldali, MD, PhD; Julie Toubiana, MD, PhD; Denise Antona, MD; Etienne Javouhey, MD, PhD; Fouad Madhi, MD; Mathie Lorrot, MD, PhD; Pierre-Louis Léger, MD, PhD; Caroline Galeotti, MD, PhD; Caroline Claude, MD; Arnaud Wiedemann, MD, PhD; Noémie Lachaume, MD; Caroline Ovaert, MD, PhD; Morgane Dumortier, MD; Jean-Emmanuel Kahn, MD, PhD; Alexis Mandelcwajg, MD; Lucas Percheron, MD; Blandine Biot, MD; Jeanne Bordet, MD; Marie-Laure Girardin, MD; David Dawei Yang, MD; Marion Grimaud, MD; Mehdi Oualha, MD, PhD; Slimane Allali, MD, PhD; Fanny Bajolle, MD; Constance Beyler, MD; Ulrich Meinzer, MD, PhD; Michael Levy, MD, PhD; Ana-Maria Paulet, MD; Corinne Levy, MD; Robert Cohen, MD; Alexandre Belot, MD, PhD; François Angoulvant, MD, PhD; for the French Covid-19 Paediatric Inflammation Consortium

Ouldali et al. JAMA 2021


181 Children with suspected MIS-C reported to the French National Public Health Agency[a]
70 Excluded
38 Lacking sufficient clinical detail for classification
32 Without WHO criteria for MIS-C[b]
22 No evidence of COVID-19
4 Bacterial sepsis
4 No multisystemic WHO criteria[c]
1 No elevated inflammatory parameters
1 Older than 19 y
111 With confirmed MIS-C
5 Received neither IVIG nor steroids[d]
106 With confirmed MIS-C
34 Received IVIG and methylprednisolone
72 Received IVIG alone

	IVIG group + methylprednisolone (n=34)	IGIV alone group (n=72)
Primary outcome		
Treatment failure (Persistent fever > 24H)	3 (9%)	37 (51%)
Secondary outcomes		
Second-line treatment	3 (9%)	33 (46%)
Hemodynamic support	2 (6%)	17 (24%)
LVEF <55%	2/12 (17%)	16/44 (36%)
Duration of PICU stay, median (IQR) d	4 (2-5)	6 (4-8.5)

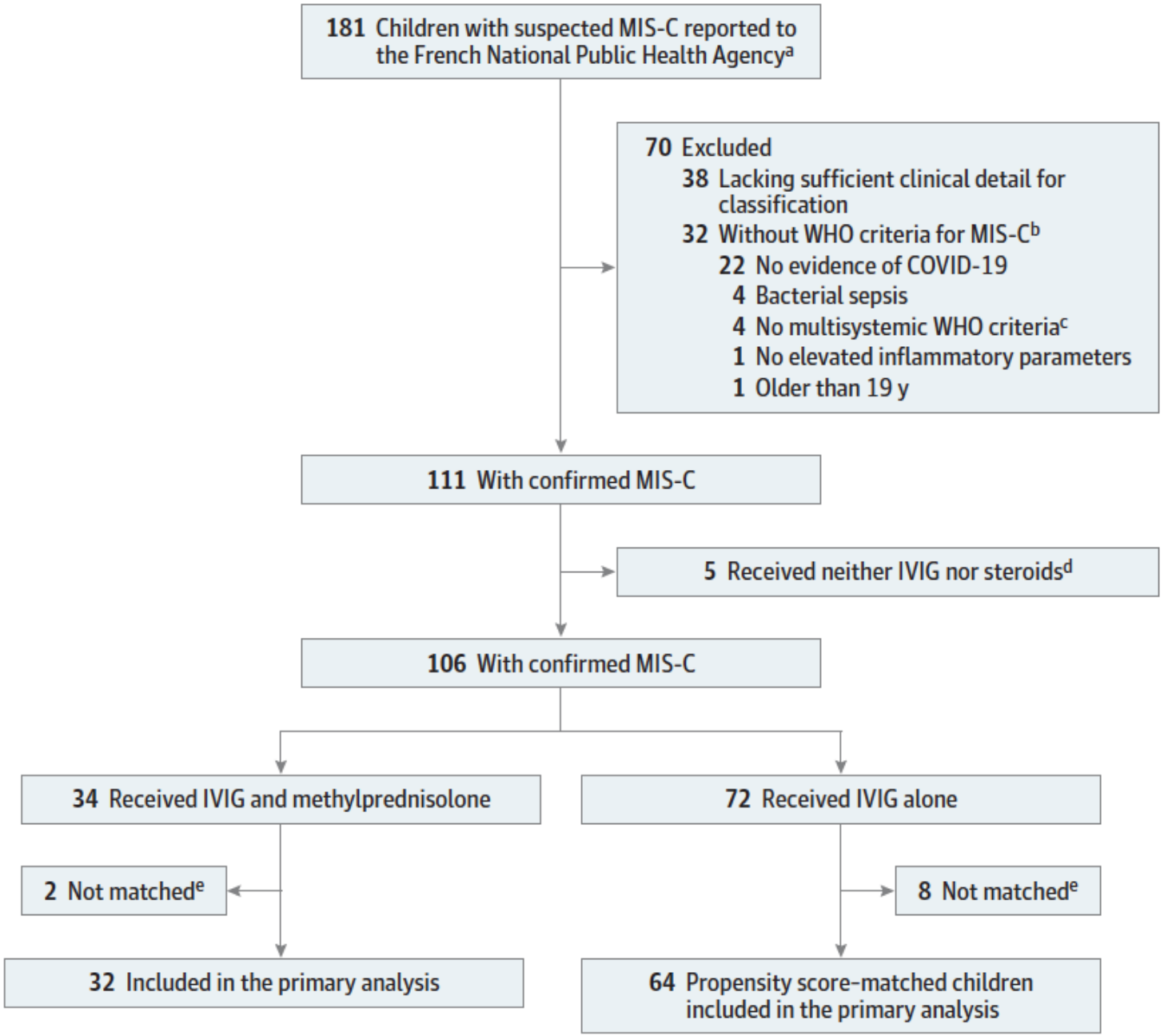

181 Children with suspected MIS-C reported to the French National Public Health Agency[a]
70 Excluded
38 Lacking sufficient clinical detail for classification
32 Without WHO criteria for MIS-C[b]
22 No evidence of COVID-19
4 Bacterial sepsis
4 No multisystemic WHO criteria[c]
1 No elevated inflammatory parameters
1 Older than 19 y
111 With confirmed MIS-C
5 Received neither IVIG nor steroids[d]
106 With confirmed MIS-C
34 Received IVIG and methylprednisolone
72 Received IVIG alone
2 Not matched[e]
8 Not matched[e]
32 Included in the primary analysis
64 Propensity score-matched children included in the primary analysis

Table 2. Primary and Secondary Analyses in the Propensity Score–Matched Cohorts

Outcomes	After propensity score matching				
	No. (%)		Absolute risk difference between groups (95% CI) [reference: IVIG alone]	Odds ratio (95% CI) [reference: IVIG alone]	*P* value
	IVIG and methylprednisolone (n = 32)	IVIG alone (n = 64)			
Primary outcome					
Treatment failure[a]	3 (9)	24 (38)	−0.28 (−0.48 to −0.08)	0.25 (0.09 to 0.70)	.008
Secondary outcomes					
Second-line treatment[b]	3 (9)	20 (31)	−0.22 (−0.40 to −0.04)	0.19 (0.06 to 0.61)	.004
Hemodynamic support[c,d]	2 (6)	15 (23)	−0.17 (−0.34 to −0.004)	0.21 (0.06 to 0.76)	.01
LVEF <55%[c]	2/12 (17)	14/40 (35)	−0.18 (−0.35 to −0.01)	0.20 (0.06 to 0.66)	.007
Duration of PICU stay, median (IQR), d	4 (2 to 5)	6 (4 to 8.5)	Reduction of days: −2.4 (−4.0 to −0.7)		.005

Ouldali et al. JAMA 2021

Treatment

- IV IG 2g/kg (as for Kawasaki Disease)
- **Steroids ++**

(quasi-randomized propensity score matching analysis in 111 children)

- Cs or biologicals in 31%.

(1 cas anakinra 1 cas tocilizumab)

Traitement immunomodulateur (MAJ18/03/2021)

Instabilité hémodynamique ou Lactate élevé ou défaillance myocardique à l'échographie

- Corticothérapie anti-inflammatoire (2mg/kg) IV*

-IVIG* haute dose fractionnée (fractionnée 1g/kg/j sur 2j), débit très lent voire à différer si dysfonction auriculaire / défaillance diastolique (selon avis réanimateur)
-Antibiothérapie* (à suspendre selon microbiologie)
-Vasopresseurs/inotropes
-Anticoagulation, pas d'aspirine*

Pas d'instabilité hémodynamique et Lactate normaux

-Corticothérapie anti-inflammatoire (2mg/kg) IV*

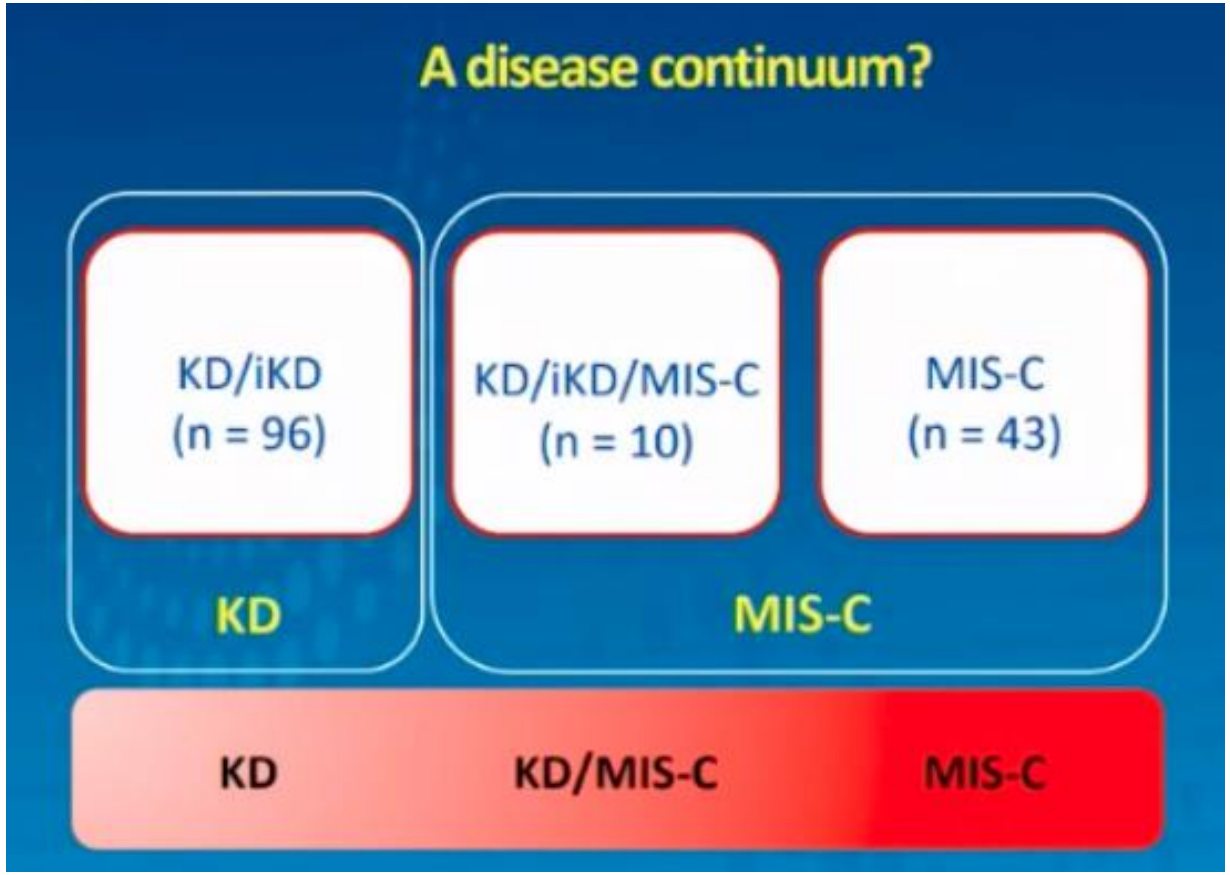
-IVIG* haute dose fractionnée 1g/kg/j sur 2j

-Aspirine antiagrégant* si atteinte coronarienne

En USC si elevation enzyme myocardique sans insuffisance circulatoire

ATTENTION NE PAS MECONNAITRE choc toxinique / septique / hémopathie maligne
⇒ PEC Sepsis Survival campaign & reco européenne
⇒ En cas de doute, contacter le réanimateur pédiatre
Si échec du traitement de première ligne, contacter rhumatopédiatre/ Immunologiste

MIS-C : A new inflammatory disease ?



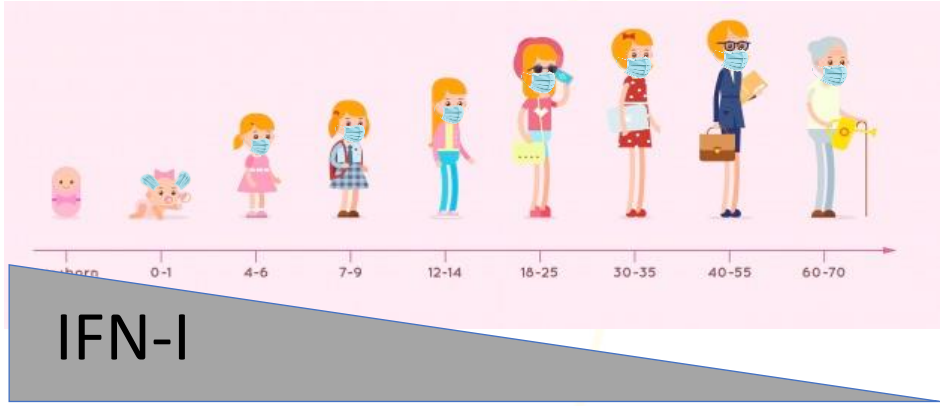
- KD et MISC : Serology or positive PCR
- Same population = children
- Fever, rash, conjonctivitis et cheliitis
- PasNo other circulating viruses

Ravelli et al. ISSAID 2021

What is the pathogenesis of MIS-C ?

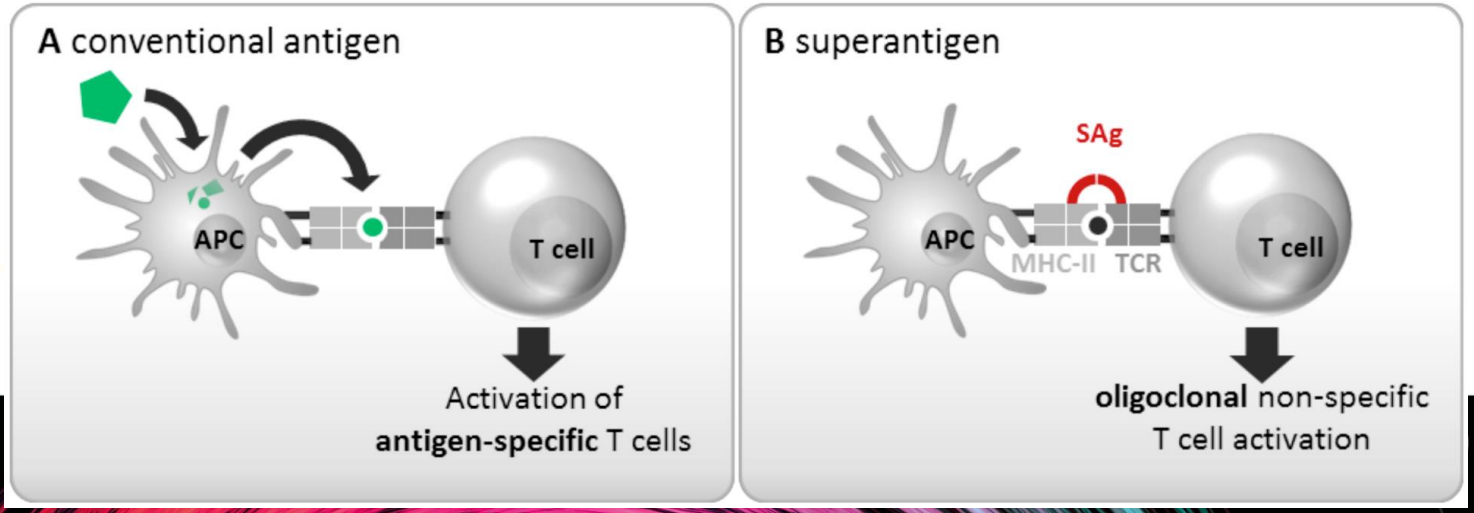
Phenotype of Kawaski disease versus Toxic Shock Syndrome

Excess of Type I IFN ?



Low IFN in severe COVID-19
Trouillet Assant 2020
Hadjadj et al 2020
Bastard et al 2020

Superantigenic effect ?



PIMS/MIS-C Study

Marion Moreews
PhD *Student*

Science Immunology

RESEARCH ARTICLES

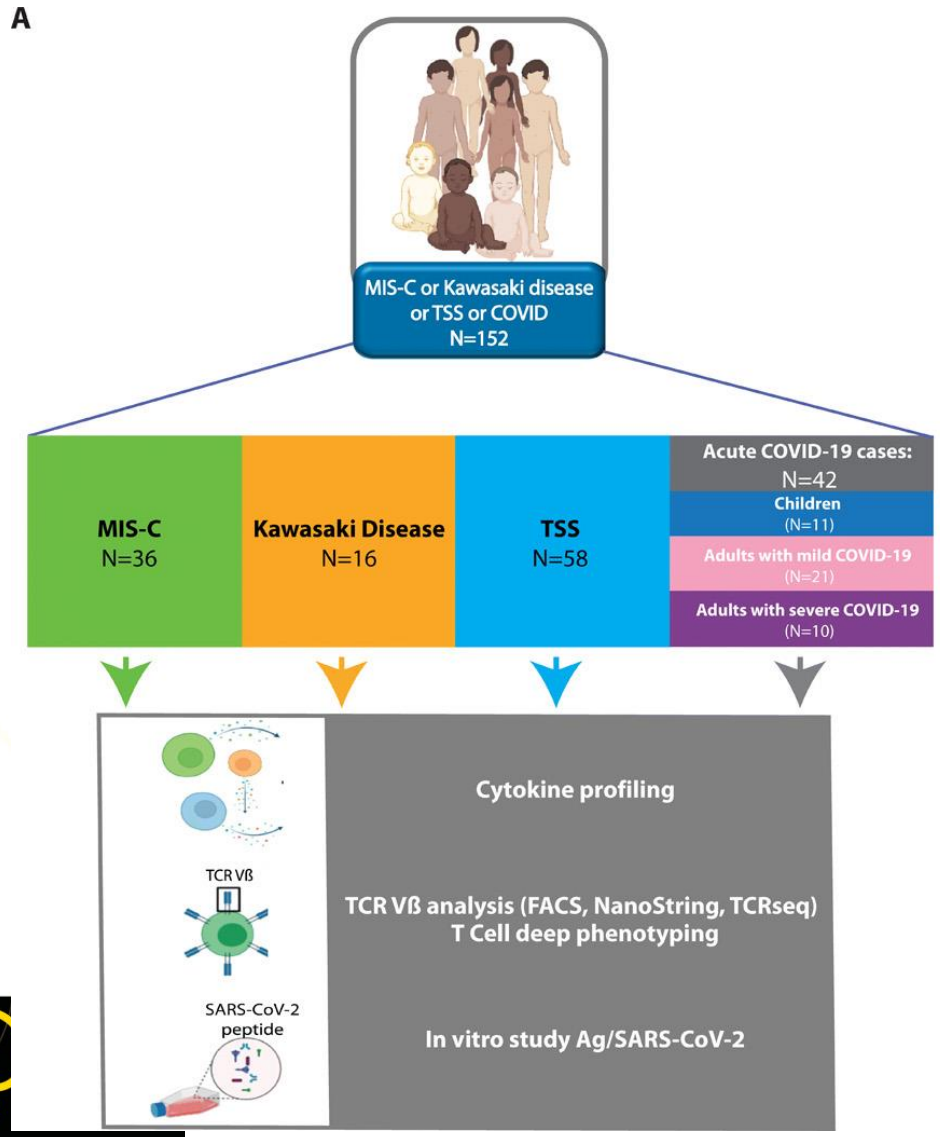
Cite as: M. Moreews *et al.*, *Sci. Immunol.* 10.1126/sciimmunol.abh1516 (2021).

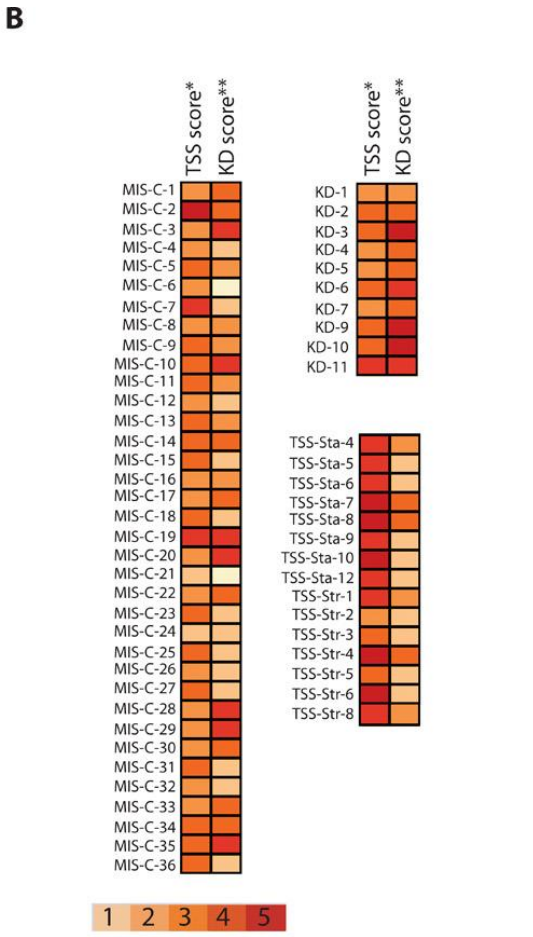
CORONAVIRUS

Polyclonal expansion of TCR Vbeta 21.3^{+} CD4^{+} and CD8^{+} T cells is a hallmark of Multisystem Inflammatory Syndrome in Children

Marion Moreews[1], Kenz Le Gouge[2]†, Samira Khaldi-Plassart[3,4]†, Rémi Pescarmona[1,4,5]†, Anne-Laure Mathieu[1*], Christophe Malcus[6,7], Sophia Djebali[1], Alicia Bellomo[1], Olivier Dauwalder[1,8], Magali Perret[1,5], Marine Villard[1,5], Emilie Chopin[9], Isabelle Rouvet[9], Francois Vandenesh[1,8], Céline Dupieux[1,8], Robin Pouyau[10], Sonia Teyssedre[10], Margaux Guerder[10], Tiphaine Louazon[11], Anne Moulin-Zinsch[12], Marie Duperril[13], Hugues Patural[13,14], Lisa Giovannini-Chami[15,16], Aurélie Portefaix[17], Behrouz Kassai[17], Fabienne Venet[1,6], Guillaume Monneret[6,7], Christine Lombard[5], Hugues Flodrops[18], Jean-Marie De Guillebon[19], Fanny Bajolle[20], Valérie Launay[21], Paul Bastard[22,23], Shen-Ying Zhang[22,23,24], Valérie Dubois[25], Olivier Thaunat[1,25,26,27], Jean-Christophe Richard[28,29], Mehdi Mezidi[28,29], Omran Allatif[1], Kahina Saker[1,30], Marlène Dreux[1], Laurent Abel[22,23,24], Jean-Laurent Casanova[22,23,24,31], Jacqueline Marvel[1], Sophie Trouillet-Assant[1,30], David Klatzmann[2,32], Thierry Walzer[1]†, Encarnita Mariotti-Ferrandiz[2,32]†, Etienne Javouhey[7,10]†, Alexandre Belot[1,6*]

PIMS/MIS-C Study





* TSS majors criterias according https://wwwn.cdc.gov/nndss/conditions/toxic-shock-syndrome-other-than-streptococcal/case-definition/2011/

**Kawasaki principle criteria other than fever :Brian W. et al., circulation.2017

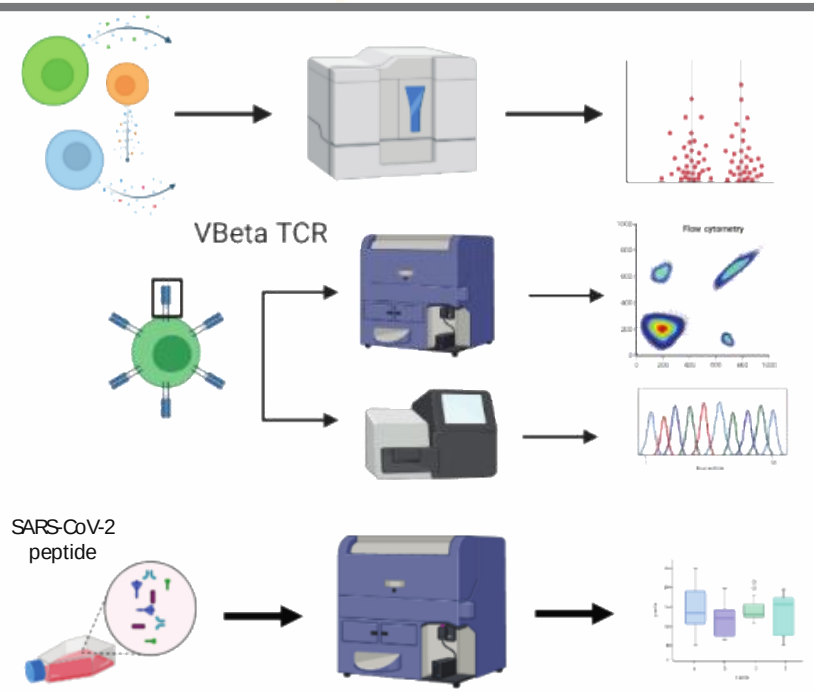
Moreews et al Science Immunol 2021

Exploration MIS-C

Cytokine profiling

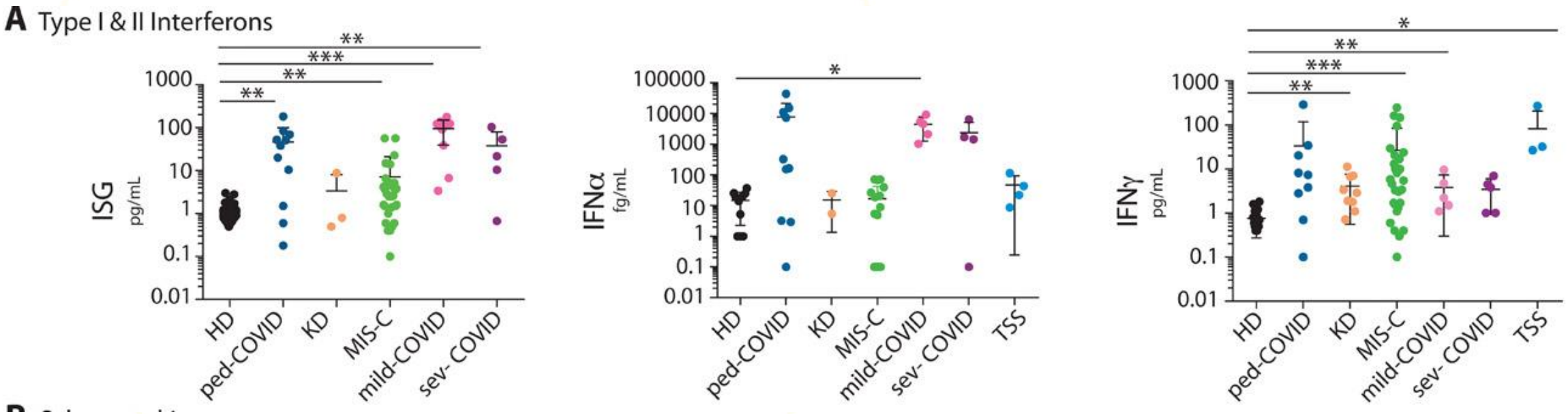
Vbeta analysis
(FACS, NanoString, TCRseq)
T Cell deep phenotyping

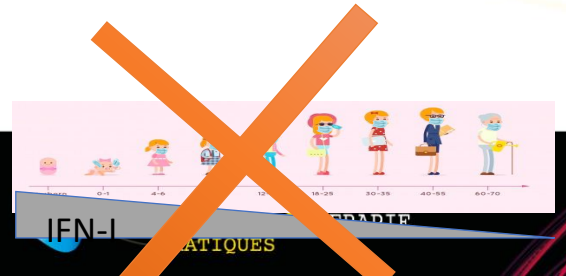
In vitro study Ag/SARS-CoV-2



Moreews et al

Interferons & MIS-C





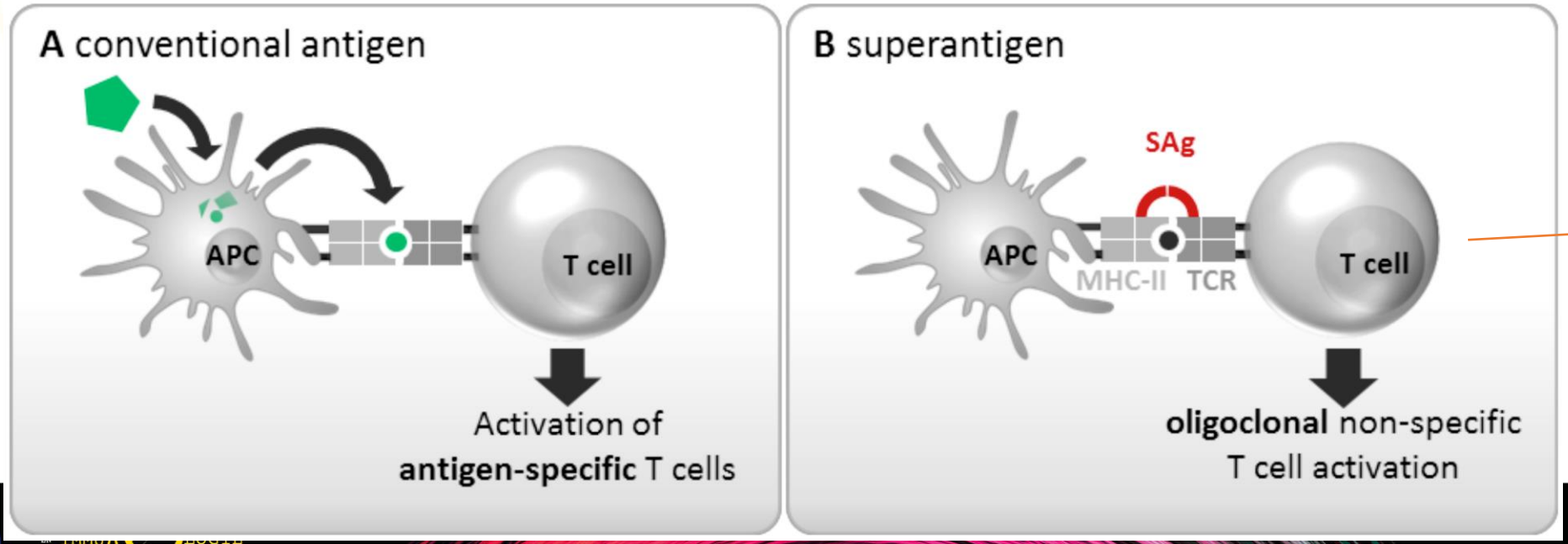
No increase of type IFNa in **MIS-C**

Moreews et al

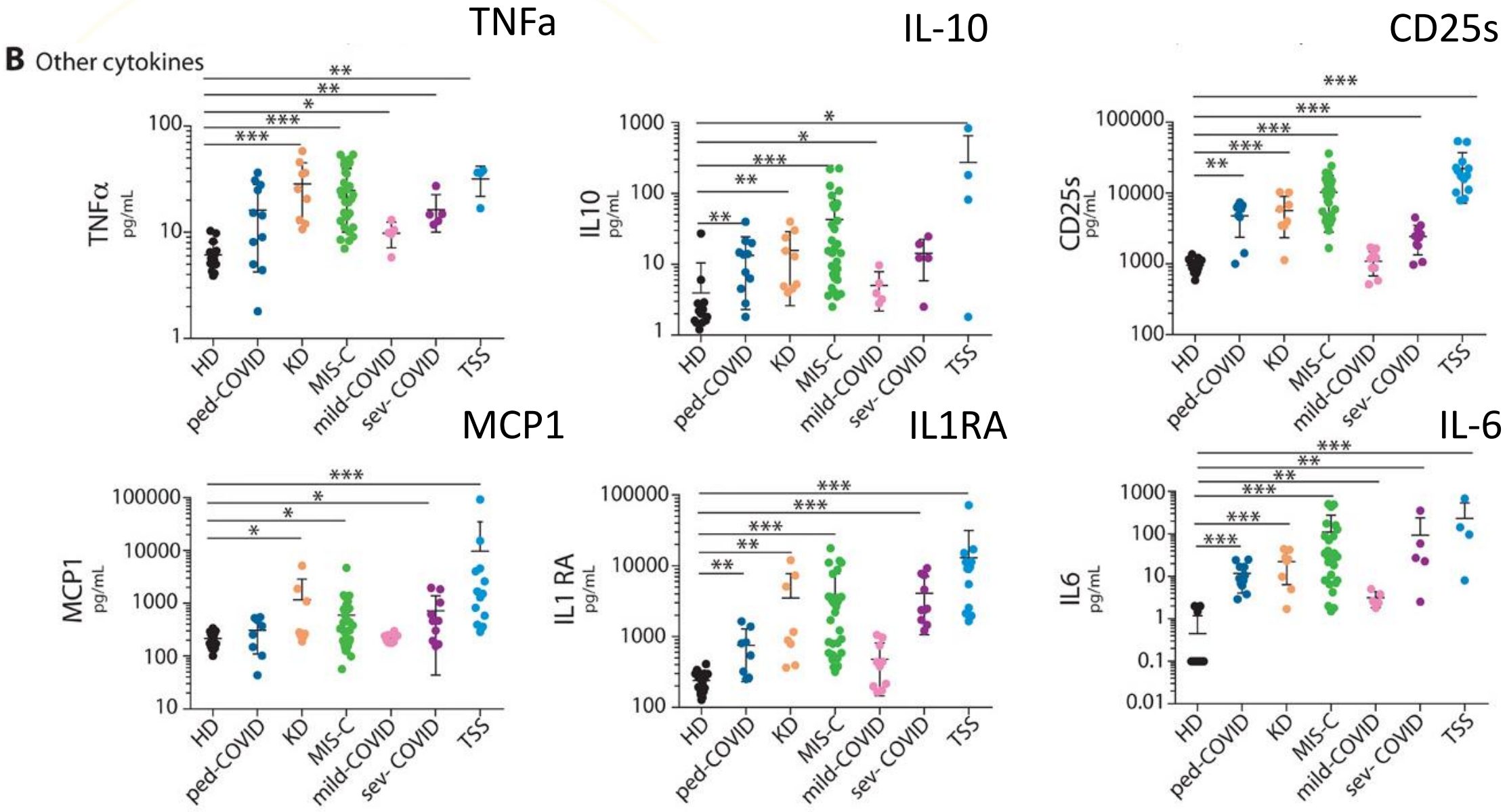
Superantigenic response

- 1/10 000
- Tcell specific monoclonal response
- MHC restricted

- 1/20
- Tcell polyclonal expansion
- MHC independent



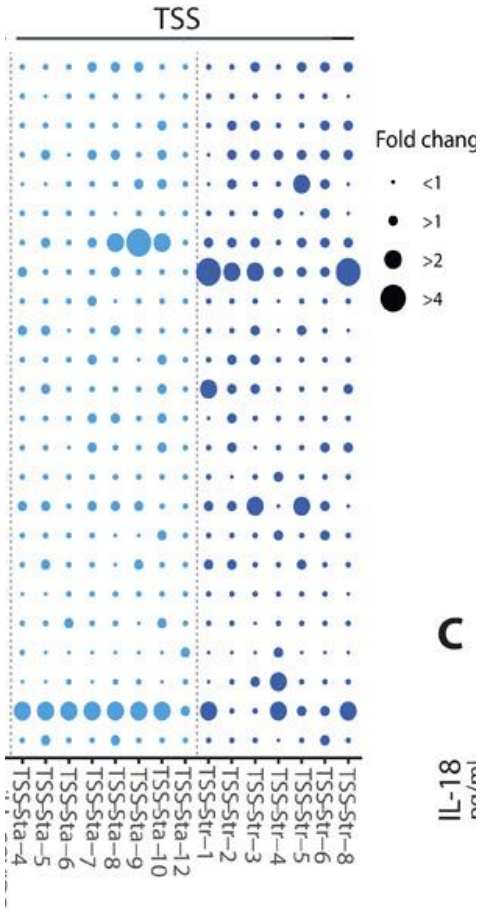
Vbeta expansion
Clonal deletion / anergy



Moreews et al

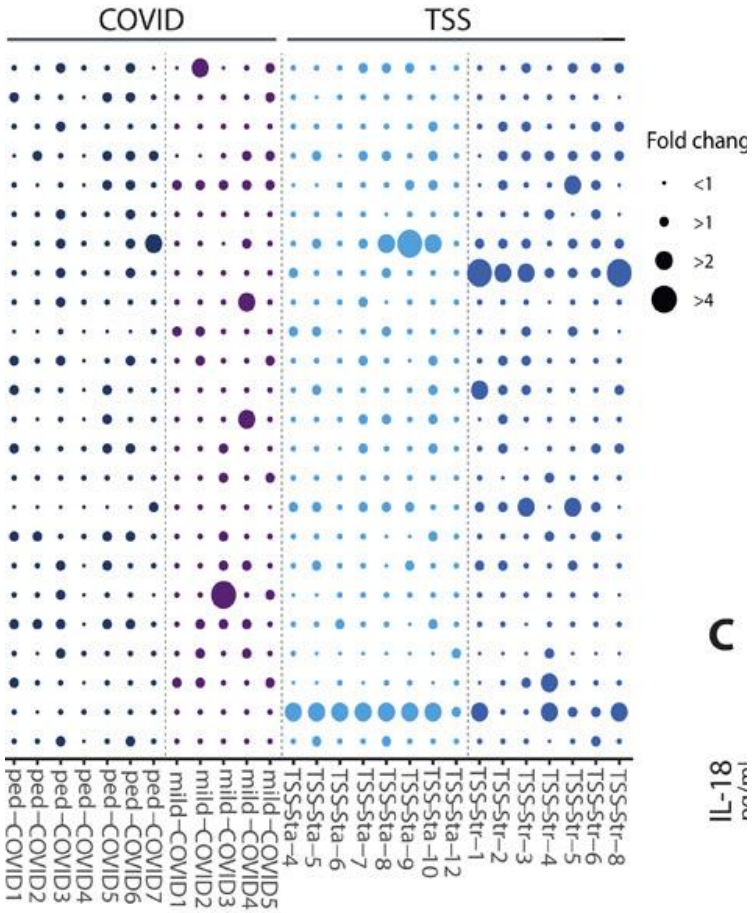
Similar cytokine pattern between MIS-C & TSS

Répertoire T & MIS-C



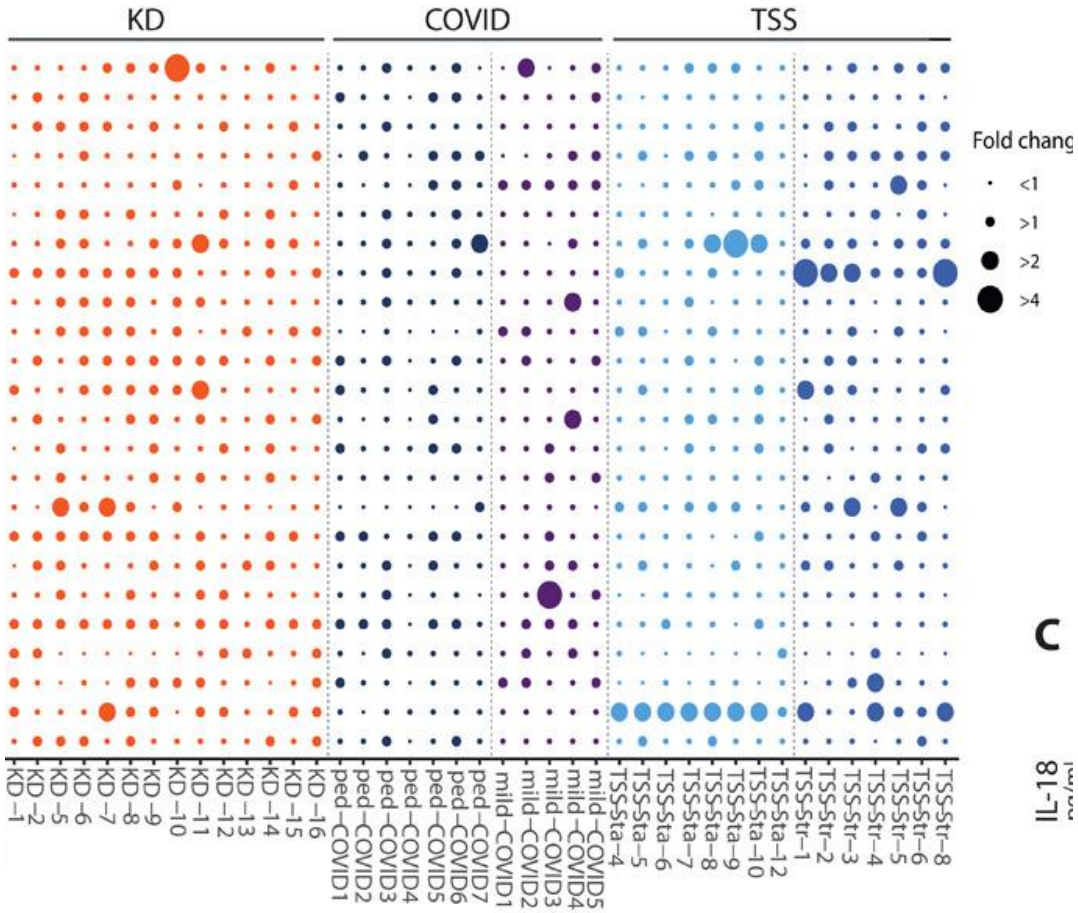
Moreews et al Science Immunol 2021

Répertoire T & MIS-C



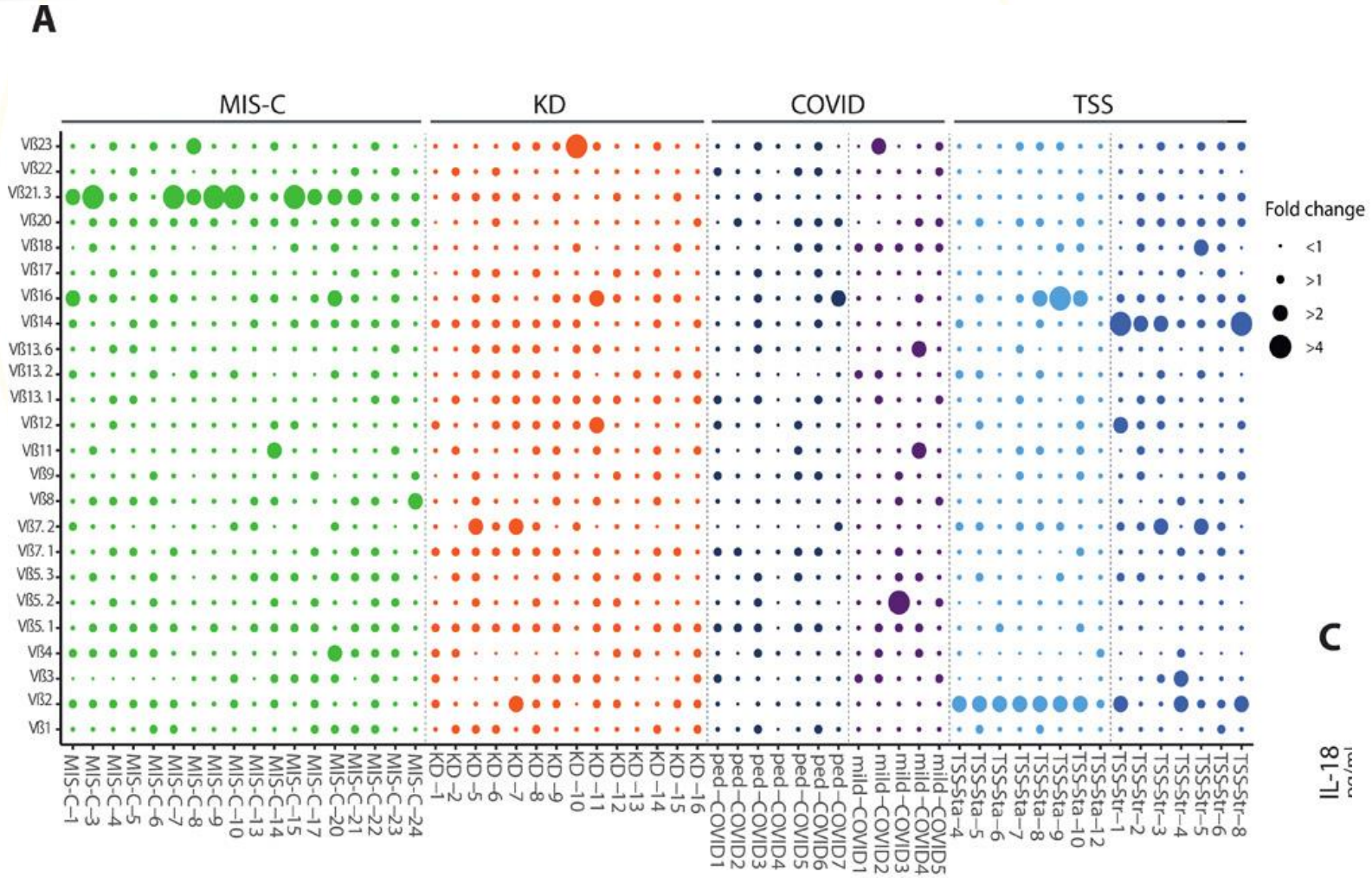
Moreews et al Science Immunol 2021

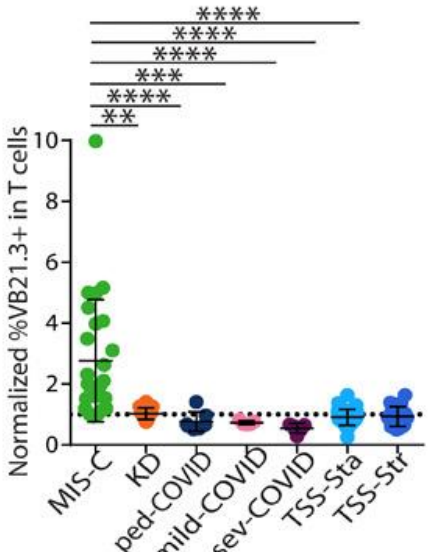
Répertoire T & MIS-C



Moreews et al Science Immunol 2021

Répertoire T & MIS-C





C

IL-18

Expansion des T Vb21.3 dans 75% des **MIS-C** (by FACS)

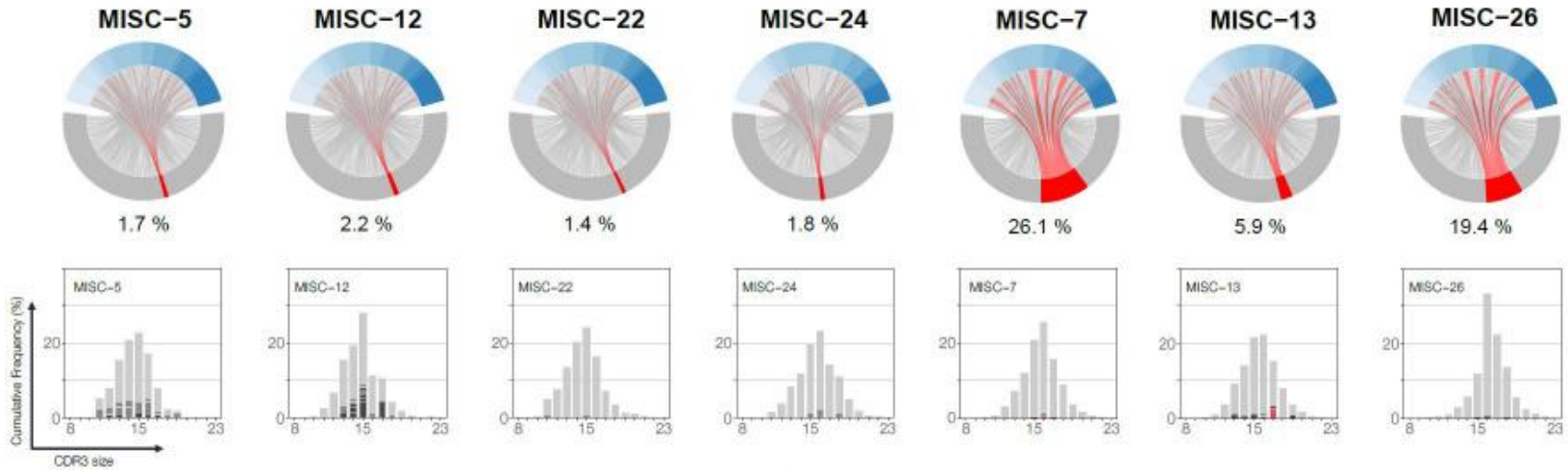
Moreews et al Science Immunol 2021

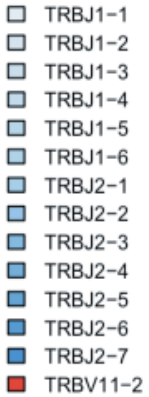
Tcells repertoire & MIS-C

TRBJ

TRBV (11-2)

CDR3 size

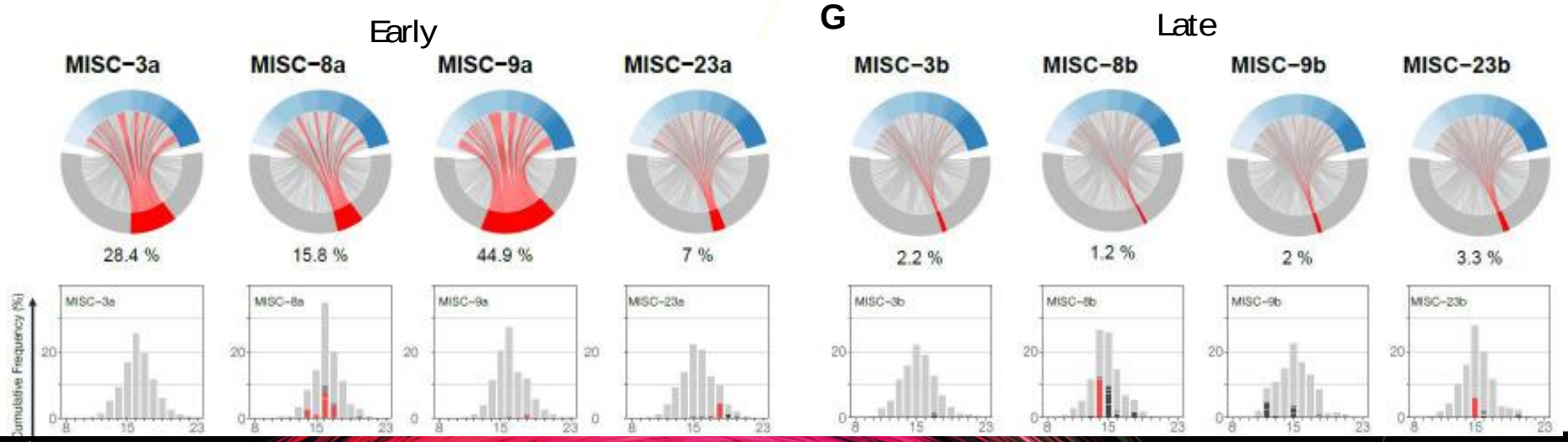




TRBJ

TRBV (11-2)

CDR3 size



Polyclonal activation of TRBV11-2/Vb21.3 expanded T cells

The Journal of Clinical Investigation RESEARCH ARTICLE

HLA class I–associated expansion of TRBV11-2 T cells in multisystem inflammatory syndrome in children

Rebecca A. Porritt,[1,2] Lisa Paschold,[1] Magali Noval Rivas,[1,2] Mary Hongying Cheng,[4] Lael M. Yonker,[1] Harsha Chandnani,[1] Merrick Lopez,[5] Donjete Simonica,[3] Christoph Schultheiß,[3] Chintda Santiskulvong,[3] Jennifer Van Eyk,[3] John K. McCormick,[6] Alessio Fasano,[5] Ivet Bahar,[4] Mascha Binder,[3] and Moshe Arditi[1,7,8]

JEM Journal of Experimental Medicine

Article | December 16 2021

TIM3+ *TRBV11-2* T cells and IFNγ signature in patrolling monocytes and CD16+ NK cells delineate MIS-C

Levi Hoste, Lisa Roels, Leslie Naesens, Victor Bosteels, Stijn Vanhee, Sam Dupont, Cedric Bosteels, Robin Browaeys, Niels Vandamme, Kevin Verstaen, Jana Roels, Karel F.A. Van Damme, Bastiaan Maes, Elisabeth De Leeuw, Jozefien Declercq, Helena Aegerter, Leen Seys, Ursula Smole, Sofie De Prijck, Manon Vanheerswynghels, Karlien Claes, Veronique Debacker, Gert Van Isterdael, Lynn Backers, Kathleen B.M. Claes, Paul Bastard, Emmanuelle Jouanguy, Shen-Ying Zhang, Gilles Mets, Joke Dehoorne, Kristof Vandekerckhove, Petra Schelstraete, Jef Willems, MIS-C Clinicians, Patrick Stordeur, Sophie Janssens, Rudi Beyaert, Yvan Saeys, Jean-Laurent Casanova, Bart N. Lambrecht, Filomeen Haerynck, Simon J. Tavernier

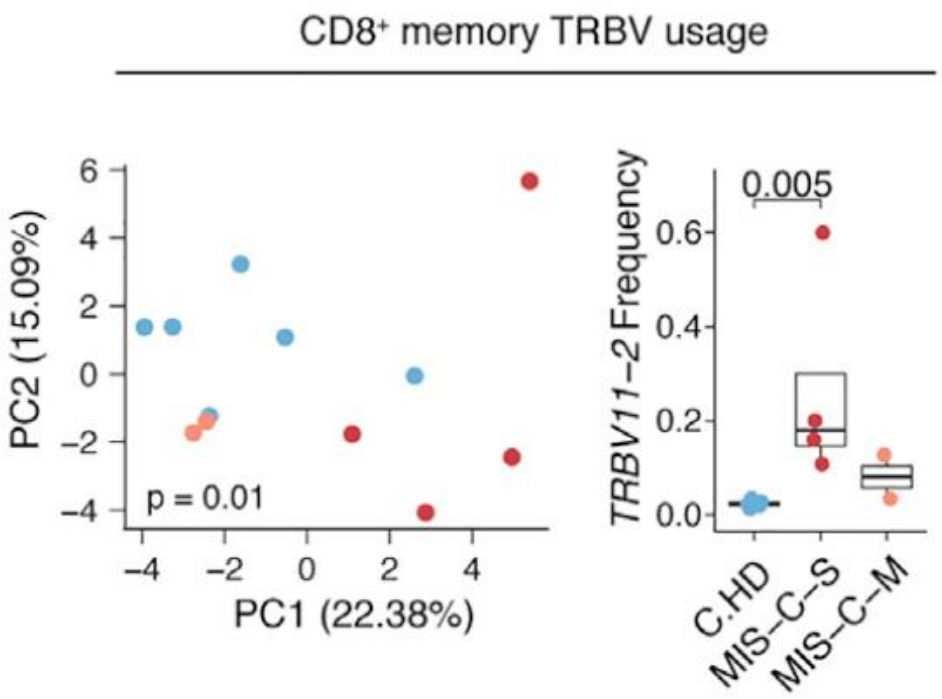
SCIENCE IMMUNOLOGY | RESEARCH ARTICLE

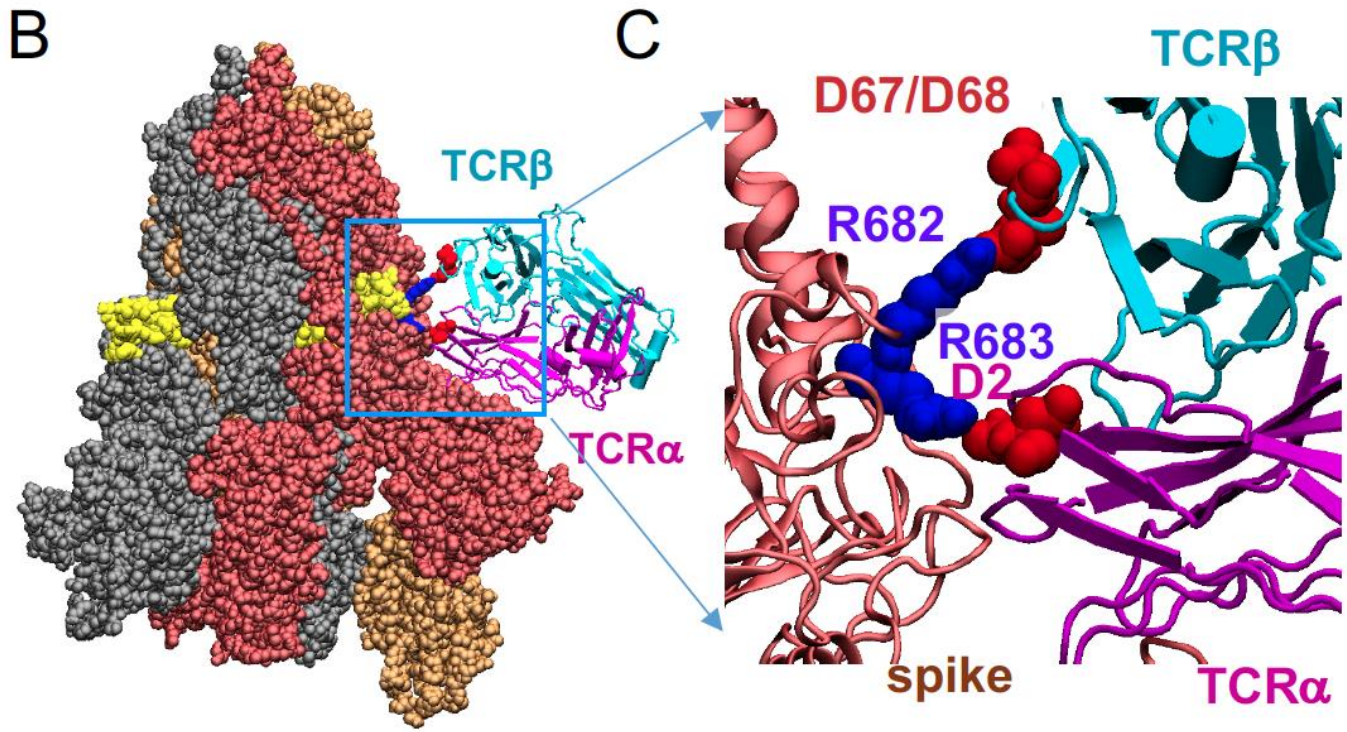
CORONAVIRUS

Deep immune profiling of MIS-C demonstrates marked but transient immune activation compared with adult and pediatric COVID-19

Laura A. Vella[1,2*†], Josephine R. Giles[2,3,4†], Amy E. Baxter[2,3†], Derek A. Oldridge[2,5,6†], Caroline Diorio[7,8], Leticia Kuri-Cervantes[2,9], Cécile Alanio[2,3,4], Maria Betina Pampena[2,9], Jennifer E. Wu[2,3,4], Zeyu Chen[2,3], Yinghui Jane Huang[2,3], Elizabeth M. Anderson[2,9], Sigrid Gouma[2,9], Kevin O. McNerney[7,8], Julie Chase[7,10], Chakkapong Burudpakdee[7], Jessica H. Lee[7], Sokratis A. Apostolidis[2,11], Alexander C. Huang[2,12], Divij Mathew[2,3], Oliva Kuthuru[2,3], Eileen C. Goodwin[2,9], Madison E. Weirick[2,9], Marcus J. Bolton[2,9], Claudia P. Arevalo[2,9], Andre Ramos[2,3], C. J. Jasen[13], Peyton E. Conrey[13], Samir Sayed[13], Heather M. Giannini[14], Kurt D'Andrea[15], The UPenn COVID Processing Unit[4], Nuala J. Meyer[14], Edward M. Behrens[2,7,16], Hamid Bassiri[1,2,7], Scott E. Hensley[2,9], Sarah E. Henrickson[2,7,3,13], David T. Teachey[7,8], Michael R. Betts[2,9], E. John Wherry[2,3,4*]

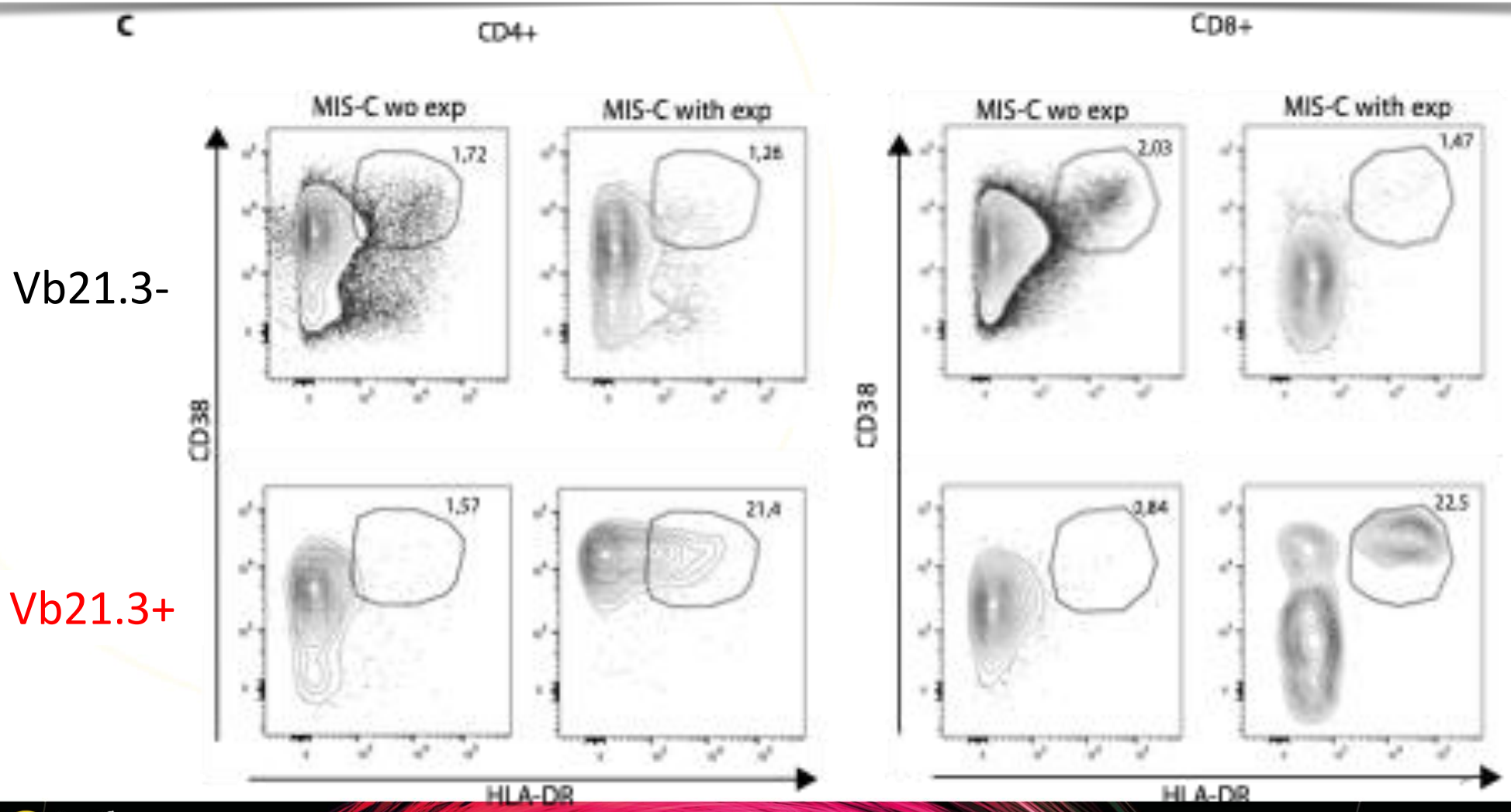
Superantigen response ?





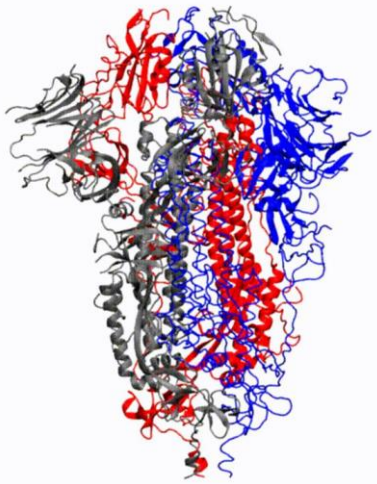
Ramaswamy et al, Immunity, 2021

Tcells in MIS-C



Massive activation of Vb21.3 expanded T cells

And vaccine ?



Le Monde | ACTUALITÉS | PRÉSIDENTIELLE 2022 | ÉCONOMIE | VIDÉOS | DÉBATS | CULTURE | M LE MAG | SERVICES

Covid-19 : seuls 2 % des enfants de 5 à 11 ans ont reçu une dose de vaccin en France

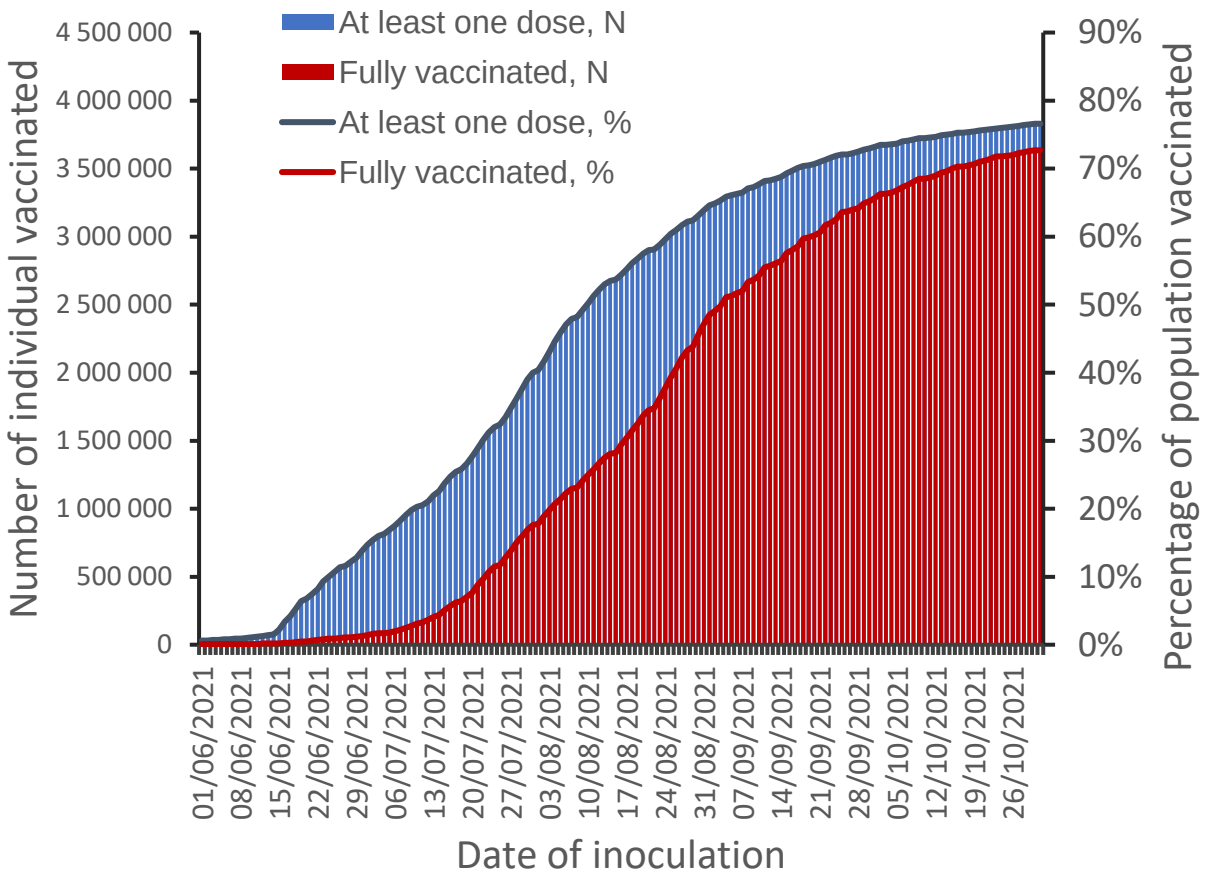
Amorcée le 20 décembre, la vaccination des 5-11 ans connaît un démarrage plus que poussif, selon les chiffres du ministère des solidarités et de la santé.

MIS-C & vaccines

August 2021
4th wave de COVID-19, delta variant
Vaccination start in adolescent

107 MISC
01/09 – 31/10/2021

- 74 < 12 years
- 33 ≥ 12 years
  - 0 fully vaccinated
  - 7 only one dose
  - 26 not vaccinated



Levy et al. JAMA 2021

COVID-19 Vaccination Status[a]	Number of MIS-C (n=33)	HR (95% CI)[b]	P-value
Unvaccinated	26	1 [reference]	
One dose	7	0.09 (0.04 – 0.21)	<.001
[c]Sensitivity analysis Day+14			
Day+14 unvaccinated	28	1 [reference]	
Day+14 one dose	5	0.07 (0.03 – 0.18)	<.001
[c]Sensitivity analysis Day+28			
Day+28 unvaccinated	31	1 [reference]	
Day+28 one dose	2	0.03 (0.01 – 0.12)	<.001
[c]Sensitivity analysis Day+42			
Day+42 unvaccinated	31	1 [reference]	
Day+42 one dose	2	0.04 (0.01 – 0.16)	<.001

Hyper inflammatory syndrome following COVID-19 mRNA vaccine in children: A national post-authorization pharmacovigilance study

Naïm Ouldali,[a,b,c,d*] Haleh Bagheri,[e] Francesco Salvo,[f,g] Denise Antona,[h] Antoine Pariente,[i] Claire Leblanc,[a] Martine Tebacher,[j] Joëlle Micallef,[k,l] Corinne Levy,[c,m] Robert Cohen,[c,m] Etienne Javouhey,[n,o] Brigitte Bader-Meunier,[p,q] Caroline Ovaert,[r,s] Sylvain Renolleau,[t,u] Veronique Hentgen,[v,w] Isabelle Kone-Paut,[w,x] Nina Deschamps,[y] Loïc De Pontual,[z] Xavier Iriart,[aa,ab,ac] Christelle Gras-Le Guen,[ad,ae,af] François Angoulvant,[a,ag] and Alexandre Belot[ah,ai,aj**], On behalf of the French Covid-19 Paediatric Inflammation Consortium£ and the French Pharmacovigilance network*

From 12 hyperinflammatory syndrome up to Jan 2022

- -2/12 explored for Vb21.3: NOT EXPANDED
- -Male predominance (10/12)
- -Cardiac involvement (10/12)
- -8/12 without exposure to virus before vaccination (Negative anti-N)
- -Milder and shorter than MIS-C

The reporting rate was 1.5 (95%CI [0.8; 2.6]) per 1,000,000 doses injected, i.e. 2.9 (95%CI [1.5; 5.1]) per 1,000,000 12–17-year-old vaccinated children.
As a comparison, 113 MIS-C (95%CI [95; 135]) occurred per 1,000,000 12–17-year-old children infected by SARS-CoV-2.
Risk of inflammation 38-75 higher after virus infection vs vaccination.

The Lancet Regional Health - Europe 2022;17: 100393
Published online 29 April 2022

Top positive Vb21.3 during the pandemics in Lyon

- Severe shock
- Purpura
- Myocarditis/ vasoplegia
- COVID-19 4 weeks before
- Vb21.3 = 31% (N<3.5%)

- Past medical history of recurrent fever and aphtosis

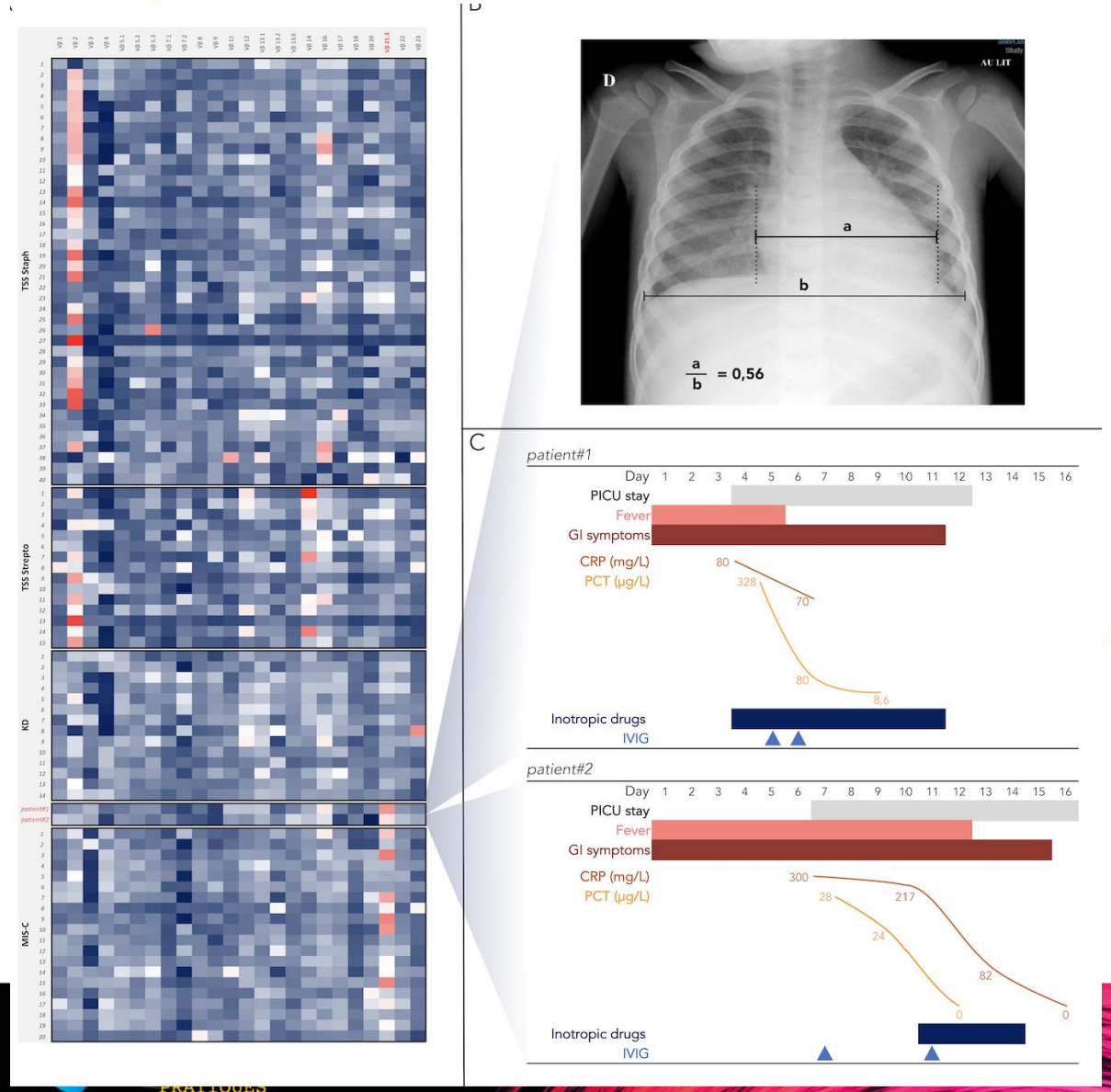
Top positive Vb21.3 during the pandemics in Lyon

- Severe shock
- Purpura
- Myocarditis/ vasoplegia
- COVID-19 4 weeks before
- Vb21.3 = 31% (N<3.5%)

- Past medical history of recurrent fever and aphtosis
- -> **A20 Hapoinsufficiency** (Mutation *TNFAIP3*)

Tusseau M, Zekre F et al. unpublished

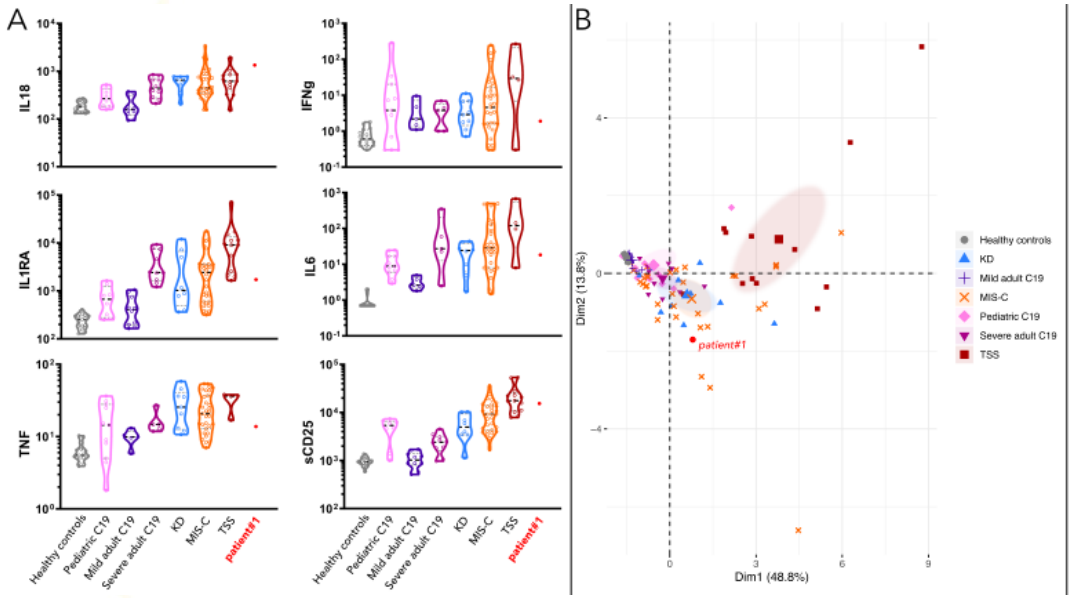
Two positive Vb21.3+ patients before the pandemics in Lyon

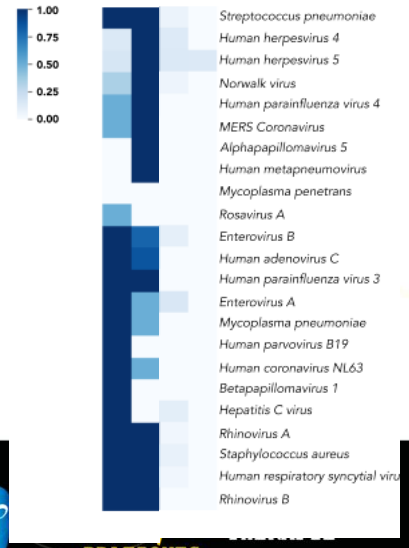


- 2 samples with Vb21.3 expansion before the Pandemics 2010 & 2015
- 2 children 4yo and 3yo
- Myocarditis / vasoplegia
- Kawasaki like syndrome…
- 1 serum left from 2015…

Benezech S et al. unpublished

Two positive Vb21.3 before the pandemics in Lyon





- 2 samples with Vb21.3 expansion before the Pandemics 2010 & 2015
- 2 children 4yo and 3yo
- Myocarditis / vasoplegia
- Kawasaki like syndrome…
- 1 serum left from 2015…

Several common virus.

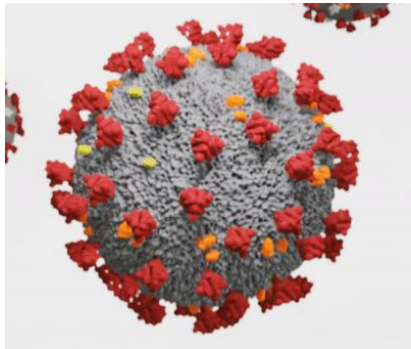
Cross reactivity with SARS-CoV.

Benezech S et al. unpublished

Conclusions

- Pediatric COVID-19: protection of young age
- MIS-C / PIMS : new emerging post-COVID19 infection
  - 75% are associated to TCR Vb 21.3 expansion
  - SARS-CoV2 and first adaptive immune response driving the superantigenic like effect ?

1st: SARS-CoV2 infection



+

2d: Pro-inflammatory state

-IL1RA autoantibodies
-HA20, SOCS1 HA, Other
-Co-infection

+

3rd: Adaptive immunity response

-Immune complex
-Ag / Ab specific
-B cell presentation

Belot's Group

Ommar Omarjee

Anne-Laure Mathieu

Maud Tusseau

Marion Moreews

& the WALZER Team

Collaborators

Clinics

Learning societies, C Gras LeGuen

F Angoulvant, V Hentgen

N Ouldali, S Renolleau, E Javouhey

C Ovaert, X Iriart

N Deschamp, L De Pontual

D Antona, V Auvigne

D Levy Bruhl, Isabelle Parent

I Kone Paut, B Bader Meunier

COVID Human GEnetic Effort

JL Casanova, H Su

SY Zhang, P Bastard

E Jouanguy, A Puel,

T Mogensen et al.

Collaborators

Research

D Klatzman, E Mariotti Fernandiz, K Le Gouge

RHU COVIFERON (JL Casanova & L Abel)

Horizon Europe UNDINE T Mogensen

Patients and families

Questions ?