Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19)

Clinician Outreach and Communication Activity (COCA) Webinar

Tuesday, May 19, 2020

Continuing Education

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To Ask a Question

- Using the Webinar System
  - Click the Q&A button.
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- For media questions, please contact CDC Media Relations at 404-639-3286, or send an email to media@cdc.gov.

For More Clinical Care Information on COVID-19

- **Call** COVID-19 Clinical Call Center at 770-488-7100 (24 hours/day).
- **Refer** patients to state and local health departments for COVID-19 testing and test results.
  - Clinicians should NOT refer patients to CDC to find out where or how to get tested for COVID-19, OR to get test results.
- **Visit** CDC's Coronavirus (COVID-19) website: https://www.cdc.gov/coronavirus
- **Visit** emergency.cdc.gov/coca over the next several days to learn about future COCA Calls.

Today's Presenters

- **Sapna Bamrah Morris, MD, MBA (no slides)**
  Clinical Team Lead
  COVID-19 Response
  Centers for Disease Control and Prevention

- **Ermias Belay, MD (no slides)**
  Special Investigations Team Lead
  COVID-19 Response
  Centers for Disease Control and Prevention

- **Michael Levin, MBE, PhD, FRCPCH, FMedSci**
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  Imperial College
  London, United Kingdom

- **James Schneider, MD, FAAP, FCCP**
  Chief, Pediatric Critical Care Medicine
  Associate Professor of Pediatrics
  Cohen Children's Medical Center

- **Vincent C. Marconi, MD**
  Professor of Medicine and Global Health
  Emory University School of Medicine
  Rollins School of Public Health

Paediatric Inflammatory Multisystem Syndrome - Temporally associated with SARS-CoV-2 – PIMS-TS

In March 2020 as COVID19 evolved in UK, Paediatricians noticed unusual illness

- Severe illness admitted to paediatric ward, or PICU
- Varied presentations - prolonged fever, sore throat, headache, abdominal pain and vomiting, rash, conjunctivitis
- Some developed shock, organ dysfunction
- In common - ↑ CRP, ↑ Neutrophil, ↓ lymphocytes, ↑ D-Dimers
- Some - typical Kawasaki disease features
- Majority SARS-CoV-2 PCR negative

We collected 37 cases from 8 hospitals in England and systematically reviewed their clinical features.

Development of a case definition

- All cases reviewed by panel of infectious diseases clinicians
- Case note review, data collated on a data base
- Initial report only Included children admitted to HDU/PICU
- **Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes; infections associated with myocarditis such as enterovirus and Macrophage activation syndromes**

- **NHS UK alerted on 24 April emerging new disorder**

RCPCH
Royal College of Paediatrics and Child Health
Leading the way in Children's Health

27 April 2020

Guidance: Paediatric multisystem inflammatory syndrome temporally associated with COVID-19

Case definition:

1. A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP and lymphopaenia) and evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder) with additional features (see listed in Appendix 1). This may include children fulfilling full or partial criteria for Kawasaki disease.

2. Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as enterovirus (waiting for results of these investigations should not delay seeking expert advice).

3. SARS-CoV-2 PCR testing may be positive or negative

38 cases identified between March 25 and May 1

Demographic features

Age	1 – 16 years (Median 11 years)
Sex	62% male (23 /37)
Co-morbidities	1 asthma, 1 epilepsy

Location of reported cases

Demographic Features

Ethnicity	PIMS-TS	London	England and Wales
Black / African / Caribbean / British	46% (17/37)	13%	3%
White	19% (7/37)	60%	86%
Asian / Asian British	11% (4/37)	19%	8%
Mixed	5% (2/37)	5%	2%
Unknown	11% (4/37)		

Clinical presentations

- **75% shock, 51% Myocardial involvement**
- 54% rash
  - 30% conjunctivitis, 20% mucus membrane
- **57% abdominal involvement**
- 38% acute kidney injury, only 1 required renal replacement therapy
- Unlike adults - only 32% respiratory symptoms

Symptom	Number	Percentage
Shock	28	75.7
Rash	20	54.1
Conjunctivitis	12	32.4
Mucus membrane Involvement	7	18.9
Swollen hands/feet	3	8.1
Abdominal pain	21	56.8
Syncope	1	2.7
Lymphadenopathy	4	10.8
Sore Throat	5	13.5
Neck Swelling	3	8.1
Diarrhoea	22	59.5
Vomiting	16	43.2
Respiratory symptoms	12	32.4
Cough	7	18.9
Oxygen requirement	19	51.4
Neurological symptoms	7	18.9
Headache	12	32.4
Meningism	2	5.4
Confusion	5	13.5
Mycoardial Involvement	19	51.4
Coronoary Artery Involvement	6	16.2
Proven Vasculitis	1	2.7
Thrombosis	1	2.7
Acute Kidney Injury	14	37.8
Renal replacement therapy	1	2.7
Peripheral Oedema	4	10.8
Ascites	9	24.3

Laboratory Features

- Lymphopaenia
- Neutrophilia
- Anaemia
- Raised D-dimer
- Raised Troponin
- Raised CRP

n=	Laboratory Test	units	Cut-off assigned	% at cut off	Number at cut off	Median	Range	IQR
30	Haemoglobin	g/L	<90	70.0	21	84.5	60-110	72-96
37	Neutrophil	x10*9/l	>8	89.2	33	16	3.4-65	11.9-26
			<2	3.0	1	6	1.0-39	3.9-10.6
37	Lymphocyte	x10*9/l	<2	94.6	35	0.6	0.1-2.9	0.4-0.8
			<1	80.0	29			
36	Platelets	x10*9/l	<100	30.6	11	146	22-457	68-200
33	D-Dimer	ug/L	>2000	93.9	31	2563	1.2-26695	11.0-5085
33	Ferritin	ug/L	>500	75.8	25	932	87-63626	506-1774
30	Troponin	ng/L	>12	90.0	27	202	3.0-5113	45-549
			>100	60.0	18			
21	Creatinine Kinase	U/L	>250	42.9	9.00	222	25-7391	98-729
36	Creatinine	umol/L	>100	33.3	12	73.5	28-302	43-121
36	ALT	U/L	>100	27.8	10	49	11-636	29-121
30	Albumin	g/L	<25	73.3	22	22.5	12.0-39	20-25
25	Lactate dehydrogenase	U/L	>750	56.0	14	810	265-6660	420-1088
29	Fibrinogen	g/L	>4	89.7	26	6	1.8-10.8	2.4-7.8
37	C reactive protein	mg/L	>100	91.9	34	301	16-556	193-359
10	pro-BNP	pg/ml	>1000	90.0	9	23093	241-35000	8783-35000

Radiology – summary of findings

- **Chest X-ray:**
  - Some normal
  - Small bilateral pleural effusions
  - Patchy consolidation
  - Focal consolidation
  - Atelectasis
- **CT chest (on a subset):**
  - Findings as for CXR
  - Nodular ground glass opacification

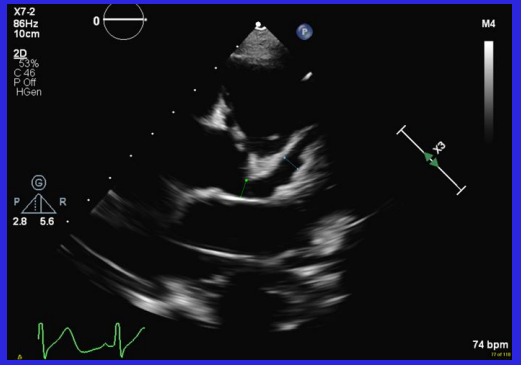
- **Abdominal USS/CT**
- Some normal
  - Free fluid
  - Ascites
  - Bowel inflammation
    - ileum/ascending colon/RIF
  - Lymphadenopathy
  - Pericholecystic oedema

Echocardiography

19/25 at least 1 echo performed

08/19 significantly impaired ventricular function (SF% <28 or equivalent)

05/19 dilated coronaries or aneurysms



Echo – LCA giant aneurysm (z+15) - Early echo had normal coronaries

LMCA mm (z)	LAD mm (z)	RCA mm (z)	comment
4.6 (+4.6)	8.0 (+15)	4.0 (+3.7)	Early echo had normal coronaries
	5.0 (+4.9)		uniformly dilated LMS to LAD coronary arteries
(<2.0)	(<2.0)	(<2.0)	dilated left circumflex
3.5 (+0.7)	3.7 (+4.2)	3.7 (+1.8)	diffuse coronary ectasia:
4.4 (+1.8)	6.8 (+12.5)	5.4 (+4.5)	Severe coronary ectasia involving both right & left coronary artery

Echocardiographic findings for the 5 children with dilated coronary arteries

Management

- All admitted to HDU/PICU for supportive care
- All required fluid resuscitation
- Inotropes required for 26 (70%)
- 38% of children did not received IVIG, just supportive care

TREATMENT	n=	%
Intravenous immunoglobulin (IVIG)	23	62.2
Corticosteroid	19	51.4
Anakinra	3	8.1
Toculizimab	0	0.0
Infliximab	2	5.4
Remdesivir	0	0.0
Lopinavir/ritonavir	0	0.0
Hydroxychloroquine	0	0.0
Azithromycin	4	10.8

Outcomes

- Majority respond to treatment
- NB – 1 child has been noted to have coronary artery dilatation at follow up ECHO, did not receive immunosuppression

OUTCOME	n=	%
Ventilatory support	25	67.6
ECMO	2	5.4
Death	1	2.70
Remain in PICU	7	19.0
Discharged from PICU	16	43.0

SARS-CoV-2 Results

- SARS-CoV-2 PCR –
  - 12 positive
  - 24 negative
  - 1 refused
- SARS-CoV-2 IgG
  - 19 positive total
  - 11 IgG pos, PCR neg
  - 5 IgG pos, PCR pos
  - 3 IgG neg, PCR neg
  - 18 not done, 7 PCR pos
- Total SARS-CoV-2 pos (PCR & IgG) is 23

What do these children have?
Illness similar to several conditions

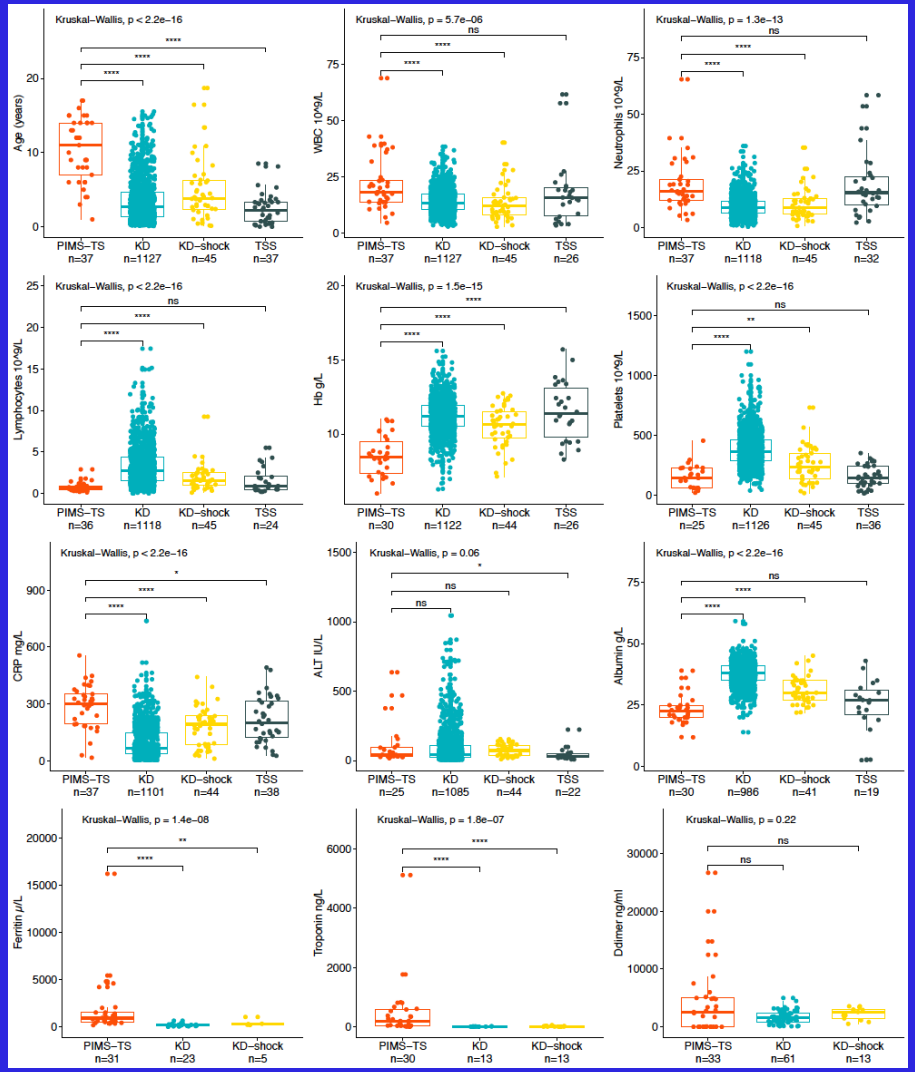
- Kawasaki disease /KD shock syndrome syndrome
- Staphylococcal or streptococcal toxic shock syndrome
- HLH / Macrophage activation syndromes
- Haemorrhagic shock and encephalopathy syndrome
- SLE/Vasculitic disease

Comparison with Kawasaki disease & Kawasaki Shock syndrome

- Rady Children's Hospital, San Diego; 2002 Jan to 2019 March

- Pre-IVIG were available from 1164 KD pts.
  - Excluding KD shock
- Pre-IVIG data were available from 45 KD shock pts

- Thanks for sharing data - Jane Burns, Chisato Shimizu, Emelia Bainto, Elizabeth Moreno, Nipha Sivilay


Kruskal–Wallis, p < 2.2e–16
Age (years)
PIMS–TS n=37
KD n=1127
KD–shock n=45
TSS n=37
Kruskal–Wallis, p = 5.7e–06
WBC 10^9/L
PIMS–TS n=37
KD n=1127
KD–shock n=45
TSS n=26
Kruskal–Wallis, p = 1.3e–13
Neutrophils 10^9/L
PIMS–TS n=37
KD n=1118
KD–shock n=45
TSS n=32
Kruskal–Wallis, p < 2.2e–16
Lymphocytes 10^9/L
PIMS–TS n=36
KD n=1118
KD–shock n=45
TSS n=24
Kruskal–Wallis, p = 1.5e–15
Hb g/L
PIMS–TS n=30
KD n=1122
KD–shock n=44
TSS n=26
Kruskal–Wallis, p < 2.2e–16
Platelets 10^9/L
PIMS–TS n=25
KD n=1126
KD–shock n=45
TSS n=36
Kruskal–Wallis, p < 2.2e–16
CRP mg/L
PIMS–TS n=37
KD n=1101
KD–shock n=44
TSS n=38
Kruskal–Wallis, p = 0.06
ALT IU/L
PIMS–TS n=25
KD n=1085
KD–shock n=44
TSS n=22
Kruskal–Wallis, p < 2.2e–16
Albumin g/L
PIMS–TS n=30
KD n=986
KD–shock n=41
TSS n=19
Kruskal–Wallis, p = 1.4e–08
Ferritin µ/L
PIMS–TS n=31
KD n=23
KD–shock n=5
Kruskal–Wallis, p = 1.8e–07
Troponin ng/L
PIMS–TS n=30
KD n=13
KD–shock n=13
Kruskal–Wallis, p = 0.22
Ddimer ng/ml
PIMS–TS n=33
KD n=61
KD–shock n=13

Conclusion from our review

New and unusual childhood illness- emerging a month behind the COVID19 curve in UK

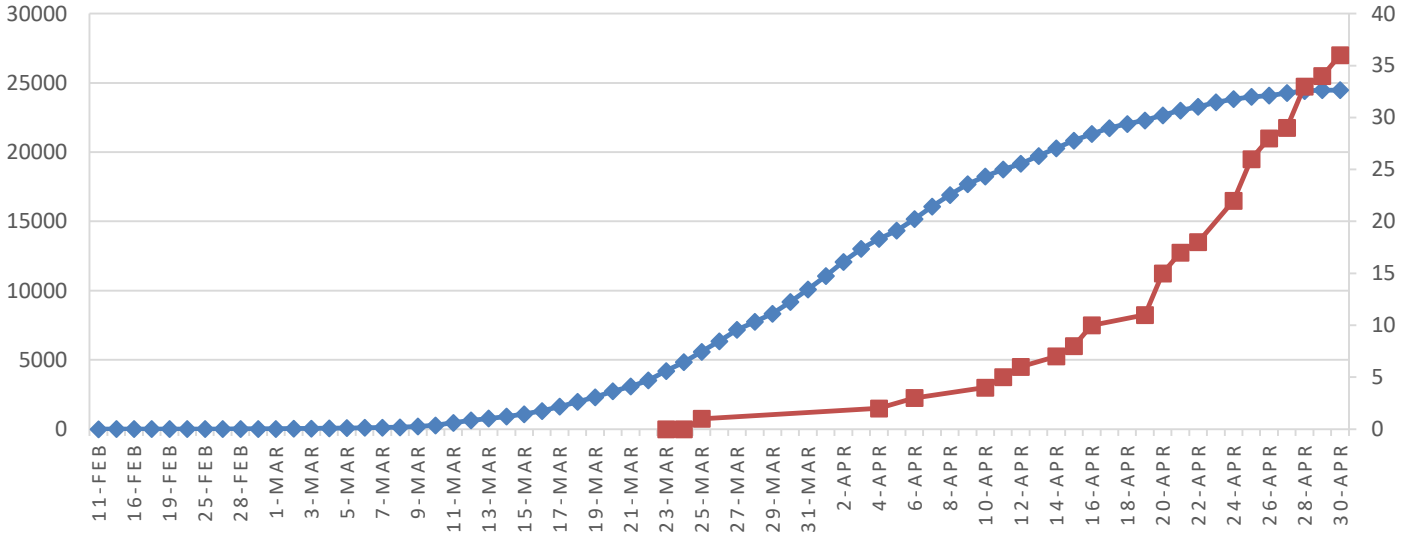
Distinctive features from other syndromes Troponin elevated, D Dimers elevated, High CRP, BNP elevated Prominent cardiac injury

What is this due to?

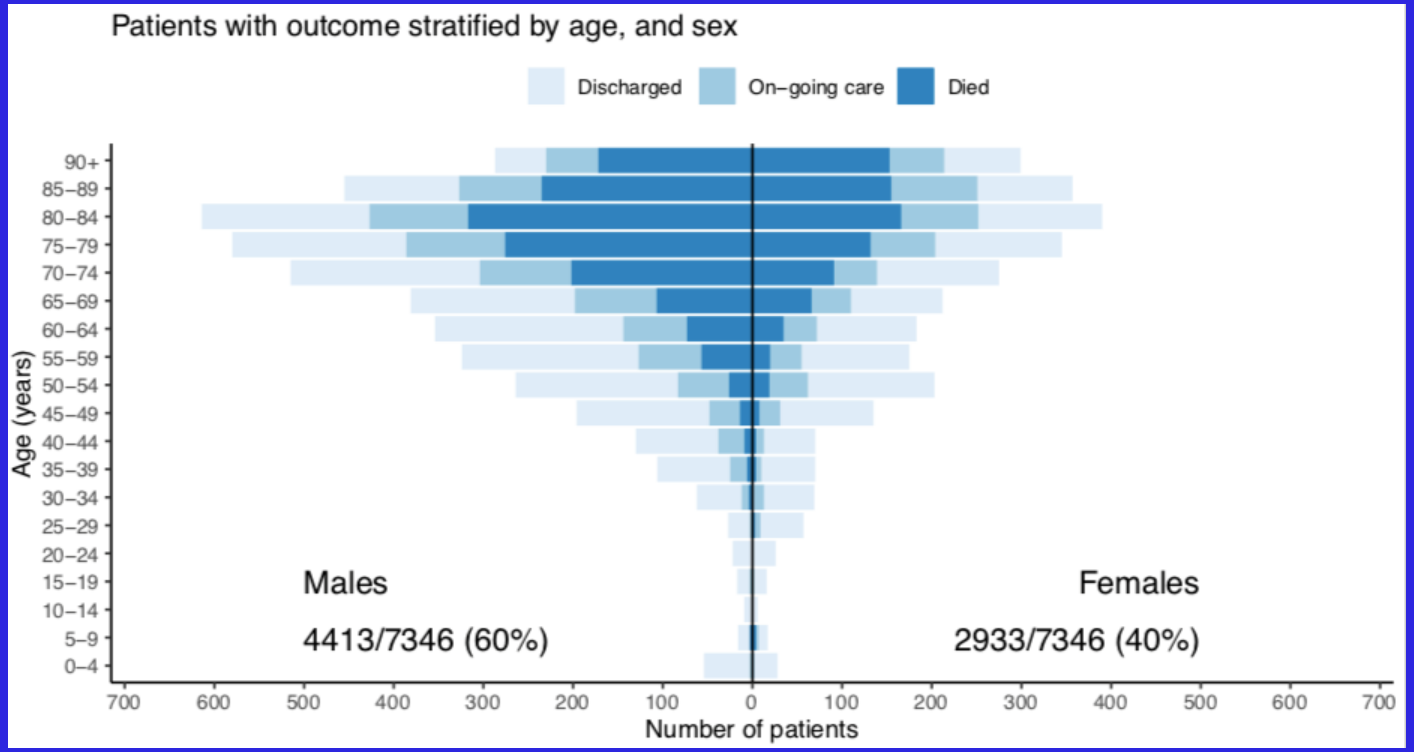
PIMS-TS appear to be a month behind the COVID19 peak in the population

Public Health England

Laboratory Confirmed COVID-19 cases, London



COVID19 age distribution in UK



Very few children with severe disease prior to these cases

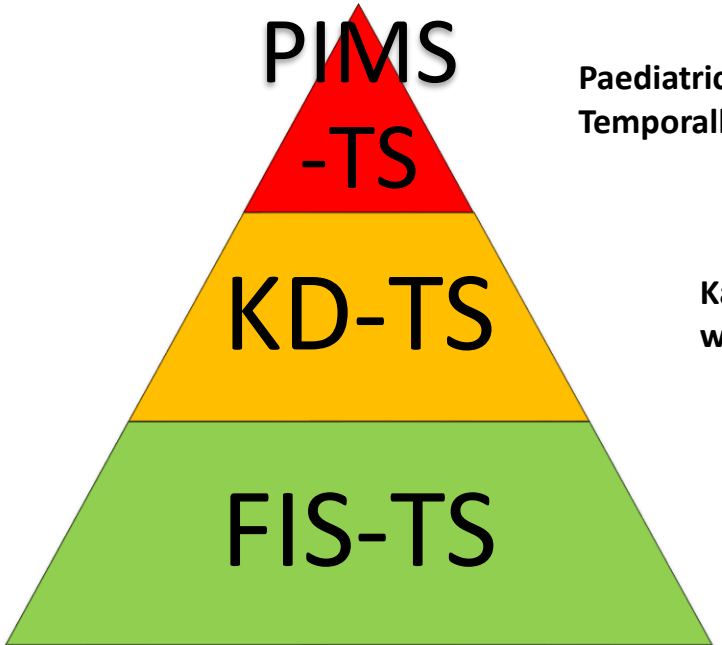
Mechanism??

- Timing a month after COVID19 curve
- Majority negative for SARS-Cov2 Virus but positive for Antibody

- This suggests the illness is mediated by the development of acquired immunity rather than by direct viral injury

An emerging new spectrum of SARSCov2 in children- not just COVID

COVID 19 in children: generally mild or asymptomatic



Paediatric Inflammatory Multisystem Syndrome-Temporally associated with SARS-CoV-2

Kawasaki Disease-Temporally associated with SARS-CoV2-

Febrile Children with Inflammation-Temporally associated with SARS-CoV-2

Urgent Research Question

- **Do patients progress from the less severe to more serious categories? i.e., FIS-TS to KD TIS or PIMS-TS; or KD -TS to PIMS TS.**
- **What is the risk of Coronary artery aneurysms in each group?**
- **What is the relationship between KD-TS and KD prior to the pandemic?**
- **Do anti-inflammatory and immuno-modulating treatment such as immunoglobulin, steroids, anti-TNF, anti-IL1, anti-IL6 or T cell inhibition, or anticoagulation or anti platelets agents improve outcome and reduce risk of coronary artery aneurysms?**
- **What are the mechanisms or pathogenesis?**
- **Are there biomarkers to distinguish each group and COVID from other conditions?**

Two studies for addressing these questions

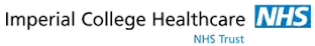
DIAMONDS
MAKING DIAGNOSIS PERSONAL

- DIAMONDS enrolling patients in 11 EU countries with COVID, and SARSov2 associated inflammatory disorders; RNA transcriptome; proteomic and genetic comparison of each disease with other infectious and inflammatory diseases
- **Best available Therapy Study (BATS)** anonymized, multi-country study of best treatment for PIMS-TS;KD-TS,FI-TS.
- **Principle is online data collection of all patients**. Each clinician gives their best "guess" treatment. Study compares rates of normalization of Inflammatory markers, development of coronary artery aneurysms, time on ventilator or inotropes in patients propensity matched for severity at enrollment.
- **BATS** is possible because we have good biomarkers of disease severity (CRP, Ferritin, Troponin) and clear endpoints for outcome (CAA, ICU). International enrollment commencing this week.

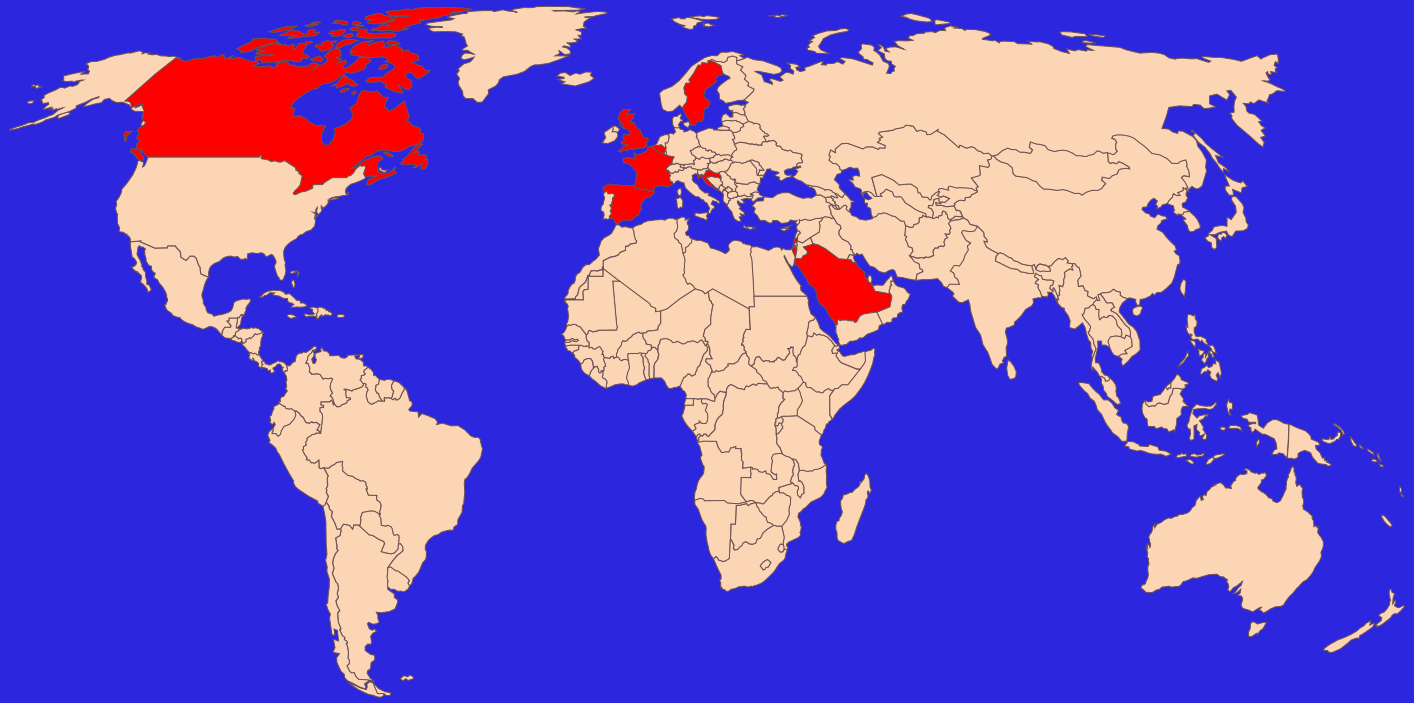
We have so much to learn

We can only understand this new threat with collaboration and placing research at the heart of clinical care.

Acknowledgements



PIMS-TS COVIDHGE Patients



World map by www.freeworldmaps.net

International Investigations

Country	Investigator	Site	Number of patients
Canada	Catherine Biggs	UBC	5
Croatia	Alenka Gagro	Children's Hospital Zagreb	1
Israel	Danny Eytan Hagit Baris Feldman	Rambam Medicat Ctr Telaviv Sourasky Medical ctr	3
France	Paul Bastard JL Casanova	Institut IMAGINE	At least 15
Belgium	Filomeen Haerynk Isabell Metys	University Gent	2
Saudi Arabia	Saleh Musen	King Saud University	1
Spain	Aurora Pujol Onofre Sergio Auilera Albesa Pere Soler Palacin	IDIBELL-Hospital Duran i Reynals Navarra Hospital Univ Hospital Vall d'Hebron	5 At least 10
Sweden	Petter Brodin	Karolinska Institute	4?

Multisystem Inflammatory Syndrome in Children Associated with COVID-19

James Schneider, MD, FAAP, FCCP
Chief, Division of Pediatric Critical Care Medicine
Associate Professor of Pediatrics

Cohen Children's Medical Center
Northwell Health

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Multisystem Inflammatory Syndrome in Children Associated with COVD-19

Fever (↑38.0) **≥ 4 days** + **ANY** of

- **GI symptoms**
  - Severe pain, v/d
  - Enteritis on imaging
- **Rash**
- **Conjunctivitis**
- **Oral changes**
- **Cough**
- **Headache/irritability**

+

Inflammation

- **CRP**
- **Ferritin**
- **Troponin**
- **Pro-BNP**

+ **Any of**

Classical Kawasaki symptoms

OR

Incomplete Kawasaki symptoms (i.e., at least 3/6 of anemia, WBC > 15,000, Platelets > 450 or <100, Albumin < 3 g/dL, Elevated ALT, Sterile pyuria >10 WBC/hpf

OR

+ echo (↓LVEF, CA dilation, valvitis)

OR

Cardiogenic and/or distributive shock with evidence of single or multi organ dysfunction (e.g., Fluid refractory hypotension with + echo and/or AKI and/or liver injury and/or oxygen requirement)

CCMC Initial Case Definition

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Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C)

- An individual aged <21 years presenting with fever[i], laboratory evidence of inflammation[ii], and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); **AND**
- No alternative plausible diagnoses; **AND**
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms

[i]Fever ≥38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours
[ii]Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin

Additional comments

- Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C
- Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection

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https://emergency.cdc.gov/han/2020/han00432.asp
Accessed 5/18/20

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CCMC Experience- Demographics

- Patients included: April 17- May 13, 2020

- Patients Included: 33 (43 currently reported to NYS DOH)
- Age: 8.6 yr (Range: 2.2-17 yr)
- Gender: 61% male
- Race: Black 24%, Asian 9%, White 9%
- Ethnicity: Hispanic 27%

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CCMC Experience- Clinical Characteristics

- No underlying medical conditions (excluding obesity): 79%
- Normal weight: 45%; Obese: 39%
- Reactive airway disease: 15%

CCMC Experience- Presenting Signs/Sx's

- Fever duration prior to presentation: 4 dy (IQR: 3, 5)
- Neurocognitive sx's: 58%
- GI sx's: 97%
- Respiratory sx's: 52%
- Shock: 76%
- Complete Kawasaki disease criteria: 64%
  - With shock: 76%

CCMC Experience- Hospital Course

- PICU Admission: 79%
- LOS: 4 dy (IQR 3, 6.5)

CCMC Experience- Initial Laboratory Results

- WBC: 9.1 K/uL
- Absolute lymphocyte count: 0.80
- Lymphopenia: 80%
- Hemoglobin: 11.2 g/dL
- Platelets: 154 K/uL
- C-reactive protein: 206 mg/L
- D-dimer: 1700 ng/mL
- Fibrinogen: 736 mg/dL
- Ferritin: 736 ng/mL
- Lactate dehydrogenase: 320 U/L
- INR: 1.31
- Pro-BNP: 3325 pg/mL
- Troponin T: 31 ng/L
- Procalcitonin: 12.05 ng/mL
- Na: 133 mmol/L
- ALT: 38 U/L
- AST: 54 U/L
- Total bilirubin: 0.5 mg/dL
- Albumin: 3.4 mg/dL

CCMC Experience- SARS-CoV-2 testing

- IgG (+) and PCR (+): 18%
- IgG (+) and PCR (-): 73%
- PCR (+) and IgG unavailable: 9%

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CCMC Experience- Organ Involvement

- Acute liver injury: 21%
- AKI: 70%
- O2 or Positive Pressure: 52%
- Mechanical ventilation: 18%
- Intubation days: 3

CCMC Experience- Cardiac involvement

- Any coronary artery abnormalities: 48%
- LAD/RCA findings: Z-score 2-2.49: 9%; Z-score >2.5: 15%; lack of tapering (Z-score <2): 24%
- Any myocardial dysfunction: 58%
  - Mild: 33%
  - Moderate: 24%
  - Severe: 0%

CCMC Experience- Medications Used

- IVIG: 100%
  - 2nd dose: 30%
- Methylprednisolone: 70%
- Aspirin: 88%
- Anakinra: 12%
- Tocilizumab: 9%
- Infliximab: 3%
- Enoxaparin: 42%

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CCMC Experience- Disposition

- Mortalities: 0
- Discharged alive: 82% (18% still hospitalized)
- Cardiac function at discharge:
  - Always normal: 42%
  - Depressed then normalized: 18%
  - Mildly depressed: 27%

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IMMUNE MODULATORS FOR COVID-19

VINCENT MARCONI, MD

PROFESSOR OF MEDICINE AND GLOBAL HEALTH

EMORY UNIVERSITY SCHOOL OF MEDICINE

ROLLINS SCHOOL OF PUBLIC HEALTH

EMORY VACCINE CENTER

DISCLOSURE

At the time this presentation was given, I have received support from Lilly, ViiV, Gilead and Bayer.

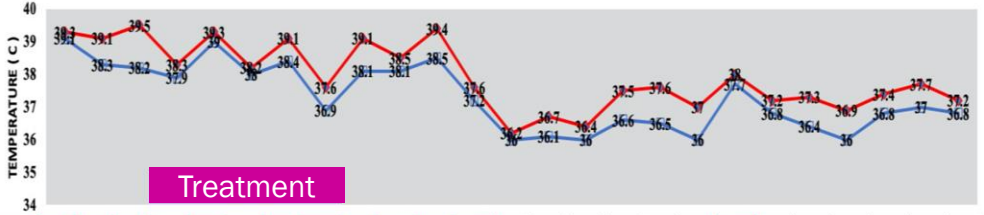
Vincent Marconi

CASE

Patient 13

Inflammatory Markers

CRP (ug/ml)	229	342	>240	>240		191.8			174	89.4	76.6	32.7
ESR (mm/hr)	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100
D-dimer (ug/ml)		15174	76022			35956		6475	3826		4499	
IL-6 (pg/ml)	155											
Day of hospitalization	2	4	6	8	10	12	14	16	18	20	22	24



Fever																									
Cough																									
Dyspnea																									
Diarrhea																									
O2 (l/min)	6	15																					8	3	
ICU admission																									
Invasive ventilation																									
PEEP(mmHg)			20	18	18	16	16	14	14	14	12	12	12	10	10	10	10	10	8	8	6	6			
FiO2(%)			80	100	100	70	70	70	65	60	50	50	50	40	40	40	40	40	40	40	40	40			
PaO2/FiO2			<100	<100	120		160			186			210				280								
Vasopressors																									
CRRT/HD																									
Vancomycin (oral)																									
Hydroxychoroquine																									
Azithromycin																									
Day of hospitalization	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24

C-difficile

Pneumo-mediastinum

Bacterial pneumonia

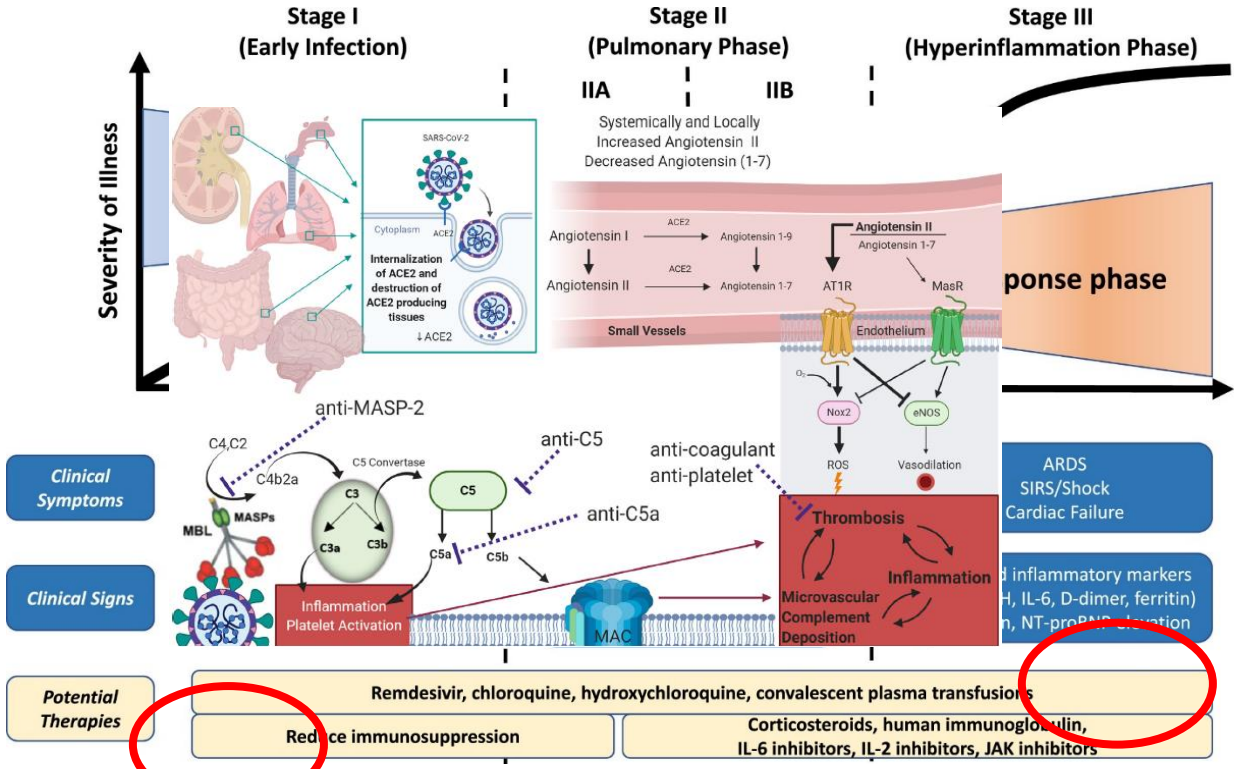
AKI

Shock

DVT

Recovery

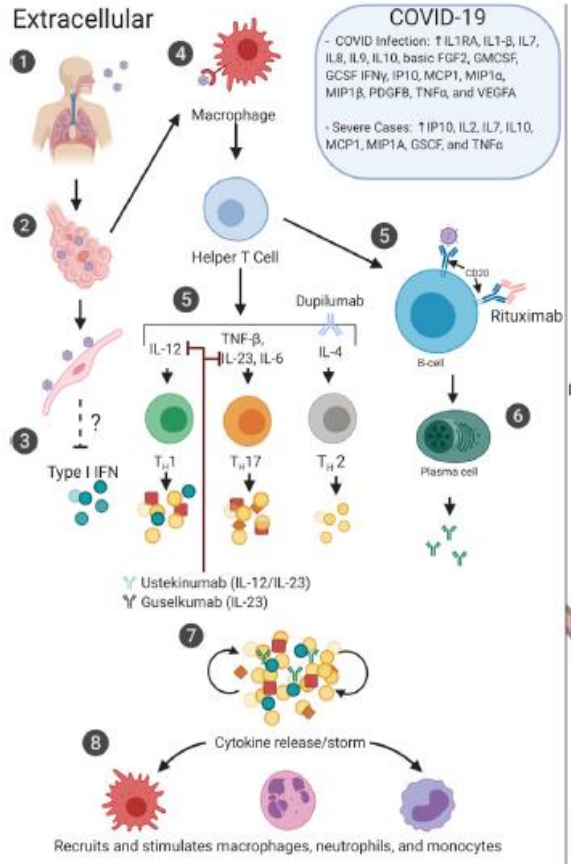
COVID-19

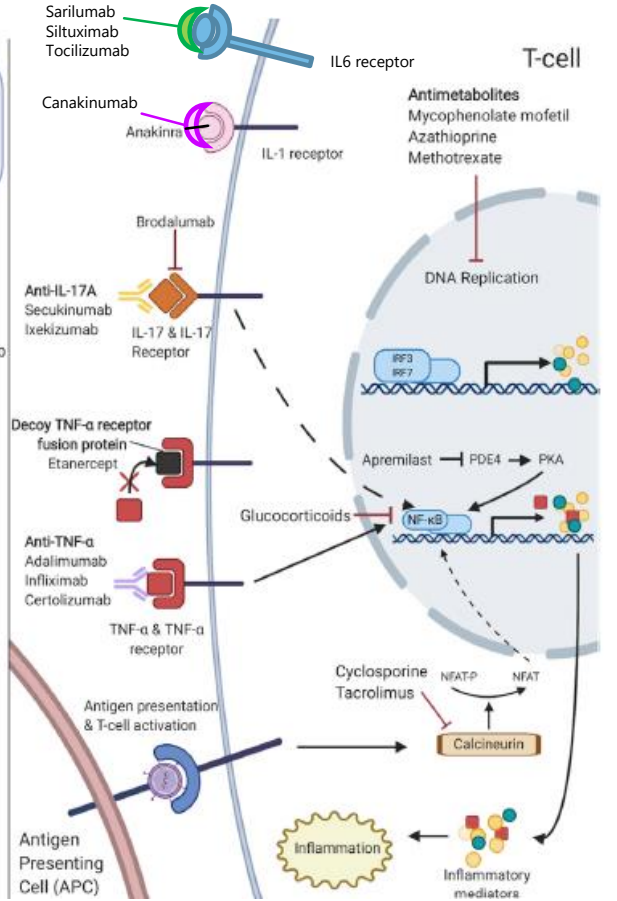


Siddiqi and Mehra, J Heart Lung Transplant, DOI: (10.1016/j.healun.2020.03.012)

Magro *Translational Research* 2020

IMMUNE MODULATORS





Price *J Am Acad Dermatol* 2020

IL-6/R BLOCKADE

Agents: sarilumab, siltuximab, sirukumab, tocilizumab

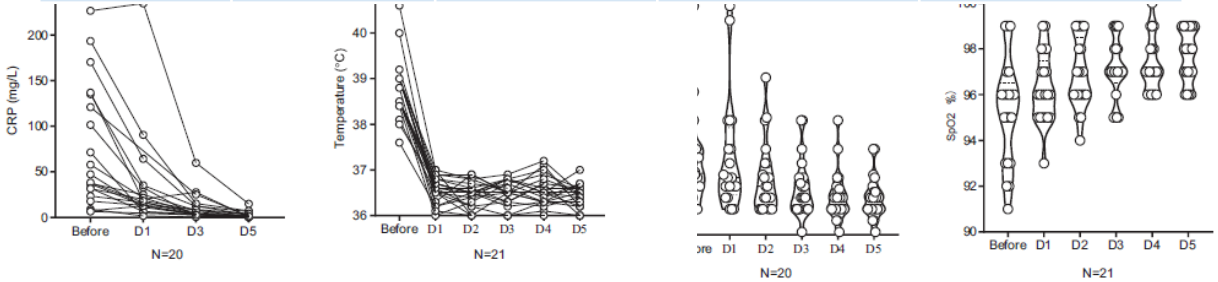
Pros: MCD, CA, RA, SoJIA, CAR-T CRS, GCA

Cons: Hypersensitivity, lipids, infections (RTI), rash, edema, IV/SC, Liver

Tocilizumab Case Series in COVID-19

Pub	Demographics	Clinical	Treatment	Outcomes
Luo *J Med Vir* 2020 China	15 patients 73y 80% Male	47% critical 40% serious 13% moderate IL6 115 pg/mL	80-600 mg x1.47 doses (33% 2+) Methylpred 53%	67% decreased IL6 20% died 80% inpt
Xu *PNAS** 2020 China	21 patients 57y 86% Male	19% critical 81% serious IL6 132 pg/mL	400 mg x1 dose LPV/r Methylpred	0% died 90% discharged
Pereira *Am J Transp* 2020 U.S.	14 patients 57 y 59% Male 6.6 y post-tran	30% severe 15% moderate	400 mg or 8 mg/kg (max 800 mg) x1 (additional doses) Antivirals+Methyl	24% died (overall) 54% discharged 6% readmit

A



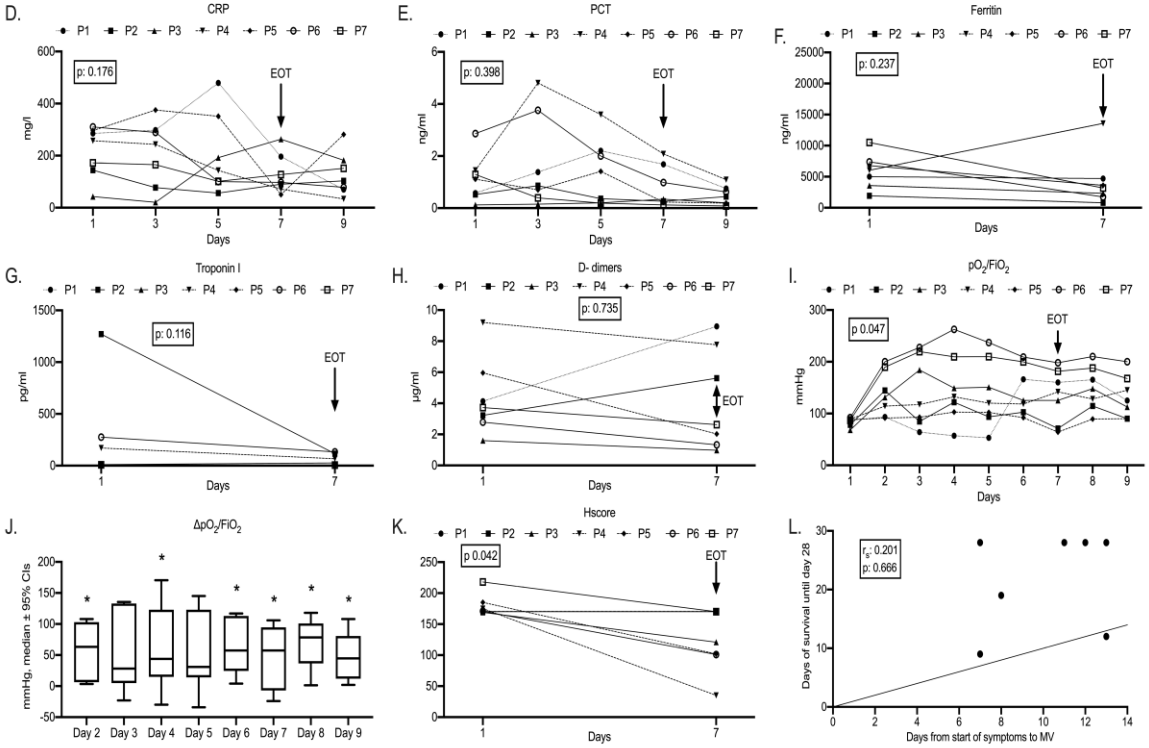
IL-1 BLOCKADE

Agents: anakinra, canakinumab

Pros: Periodic fever syndromes, SoJIA MAS, SC 26d

Cons: HA, inj rxn, lipids, infections, cytopenias, cancer?, IV QID-SC daily

Anakinra for COVID-19 Hemophagocytic Syndrome



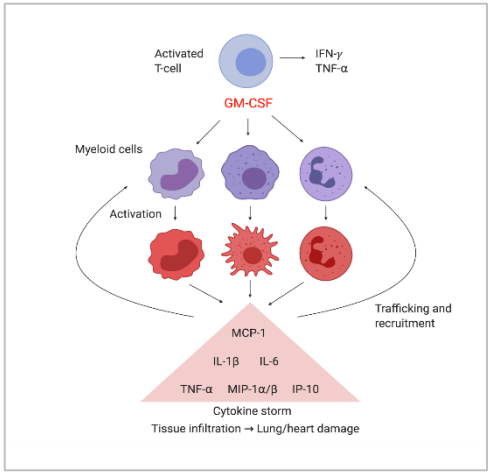
Dimopoulos *Cell Host Microbe* 2020

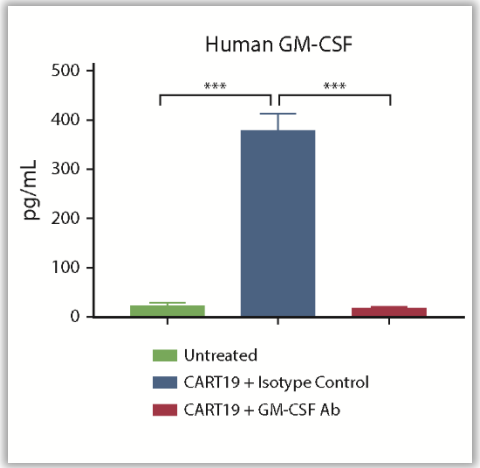
GM-CSF BLOCKADE

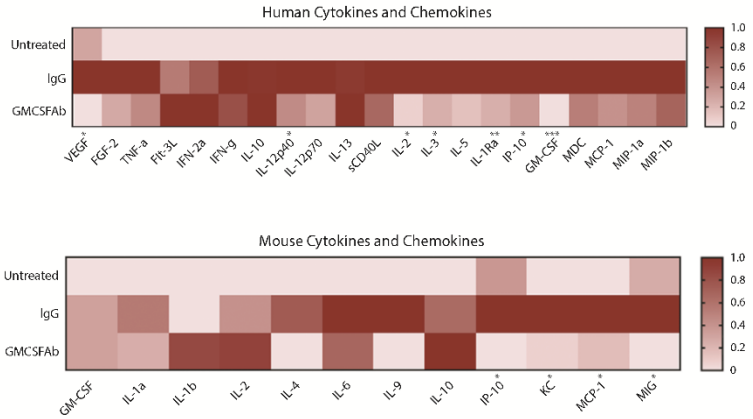
Agents: TJ003234, gimsilumab, lenzilumab, mavrilimumab, otilimab, namilumab

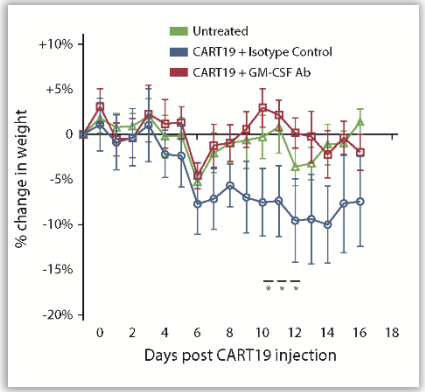
Pros: Ank Spon, CAR-T cytokine storm, RA, MS, CMML, GVHD, Eos Asthma, Th17, CNS, Gut

Cons: HTN, Hypersensitivity, Alveolar Proteinosis, SOB, IV









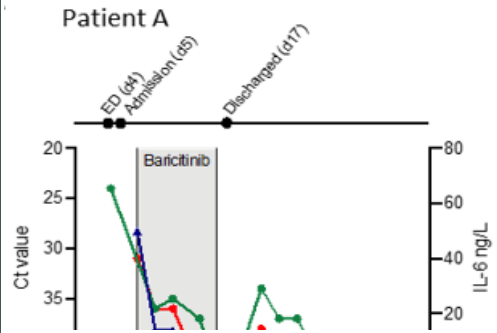
Sterner *Blood* 2019

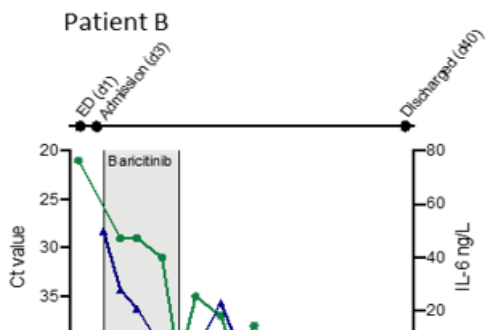
JAK BLOCKADE

Agents: baricitnib, ruxolitinib

Pros: RA, MF, PCV, oral, renal (bari), multiple cytokines, antiviral activity?

Cons: infections, thrombosis, cytopenias, liver (rux)

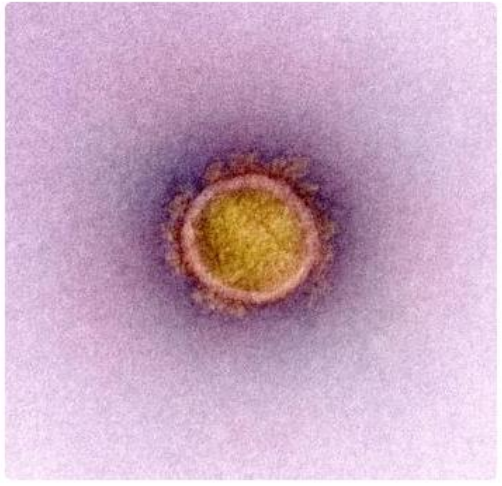




Adaptive COVID-19 Treatment Trial (ACTT)

NIAID is supporting a randomized, controlled clinical trial to evaluate the safety and efficacy of the investigational antiviral remdesivir in hospitalized adults diagnosed with coronavirus disease 2019 (COVID-19). It will take place in up to 75 locations globally.

Remdesivir, developed by Gilead Sciences Inc., is an investigational broad-spectrum antiviral treatment. It was previously tested in humans with Ebola virus disease and has shown promise in animal models for treating Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS), which are caused by other coronaviruses.



What does the study involve?

All potential participants will undergo a baseline physical exam

TNF BLOCKADE

Agents: adalimumab, certolizumab, etanercept, infliximab

Pros: RA, IBD, psoriasis, CRS, Ank Spon, Kawasaki, sepsis, SC

Cons: cytopenia, infections, anaphyl, demyelin, cancer, IV

The New York Times

15 Children Are Hospitalized With Mysterious Illness Possibly Tied to Covid-19

The health authorities in New York City issued an alert saying that the children had a syndrome that doctors do not yet fully understand.

The boardwalk in the Rockaways in Queens. Children are less likely to become seriously ill with Covid-19 than adults. But some do. Kirsten Luce for The New York Times

Charact	eath (n, %)
Overall	3%
Sulfasal	7%
mesalan	
Budesor	4%
Oral/par steroids	11%
6MP/aza monothe	2%
Methotr monothe	0%
Anti-TNF 6MP/AZ	1%
Anti-TNF 6MP/AZ	2%

RE-IBD DATABASE

emiology of Coronavirus
er Research Exclusion

CONCLUSIONS

- First large scale test of anti-inflammatory for deadly viral disease, caution for off-label use outside study
- Appear to reduce fever and cytokine storm but time to recovery and mortality data are lacking
- Unclear impact of virus control, secondary infections, thromboses or cytopenias for short term use
- More classes than can fit in 15 min, trials underway
- Steroids not recommended unless in a trial*

*NIH COVID 19 Clinical Guidelines https://www.covid19treatmentguidelines.nih.gov/critical-care/

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Special thanks to all patients, staff and my family!

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  - Click on the **Q&A** button in the Zoom webinar system.
  - Type your question in the **Q&A** box.
  - Submit your question.
  - You may also email your question to coca@cdc.gov.
- For media questions, please contact CDC Media Relations at 404-639-3286 or email media@cdc.gov.
- **For more Clinical Care information on COVID-19**
  - **Call** COVID-19 Clinical Call Center at 770-488-7100 (24 hours/day).
  - **Refer** patients to state and local health departments for COVID-19 testing and test results.
    - Clinicians should NOT refer patients to CDC to find out where or how to get tested for COVID-19 OR to get test results.
  - **Visit** CDC's Coronavirus (COVID-19) website: https://www.cdc.gov/coronavirus.

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What: Video recording

Where: On the COCA Call webpage at
https://emergency.cdc.gov/coca/calls/2020/callinfo_051920.asp

On COCA's Facebook Page **immediately** after the live call at
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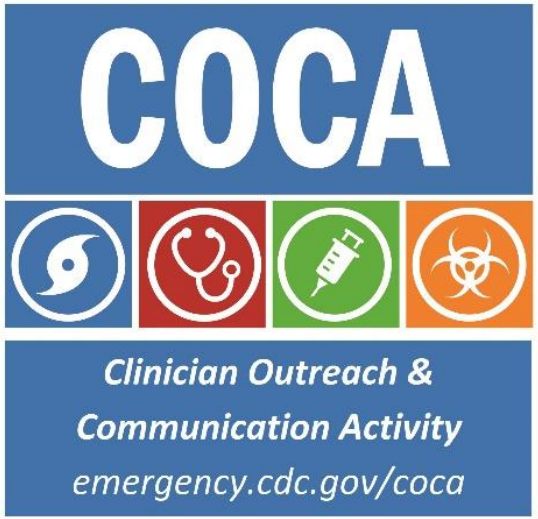

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