

# Myasthenia Gravis and COVID19

Yuebing Li, MD, PhD

Cleveland Clinic

# Symptoms of COVID19 Infection

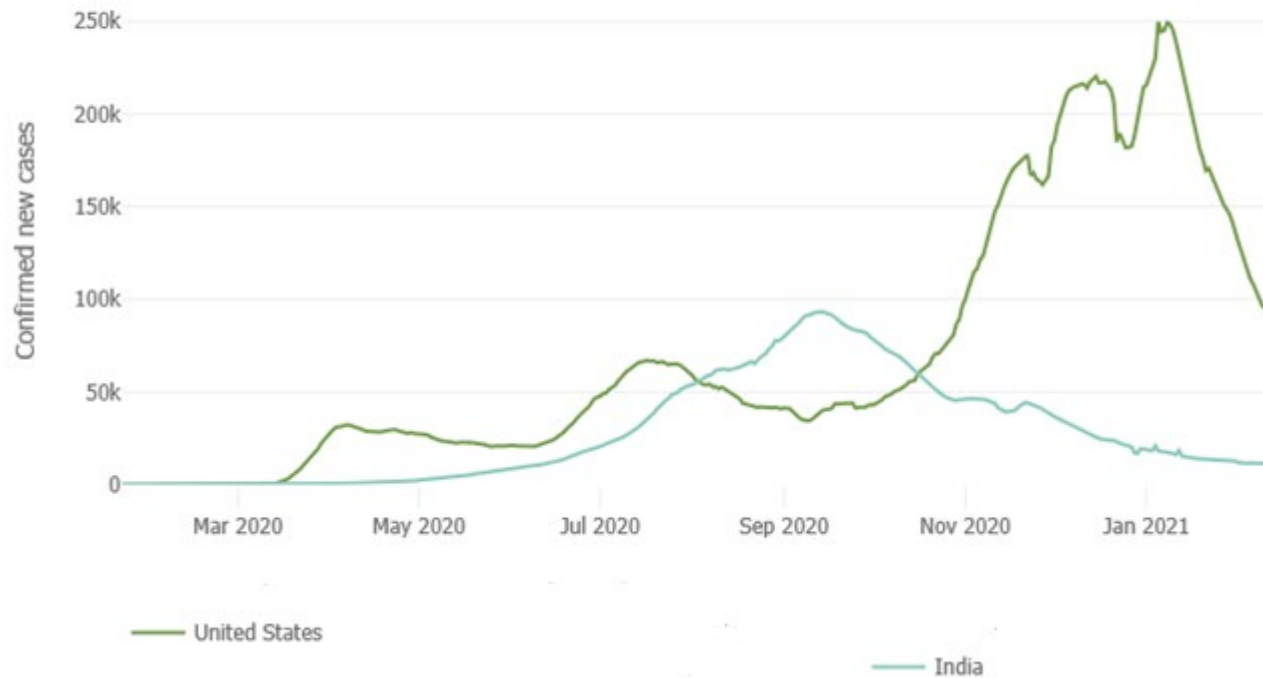
- Symptoms may appear 2-14 days after exposure to virus.
- Symptoms include:
  - Fever or chills, 80 to 99% of symptomatic patients
  - Cough, dry>wet, 60 to 80%
  - Loss of appetite 40 to 80%
  - Fatigue 40 to 70%
  - Difficulty breathing, 30%
  - Muscle or body aches, 30%
  - Loss of taste or sand/or smell, 20 to 90%
  - Sore throat
  - Congestion or runny nose
  - Headache
  - Nausea or vomiting, diarrhea
  - Confusion and other neurological symptoms

# Differences between COVID19 and flu

- Both are respiratory RNA viruses (different family) that are transmitted by droplet.
- COVID infects more people (two to three times higher than flu)
- COVID takes longer period to show up symptoms (five days versus three days)
- COVID causes more mortality (3% to 0.1%)
- COVID affects children less.
- COVID is less seasonal than flu.
- COVID vaccine is more effective: 70 to 90% versus 30 to 50%.
  
- 80% of COVID infected people have no symptoms or very mild symptoms.
  - 97.5% of COVID symptoms show up within 12 days.
- 15% of COVID infected people have significant symptoms.
- 5% of COVID infected people are placed on ventilators.

## DAILY CONFIRMED NEW CASES (7-DAY MOVING AVERAGE)

Outbreak evolution for the current most affected countries



## Does wearing a mask help?

News > World > Asia

### Coronavirus: India makes face masks mandatory for more than 300m people, punishable by up to six months in prison

Orders by major cities in India to wear face masks as a COVID-19 advice and amid a 'massive shortage' of protective equipment

Thursday 09 April 2020 18:45

Adam Withnall Delhi | @adamwithnall | Thursday 09 April 2020 18:45 | comments



# Things you can do at home when infected by COVID

- Social distancing: Stay home from work, school, and other public places.
- Stay in a specific room and away from other people in your home if possible. Use a separate bathroom, if available.
- Avoid sharing personal items with other people, like dishes, towels, and bedding.
- Rest and stay hydrated.
- Monitor your symptoms carefully.
- Cover your cough and sneezes
- Wash your hands often with soap and water for at least 20 seconds or clean your hands with hand sanitizer that contains at least 60% alcohol.
- Clean all surfaces that are touched often, like counters, tabletops, and doorknobs.

# Number of COVID vaccinations

- Number of doses of vaccines given in USA: 56.1 million doses
- Number of doses of vaccines given daily in USA: 1.5 to 2million
- Percentage of people in Ohio who have received at least one dose: 11.5%
  
- Number of doses of vaccines given in the world: 181 million doses
- Israel and UAE leading the trend.
- It takes about 5 years to immunize 70% of world population.

# Types of COVID vaccines

👤 44K 💧 2 ❄️ -70°C ✅ 95%

Pfizer was the first company to report positive phase 3 clinical data. It plans to produce 50M doses in 2020 and 1.3B in 2021.

## Moderna

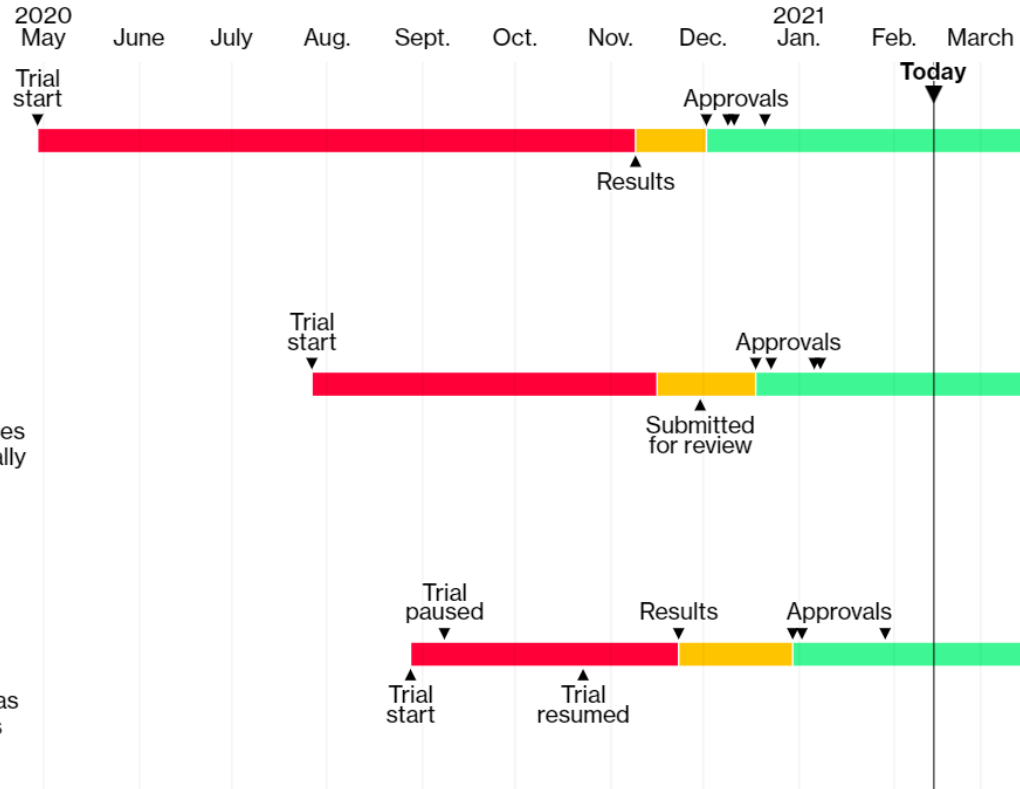
👤 30K 💧 2 ❄️ 2-8°C ✅ 95%

Moderna and Pfizer both use a new vaccine approach involving messenger RNA. Moderna expects to have 20M doses for the U.S. in December and 100M globally in Q1.

## AstraZeneca/Oxford

👤 65K 💧 2 ❄️ 2-8°C ✅ 70%

AstraZeneca struck deals for 3 billion doses even before any late-stage study results. That's more than twice as many as any other candidate. Initial clinical results were mixed.



- Two more: Johnson & Johnson (66%), Novavax (89%).

# Safety and Side Effects of COVID vaccine

- SAERS system, 2 million reported their experience.
- 4.5% reported side effects. Percentages of side effects.
  - 70% pain
  - 30% fatigue
  - 30% headache
  - 23% muscle ache
  - 11% fever/chills
  - Reaction to second dose > first dose
  - Pfizer = Moderna
- Anaphylaxis
  - Pfizer 50/9 million, Moderna 21/8 million
  - 90% occurred within first 30 minutes.
- Death: <1000 among 50 million. No clear direct relationship



## MGFA Official Statement on the COVID-19 Vaccine for the MG Community (February 11, 2021)

- Vaccines manufactured by Pfizer and Moderna are non-live vaccines that use modified RNA. The Johnson & Johnson "1 dose" vaccine is non-live.
- There is no risk of developing Covid-19 infection from the vaccines.
- These vaccines were tested in study subject which majority did not have underlying medical conditions. Patients with autoimmune conditions, like myasthenia gravis, were not included in the testing of these vaccines to date.
- MGFA recommend that these Covid-19 vaccines to be given to patients with autoimmune conditions like myasthenia gravis and for those patients who take medications that suppress the immune system.



## **Known** factors associated with severe COVID infection

- Age
- Chronic condition:
  - Cancer
  - Heart disease
  - Chronic kidney disease
  - COPD
  - Severe obesity (BMI>40)
  - Organ transplant
  - Type 2 diabetes

## Possible factors associated with severe COVID infection

- Type I diabetes
- Asthma
- Stroke
- Dementia
- Liver problem
- Weakened immune system from medical treatment

## COVID-19 in patients with myasthenia gravis

Pria Anand MD<sup>1</sup>  | Michaël C. C. Slama MD, PhD<sup>2,3</sup> | Michelle Kaku MD<sup>1</sup> |  
Charlene Ong MD<sup>1</sup> | Anna M. Cervantes-Arslanian MD<sup>1</sup> | Lan Zhou MD PhD<sup>1</sup> |  
William S. David MD PhD<sup>2</sup> | Amanda C. Guidon MD<sup>2</sup> 

- Five patients, two males, three females
- Age: 42, 57, 64, 64, 90 years old
- Duration of MG: 6, 20, 2, 4, 1 years.
- Four AChR (+), one MuSK (+)
- Evidence of MG exacerbation: YES in one, NO in two, UNCLEAR in two.
- MG meds adjust: ONE received IVIG and increased prednisone. No additional medication augmentation needed in FOUR.
- Outcome: THREE discharged home, ONE went to nursing home, ONE still in hospital.
- Impression: Majority of MG patients did okay.

## Management of patients with generalised myasthenia gravis and COVID-19: four case reports

Annemarie Hübers<sup>1</sup>, Agustina M Lascano<sup>2</sup>, Patrice H Lalive<sup>3</sup>

**Table 1** Clinical data of four patients with generalised gravis and SARS-CoV-2

Patient	1	2	3	4
Disease duration	6 years	4 years	2 years	3 years
MGFA classification	Ila	IIIb	Ila	V
Thymectomy	Yes	Yes	No	Yes
AB status	Anti-ACh-Rab	Anti-ACh-Rab	Negative	Anti-ACh-Rab
Main symptoms prior to admission	Ocular, bulbar, lower limb weakness.	Respiratory muscles, limb weakness.	Unilateral ptosis, double vision.	Ocular (double vision).
Comorbidities	M Basedow (resolved in 2015).	Behçet's disease, chronic migraine, hypogonadotrope hypogonadism, hypothyroidism, obesity, thymoma.	Arterial hypertension.	Obesity, left phrenic nerve damage, sleep apnoea.
MG baseline treatment	AZA 50 mg/day, pyridostigmine 60 mg 5–6×/day.	Pyridostigmine 60 mg 4–5×/day, prednisone 25 mg/day, subcutaneous immunoglobulins 12 g every 4 days.	Pyridostigmine 3×30 mg/day.	Pyridostigmine 60 mg 3×/day, rituximab 1 g every 6 months.
MG treatment change	AZA stopped during COVID-19; IVIG 5 days.	None.	None.	Pyridostigmine increased to 360 mg/day.
COVID-19 disease course	Anosmia after 4 weeks.	Fluctuating headaches and respiratory symptoms over 6 weeks.	Fully recovered after around 3 weeks.	Mechanical ventilation >14 days, tracheostoma for 9 weeks.

AZA, azathioprine; IVIG, intravenous immunoglobulin; MG, myasthenia gravis; MGFA, Myasthenia Gravis Foundation of America; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

# Myasthenia Gravis and COVID-19: Clinical Characteristics and Outcomes

Antonio E Camelo-Filho <sup>1</sup>, André M S Silva <sup>1</sup>, Eduardo P Estephan <sup>1 2</sup>, Antônio A Zambon <sup>1</sup>, Rodrigo H Mendonça <sup>1</sup>, Paulo V S Souza <sup>3</sup>, Wladimir B V R Pinto <sup>3</sup>, Acary S B Oliveira <sup>3</sup>, Iron Dangoni-Filho <sup>1</sup>, Ana F P Pouza <sup>1 4</sup>, Berenice C O Valerio <sup>5</sup>, Edmar Zanoteli <sup>1</sup>

- An observational retrospective study with 15 consecutive adult MG patients admitted with COVID-19 at four hospitals in **São Paulo, Brazil**.
- Most patients with MG hospitalized for COVID-19 had severe courses of the disease: 13 (87%) were admitted in the ICU, 73% needed mechanical ventilation, and 30% died.
- Immunoglobulin use and the plasma exchange procedure were safe.
- Immunosuppressive therapy seems to be associated with better outcomes, as it might play a protective role.
- Problem: Authors considers all patients intubated were due to MG exacerbation. It may be due to COVID pneumonia.

## COVID-19-associated risks and effects in myasthenia gravis (CARE-MG)

Srikanth Muppidi <sup>1</sup>, Jeffrey T Guptill <sup>2</sup>, Saiju Jacob <sup>3</sup>, Yingkai Li <sup>2</sup>, Maria E Farrugia <sup>4</sup>,  
Amanda C Guidon <sup>5</sup>, Jinny O Tavee <sup>6</sup>, Henry Kaminski <sup>7</sup>, James F Howard Jr <sup>8</sup>, Gary Cutter <sup>9</sup>,  
Heinz Wiendl <sup>10</sup>, Matthew B Maas <sup>6</sup>, Isabel Illa <sup>11</sup>, Renato Mantegazza <sup>12</sup>, Hiroyuki Murai <sup>13</sup>,  
Kimiaki Utsugisawa <sup>14</sup>, Richard J Nowak <sup>15</sup>, CARE-MG Study Group

- Physician reported registry, COVID-19 Associated Risks and Effects in Myasthenia Gravis (CARE-MG), joint effort of the International MG/COVID-19 Working Group and neurologists was formally launched on April 9, 2020.
- A total of 91 MG patients were included at the time of interim analysis (Oct 5, 2020).
  - MG worsening or crisis requiring rescue therapy (eg, intravenous immunoglobulin, plasma exchange, or steroids) in the setting of COVID-19 was reported in 36 (40%) of 91 patients.
  - Complete recovery or discharge to home was reported in 39 (43%) patients.
  - 22 (24%) patients died due to COVID-19.
- Most patients were from early non-USA populations

## Impact of Coronavirus Disease 2019 in a French Cohort of Myasthenia Gravis

[Guilhem Solé](#)<sup>1</sup>, [Stéphane Mathis](#)<sup>2 3</sup>, [Diane Friedman](#)<sup>4</sup>, [Emmanuelle Salort-Campana](#)<sup>5</sup>,

**Methods:** A multicenter, retrospective, observational cohort study conducted in by the FILNEMUS network, including MG patients with a confirmed or highly-suspected diagnosis of COVID-19.

**Results:** Among 3,558 MG patients registered in the French database for rare disorders, 34 (0.96%) had COVID-19.

The mean age at COVID-19 onset was  $55.0 \pm 19.9$  years (mean MG duration:  $8.5 \pm 8.5$  years).

By the end of the study, 28 patients recovered from COVID-19, 1 remained affected, and **5 died**.

Only high Myasthenia Gravis Foundation of America (MGFA) class ( $\geq IV$ ) before COVID-19 was associated with severe COVID-19 ( $p=0.004$ )

**Conclusions:** COVID-19 had a limited effect on most patients, and immunosuppressive medications and corticosteroids used for MG management are not risk factors for poorer outcomes.

However, the risk of severe COVID-19 is elevated in patients with high MGFA classes (severer MG disease at the time of COVID infection).



## Impact of Coronavirus Disease 2019 in a French Cohort of Myasthenia Gravis

Guilhem Solé <sup>1</sup>, Stéphane Mathis <sup>2</sup> <sup>3</sup>, Diane Friedman <sup>4</sup>, Emmanuelle Salort-Campana <sup>5</sup>,

Patient	1	2	3	4	5
M/F	M	F	F	M	M
Age, y	62	83	39	44	92
BMI, kg/m <sup>2</sup>	19.9	25.2	20.0	26.1	27.1
Other comorbidities	Dyslip	HBP, Dyslip	Inv Vent, DM Biemer	-	HBP
<b>Myasthenia Gravis</b>					
Antibody type	AntiAChR Ab	AntiAChR Ab	AntiAChR Ab	AntiAChR Ab	AntiAChR Ab
Duration, y	3	1	23	16	7
Thymectomy	Thymoma (2014)	-	-	-	-
MGFA severity class at the beginning of MG	IIb	IIIa	V	IVb	IVb
MGFA severity class at beginning of COVID-19	IIb	IIIa	V	IVb	II
MG treatment at the beginning of COVID-19	Pyr 180mg/d	Abe 100mg/d Pred 70mg/d	Abe 40mg/d Pred 15mg/d Tacro 3mg/d	Pyr 60mg/d AZA 100mg/d	Pyr 180mg/d MFM 2g/d
Causes of death	ARDS several bacterial infections	ARDS	ARDS Multi-organ failure	ARDS Multi-organ failure	ARDS
COVID-19 total duration, d	25	7	9	28	21
Total duration of hospital stay, d	18	7	6	20	17
Total duration of ICU stay, d	18	7	6	20	0
MG treatment during COVID-19	Not Modified	Not Modified	Not Modified	Stop AZA	Not Modified
COVID-19 treatment	Pred	Tocilizumab	HCQ Ritonavir Darunavir	HCQ Azi	-

Epub 2020 Aug 10.

## Myasthenia Gravis Associated With SARS-CoV-2 Infection

Domenico A Restivo<sup>1</sup>, Diego Centonze<sup>2</sup>, Alessandro Alesina<sup>3</sup>, Rosario Marchese-Ragona<sup>4</sup>

- MG caused by COVID?

Table. Clinical and Demographic Data of 3 Patients With Myasthenia Gravis Associated With COVID-19 Infection

Patient	Age, y	Sex	Previous Neurologic or Autoimmune Diseases	Body Temperature at Hospitalization, °C	Myasthenia Gravis Symptom Onset	Pulmonary Manifestations on CT scan	Therapy
1	64	M	No	36.5	5 d after fever	None	Pyridostigmine bromide: 60 mg 4× daily Prednisone: 75 mg/d
2	68	M	No	36	7 d after fever	None	IVI: 0.4 g/kg/d for 5 d
3	71	F	No	37.6	5 d after fever	Bilateral interstitial pneumonia	Plasmapheresis: 3 sessions the 1st wk, 2 sessions the 2nd wk, 1 session the 3rd wk; dosage: 1 volume plasma/1 volume saline + 2 L albumin Lopinavir/ritonavir: 400/100 mg 2× daily Hydroxychloroquine: 200 mg 2× daily

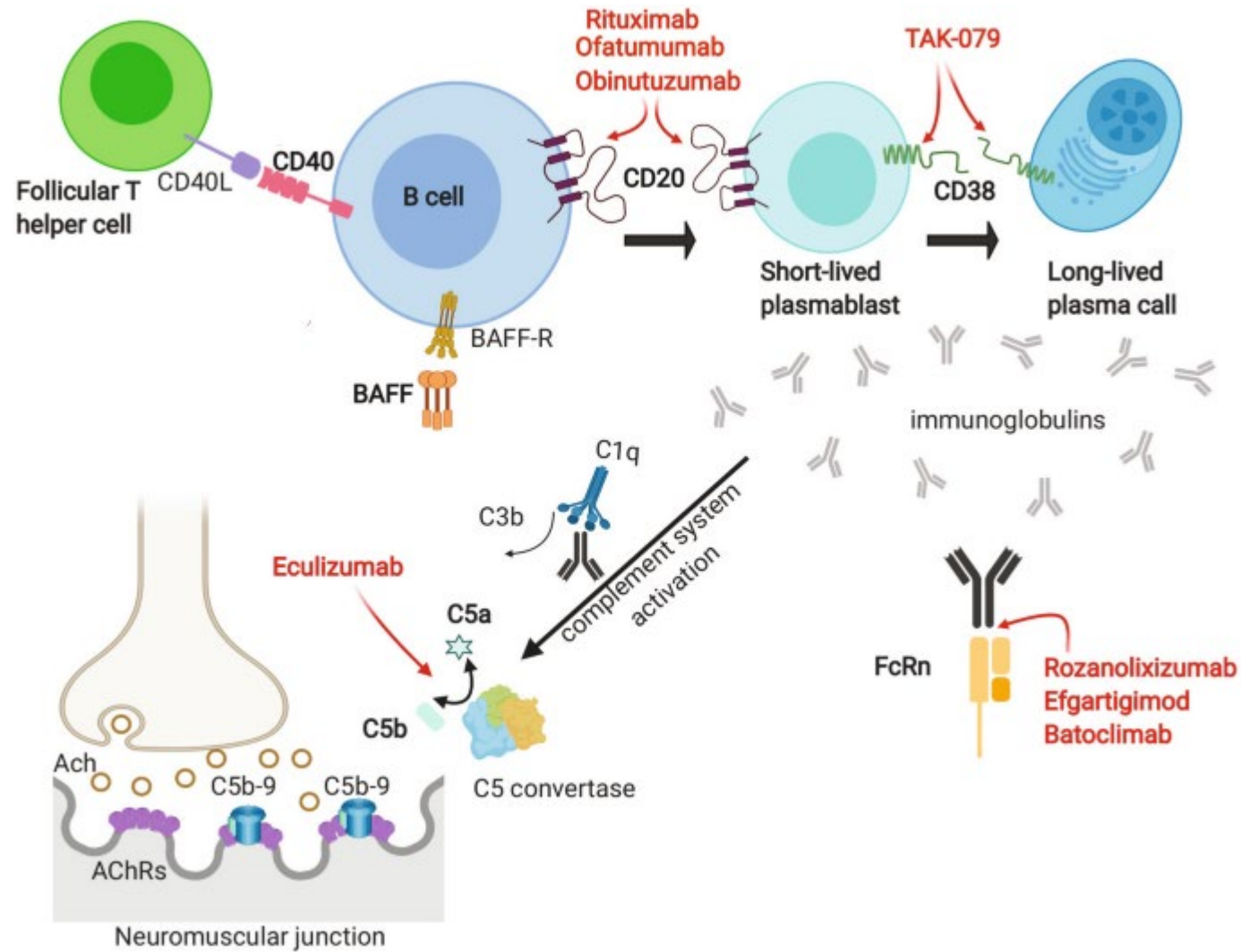
COVID = coronavirus disease 2019; CT = computed tomography; F = female; IVI = intravenous immunoglobulin; M = male.

## Guidance for the management of myasthenia gravis (MG) and Lambert–Eaton myasthenic syndrome (LEMS) during the COVID–19 pandemic

International MG/COVID-19 Working Group; Saiju Jacob <sup>1</sup>, Srikanth Muppidi <sup>2</sup>, Amanda Guidon <sup>3</sup>, Jeffrey Guptill <sup>4</sup>, Michael Hehir <sup>5</sup>, James F Howard Jr <sup>6</sup>, Isabel Illa <sup>7</sup>, Renato Mantegazza <sup>8</sup>, Hiroyuki Murai <sup>9</sup>, Kimiaki Utsugisawa <sup>10</sup>, John Vissing <sup>11</sup>, Heinz Wiendl <sup>12</sup>, Richard J Nowak <sup>13</sup>

- MG/LEMS patients should continue their current treatment and should not stop any existing medications/treatment (including IVIG, plasma exchange or Soliris).
- Whenever possible, consider home infusion rather than traveling to hospitals or infusion centers
- B-cell depleting therapy: delay initiation of B-cell depleting therapy (e.g., rituximab), until the peak of the outbreak is over in their region.
- Treatment trial medications: no clear indication of COVID risk increase.
- For those MG patients who developed COVID, there might be a need to increase the dose of corticosteroids as in standard infection/stress steroid protocols. However, if the symptoms are severe (requiring hospitalization), it may be necessary to consider pausing current immunosuppression temporarily, especially if there is concurrent infections/sepsis.

# New Treatment in Myasthenia Gravis



# New Treatment in Myasthenia Gravis

- Complement inhibitors
  - **Eculizumab** (Soliris). Alexion. FDA approved for MG. Expensive.
  - **Ravulizumab** (Ultomiris), Alexion. Extended version of eculizumab. Phase III trial ongoing.
  - **Zilucoplan**. Ra Pharma-UCB. Phase III trial ongoing.
  - **Pozelimab** and **Cemdisiran** combination. Regeneron. Phase III trial planned.
- Neonatal Fc receptor (FcRn) therapy
  - **Efgartigimod**. Argenx. Phase III trial finished. FDA submission soon.
  - **Rozanolixizumab**. UCB Pharma. Phase III trial ongoing.
  - **Nipocalimab**. Momenta. Phase III trial in the initiation stage.
  - **Batoclimab**. Immunovant. Phase III trial being planned.
- **Inebilizumab** (Uplizna), CD19 directed monoclonal antibody, FDA approved for neuromyelitis optica. Similar to Rituximab. Sponsored by Viela Bio. MINT trial just started.
- **Amifampridine phosphate** (Firdapse). Catalyst. Trial on MuSK-MG failed. Company may consider another trial.