

# Omeros Corporation

October 2020

Analyst information

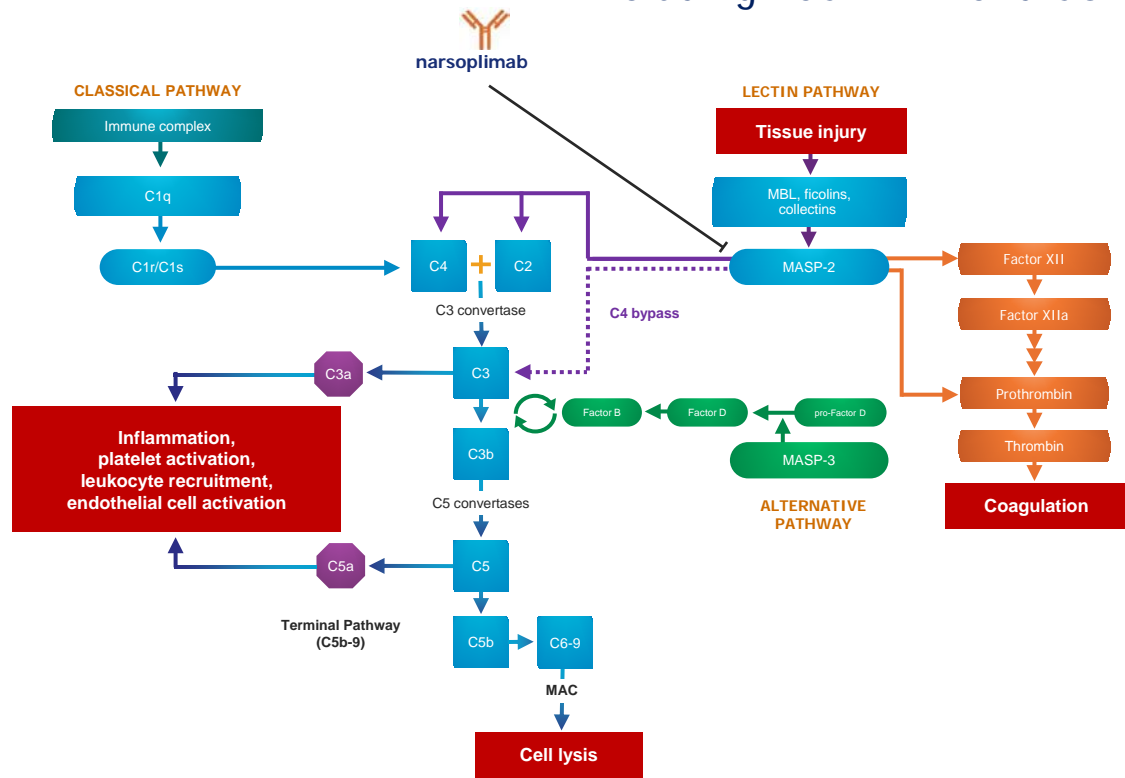
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## Narsoplimab and Regulatory Status

- Narsoplimab is a fully human IgG4 antibody against MASP-2, the effector enzyme of the lectin pathway of complement
- Completed pivotal clinical program in hematopoietic stem cell transplant-associated-TMA (HSCT-TMA). Rolling BLA for HSCT-TMA will be submitted soon.
- Enrolling 2 additional Phase 3 clinical programs - IgA nephropathy (IgAN) and atypical hemolytic uremic syndrome (aHUS)
- ~250 patients and healthy volunteers have been dosed with narsoplimab
- No significant safety concerns have been observed
- FDA has granted narsoplimab Breakthrough Therapy designation in both HSCT-TMA and IgAN
- Broad therapeutic areas for lectin pathway inhibition:
  - Endothelial injury syndromes
  - Proteinuric diseases
  - Ischemia-reperfusion injury
  - Dysregulation of inflammation (e.g., CNS)

# Narsoplimab is a Potential Therapeutic for a Broad Range of Disorders, Including HSCT-TMA and COVID-19



## Lectin Pathway Disorders

- COVID-19
- HSCT and TMA-related EIS
  - aGVHD
  - CLS
  - DAH
  - IPS
  - SOS/VOD
  - HELLP/CAPS
- Oncology
  - Colorectal Cancer
  - Cervical Cancer
  - ESCC
- Acute transplant & surgery-related conditions
  - Delayed Graft Function-solid organ transplant
- Chronic nephrology/proteinuria diseases
  - IgAN
  - MGN
  - Lupus nephritis

## Endothelial Injury Plays a Major Role in Pathogenesis of a Wide Range of Diseases

Endothelial injury plays a role in the pathogenesis of:



Stroke	Viral infections (e.g. COVID-19)	Chronic kidney disease
Peripheral vascular disease	Stem cell transplant-related complications (e.g., TMA, aGVHD, VOD, DAH, IPS, CLS)	Venous thrombosis
Cancer	Heart disease	Diabetes

Injury to endothelial cells occurs in many ways: physically, chemically, and immunologically

Damage to the vascular endothelium results in a procoagulant state and complement pathway activation

- Lectin pathway is a pattern-recognition system
- Lectin pathway is activated by carbohydrate patterns on microbes and surfaces of damaged cells

# Role of Endothelial Injury in COVID-19 Published Across Numerous Peer-reviewed Journals

**OXFORD ACADEMIC**  
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**MASP2 levels are elevated in thrombotic m association with microvascular endothelial suppression by anti-MASP2 antibody narsc**  
 S. Elhadad, J. Chapin, D. Copertino, K. Van Besien, J. Ahamed, J. Lai  
 First published: 18 July 2020 | <https://doi.org/10.1111/cei.13497>

**COVID-19 as a cardi potential role of chr dysfunction**

**Endotheliopathy in COVID-19-associated coagulopathy: A multi-centre, cross-sectional study**  
 Matthew L Meizlish, MPhil | C-Hong Cha

**COVID-19: the vasculature unleashed**  
 Laure-Anne Teuwen, Vincent Geldhof, Alessandra Pasut & Peter Carmeliet  
*Nature Reviews Immunology* 20, 389–391(2020) | Cite this article  
 39k Accesses | 8 Citations | 693 Altmetric

**Is COVID-19 an Endothelial Disease? Clinical and Basic Evidence**  
 An Author Co-Editorial  
 Celestino Sardu, Jessica Gambardella, Marco Bruno Morelli, Xujun Wang, Raffaele Marfella, Gaetano Santulli

**Mount Sinai Study Indicates COVID-19 May be Driven by Pulmonary Thrombi & Pulmonary Endothelial Dysfunction**  
 April 28, 2020 | COVID-19: ENDOTHELIAL DYSFUNCTION, MOUNT SINAI SCHOOL OF MEDICINE, MOUNT SINAI THROMBOSIS, THROMBOSIS

**Endothelial Injury May Play a Major Role in COVID-19-Associated Coagulopathy**  
 Alm F. Iyck, MD  
 DISCLOSURES | June 20, 2020

**The NEW ENGLAND JOURNAL of MEDICINE**  
 ORIGINAL ARTICLE  
 Ticagrelor and Aspirin or Aspirin Alone in Acute Ischemic Stroke  
 NEJM Catalyst eBook  
 The Clinician Role in Health Care Delivery and Innovation  
 ORIGINAL ARTICLE  
 Timing of Initiations of Renal-Replacements Therapy in Acute Kidney Injury  
 EDITORIAL  
 WHO's Next — The United States and the World Health Organization

**Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19**  
 Maximilian Ackermann, M.D., Stijn E. Verleden, Ph.D., Mark Kuehnel, Ph.D., Axel Haverich, M.D., Tobias Welte, M.D., Florian Laenger, M.D., Arno Vanstapel, Ph.D., Christopher Werlein, M.D., Helge Stark, Ph.D., Alexandar Tzankov, M.D., William W. Li, M.D., Vincent W. Li, M.D., et al.

## Endothelial Injury with Complement Activation is Central to Pathophysiology of HSCT-TMA and COVID-19

- Once endothelial injury occurs, pathophysiology of HSCT-TMA and COVID-19 are similar
- Endothelial injury activates the lectin pathway of complement
- In HSCT-TMA, endothelial injury is caused by conditioning regimen, immunosuppressants, GVHD and infection
- In COVID-19, endothelial injury is caused by direct viral infection
- MASP-2, the lectin pathway's effector enzyme, binds the nucleocapsid protein of SARS-CoV-2 and activates the lectin pathway, leading to amplification of underlying cellular injury and inducing cytokine response (e.g., IL-6)
- Viral load has no correlation in COVID-19 patients to clinical status or disease severity

### *Components of COVID-19:*

- *Complement activation*
- *Inflammation*
- *Coagulation*

***Narsoplimab inhibits all 3***

## Parallels Between COVID-19 and HSCT-TMA

Comparator	COVID-19	HSCT-TMA
<b>Lectin-Pathway Activation from Endothelial Damage</b>	✓	✓
<b>Cause of Endothelial Injury</b>	Viral	Conditioning regimen, Immunosuppressants, GVHD, infection
<b>MASP-2 Activation</b>	✓	✓
<b>Multi-Organ TMA</b>	✓	✓

- Approximately 50 patients have been dosed with narsoplimab across the two EIS
- Marked improvement seen in narsoplimab-treated patients in these studies



## Compassionate Use of Narsoplimab for COVID-19 Patients in Bergamo, Italy

- 6 patients treated with narsoplimab, each included for presence of ARDS requiring mechanical ventilation (4 on CPAP, 2 intubated)
- Dosing IV twice weekly for 2 to 4 weeks
- All patients fully recovered, survived and were discharged
- 2 patients with massive bilateral pulmonary thromboses that resolved after narsoplimab treatment
- Temporal patterns of laboratory markers (CEC, IL-6, IL-8, CRP, LDH, AST and D-dimer) were consistent with the observed clinical improvement; in particular, CEC counts appear to be a reliable tool to evaluate endothelial damage and treatment response
- All patients received routine supportive care (prophylactic enoxaparin, azithromycin, hydroxychloroquine, darunavir/cobicistat) and, during the study, steroids (patient #1 did not receive steroids and patients 2 and 3 likely received no benefit from steroids given timing of initiation)
- Two control groups with similar entry criteria and baseline characteristics were selected for retrospective comparison showing substantial mortality rates of 32 percent and 53 percent
- Manuscript published in peer-reviewed *Immunobiology*

## Data from the COVID-19 Study in Italy

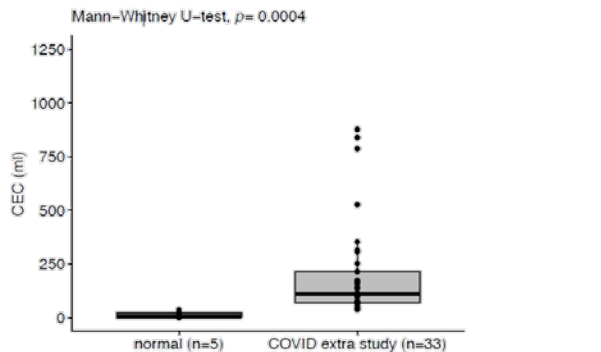
### Demographics and Treatment Summary

Demographic	Median (range) or n (%)
<b>Age</b>	57 years (47-63)
<b>Male sex</b>	5 (83%)
<b>Weight</b>	86 Kg (82-100 Kg)
<b>Comorbidities</b>	Diabetes (n=1); Hypertension (n=1); Dyslipidemia (n=2); Obese/Overweight (n=6)

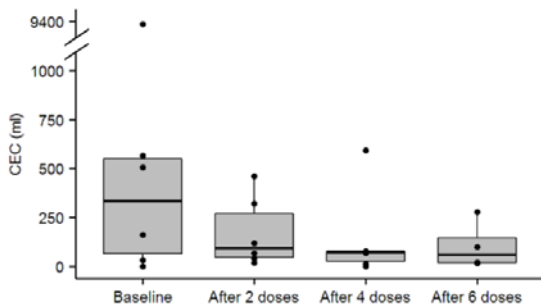
Treatment Summary	n (%) or Median (range)
<b>Timing of narsoplimab treatment from start of CPAP oxygen support</b>	
<i>Within 24 hours</i>	4 (67%)
<i>Within 48 hours</i>	2 (33%)
<b>Time from hospital admission to treatment</b>	2 days (1-4)
<b>Duration of follow-up (to date) after first dose</b>	27 days (16-90)

## Data from the COVID-19 Study in Italy

### Evidence of Endothelial Damage (CEC Counts) in COVID-19

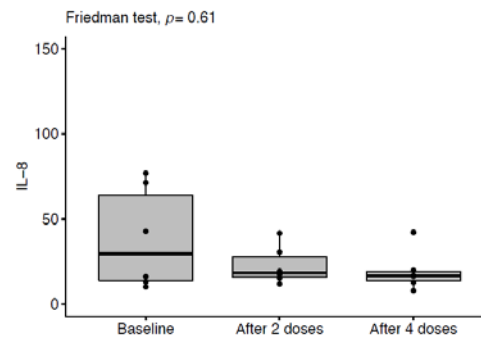
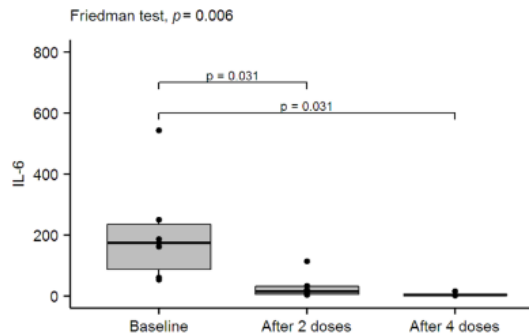


5 normal (uninfected) and 33 infected patients without  
Friedman test,  $p = 0.01$



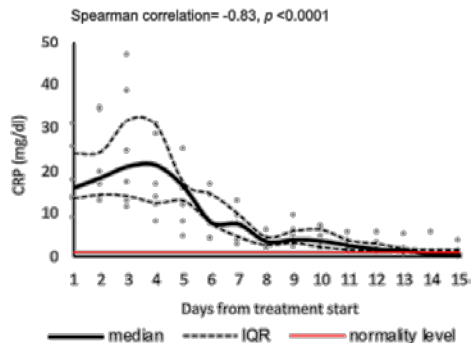
6 infected patients treated with Narsoplimab

### IL-6 / IL-8 Levels Improved in 6 Patients Treated with Narsoplimab

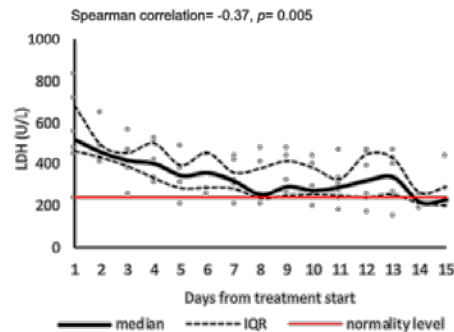


## Data from Narsoplimab-treated COVID-19 Patients

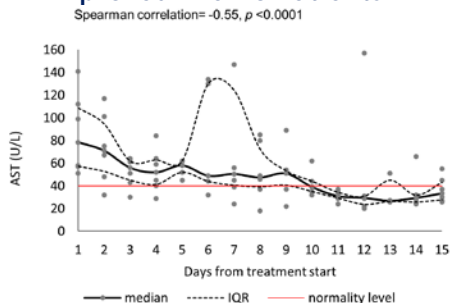
### C-Reactive Protein Improved in all 6 Patients



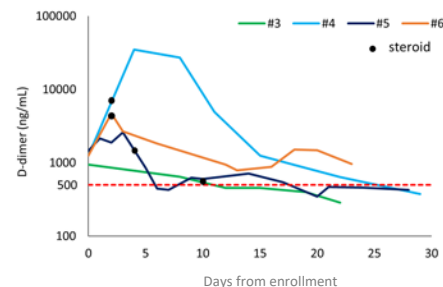
### Lactate Dehydrogenase Improved in all 6 Patients



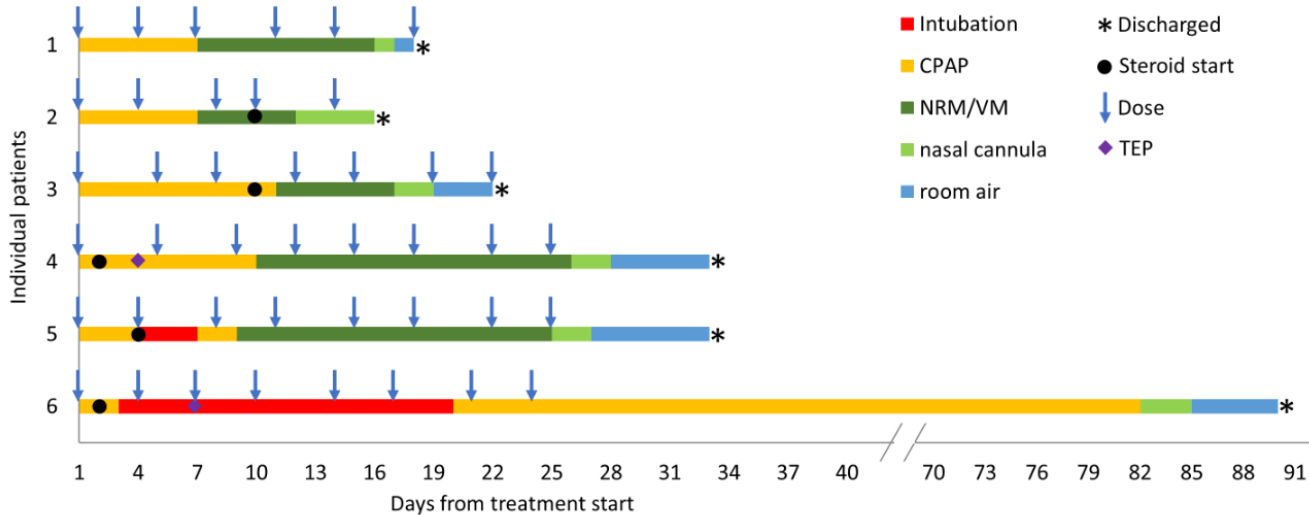
### Aspartate Aminotransferase (AST) Improved in all 6 Patients



### D-Dimer Improved in all Assessed Patients



## Clinical Outcomes of COVID-19 Patients Treated with Narsoplimab



- The bar colors indicate the different oxygen support (CPAP = yellow; mechanical ventilation with intubation = red; non-rebreather oxygen mask/Venturi mask = green; low-flow oxygen by nasal cannula = light green; room air = blue)
- Narsoplimab doses are marked by blue arrows
- Black circle indicates the beginning of steroid treatment
- CPAP = continuous positive airway pressure; NRM = non-rebreather oxygen mask; VM = Venturi mask; TEP = pulmonary thromboembolism

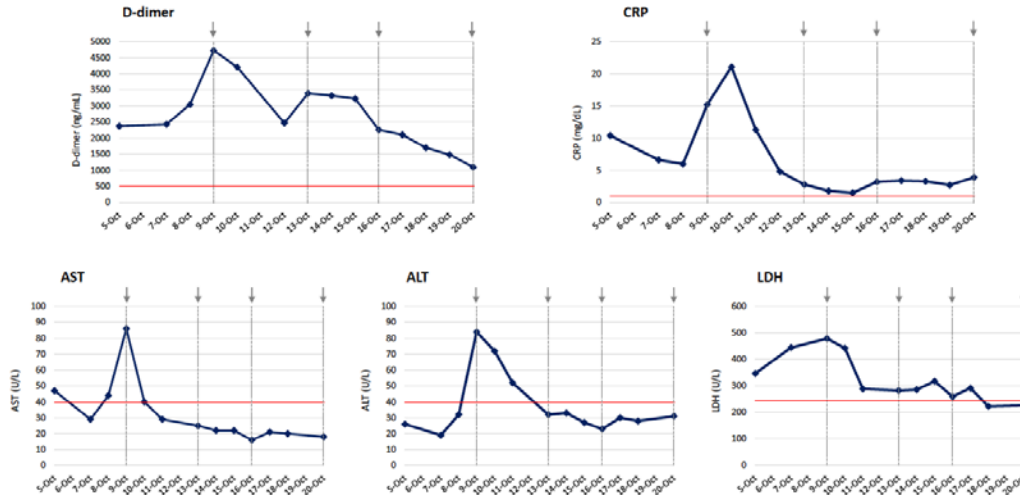
## At 5-6 Month Follow-Up, All 6 Patients Without Clinical or Laboratory Evidence of Sequelae

Laboratory Findings	Baseline	Last Evaluation (5-6 Mos. Post-Discharge)
White cell count - per mm <sup>3</sup> , median (range)	8335 (6420-10,120)	7320 (3200-8770)
> 10,000 per mm <sup>3</sup> - no. (%)	2 (33)	0 (0)
< 4000 per mm <sup>3</sup> - no. (%)	0 (0)	1 (17)
Lymphocyte count - per mm <sup>3</sup> , median (range)	875 (410-1290)	2815 (810-3780)
Platelet count - x 10 <sup>3</sup> per mm <sup>3</sup> , median (range)	282 (199 -390)	238 (170-354)
Hemoglobin - g/dL, median (range)	13.4 (13.2-14.1)	14.8 (13.4-15.8)
Distribution of other findings (laboratory reference ranges)		
C-reactive protein (0.0-1.0 mg/dL)	14 (9.5-31.3)	0.15 (0-0.5)
Lactate dehydrogenase (120/246 U/L)	518.5 (238-841)	212 (119-249)
Aspartate aminotransferase (13-40 U/L)	78.5 (51-141)	18 (12-29)
Alanine aminotransferase (7-40 U/L)	73 (37-183)	22.5 (20-67)
Creatinine (0.3-1.3 mg/dL)	0.85 (0.38-1.33)	0.94 (0.51-1.07)
D-dimer (< 500 ng/mL)		
< 190 - no. (%)	0 (0)	3 (50)
> 190 - median (range)	1250.5 (943-1454)	324 (202-390)

- Clinical status at last evaluation of all 6 patients - no evidence of post-COVID sequelae

## Bergamo Patient #7 Undergoing Narsoplimab Treatment

- 74-year-old man
- High-risk: diabetic, obese, long history of smoking/COPD, prostate cancer
- Rapidly deteriorating pulmonary status: nasal cannula → mask → CPAP → intubation
- Began treatment with narsoplimab following intubation; extubated around the 2<sup>nd</sup> dose



\* Grey arrows denote dosing; Red lines denote normal value threshold