

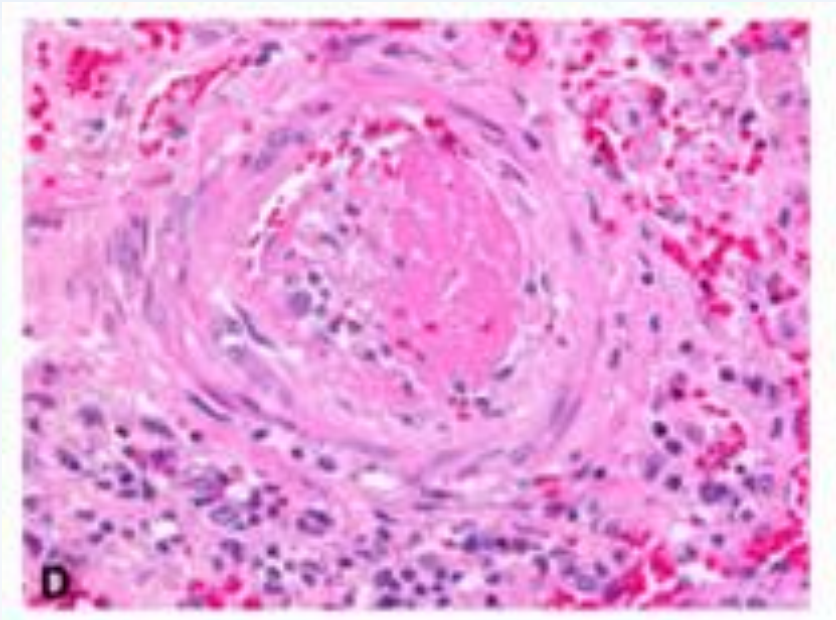
# COVID-19 – Lessons from stem cell transplant recipients

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## Miguel Perales MD disclosures

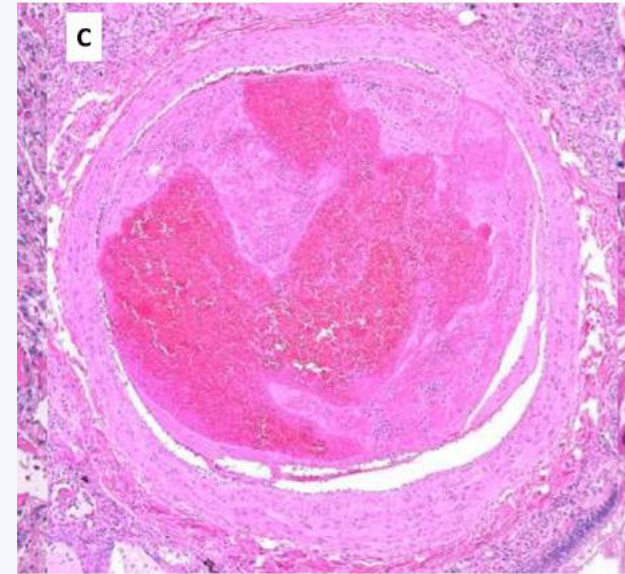
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  - MolMed, NexImmune
- Ad hoc Advisory Board:
  - Abbvie, Bellicum, Bristol-Myers Squibb, Incyte, Kite-Gilead, Nektar Therapeutics, Novartis, Omeros, Takeda
- Consulting:
  - Merck
- Member, DSMB:
  - Medigene, Servier, Cidara
- Research Funding:
  - Incyte (clinical trial), Kite-Gilead (clinical trial), Miltenyi (clinical trial)
- Academic/Not-for-Profit:
  - Board Member: Be The Match (NMDP)
  - Chair, CIBMTR Cellular Immunotherapy Data Resource (CIDR) Oversight Committee
  - Member DSMB: Tufts Cancer Center, University of Barcelona CART trial

## Lung – Transplant Associated TMA



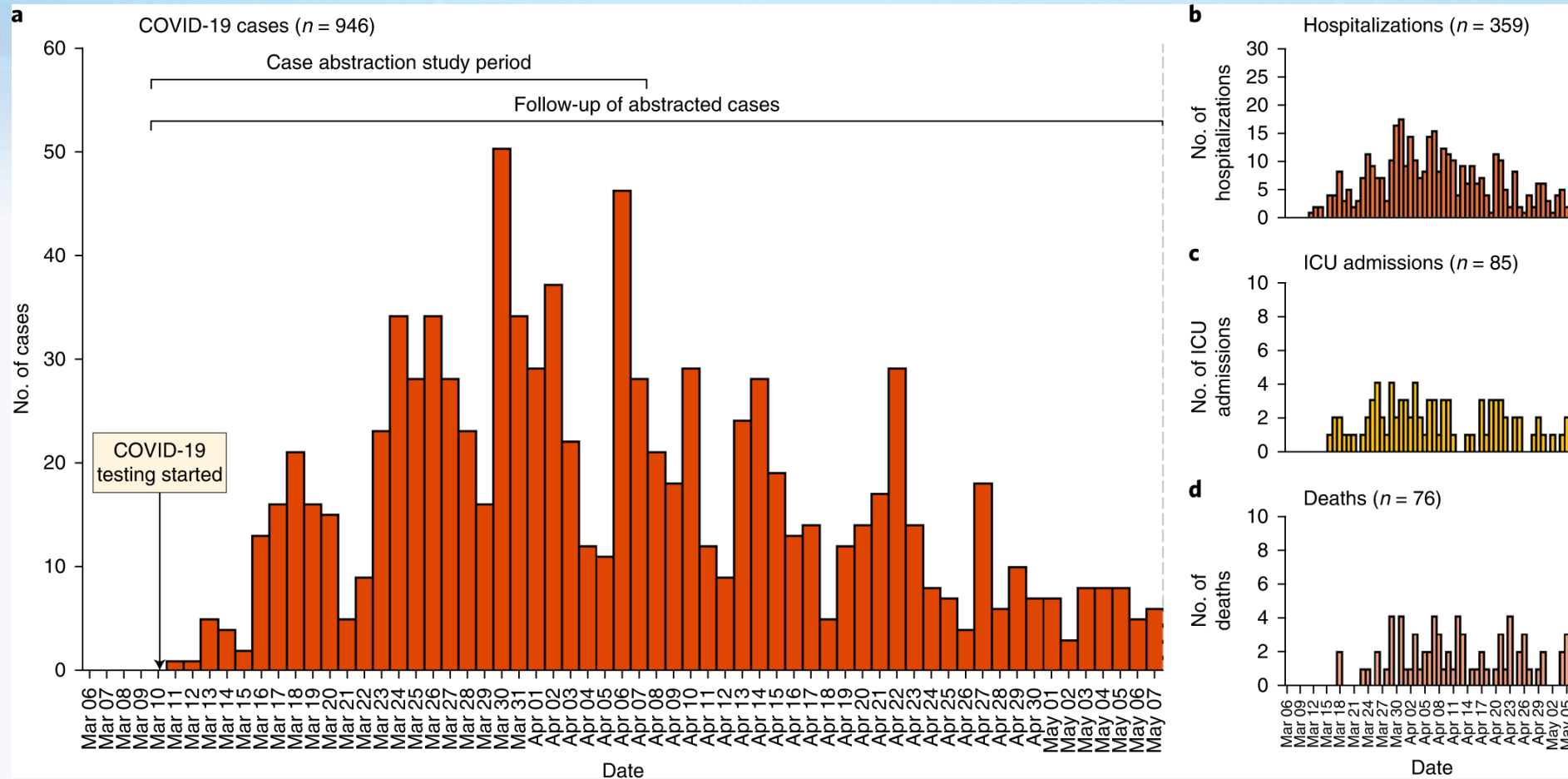
Jodele et al, Blood 2014

## Lung – COVID-19



Recalde et al, Thorax 2020

# SARS CoV-2-positive cases at MSK from 3/10/20 to 5/7/20

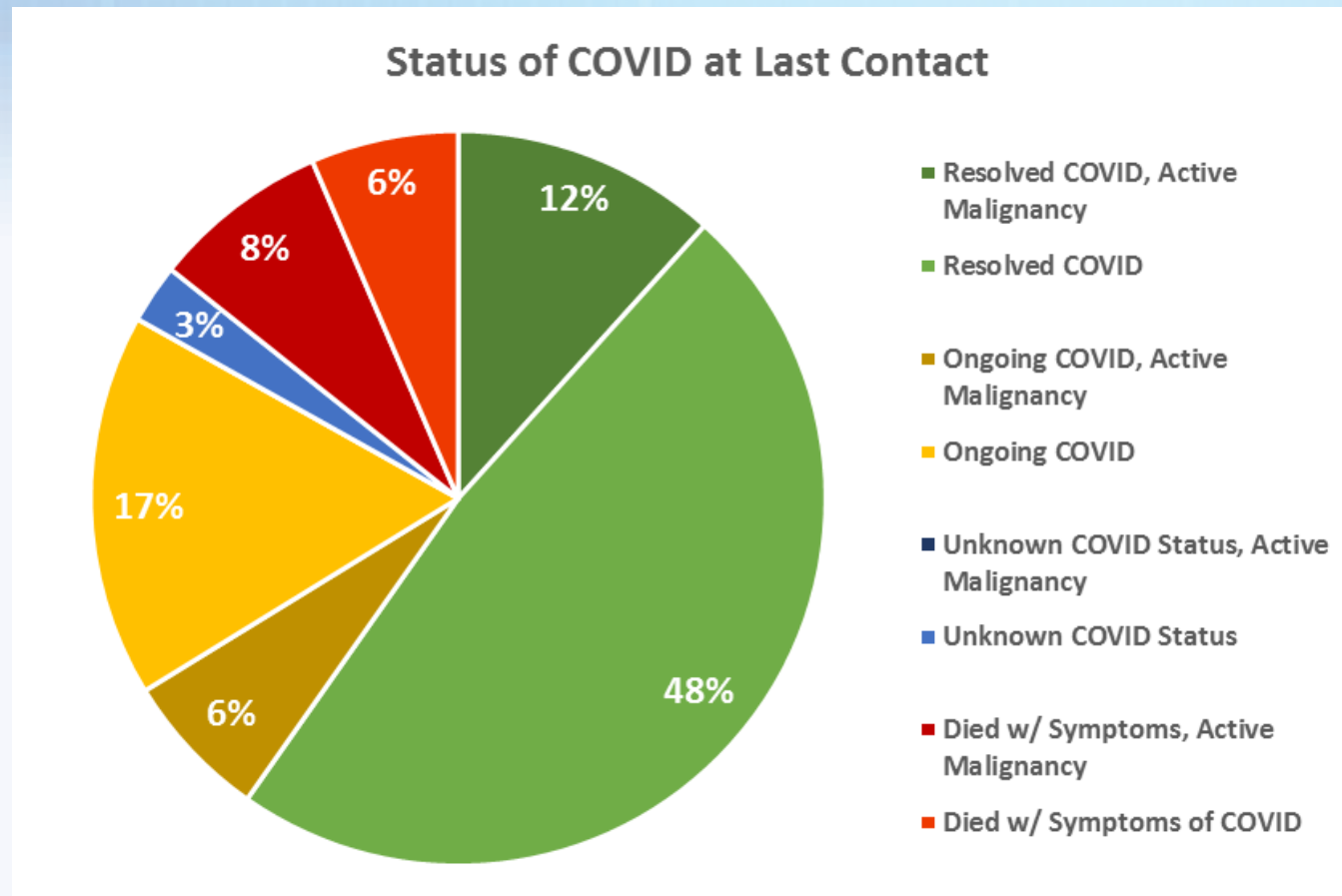


# Admission for COVID-19 infection more likely in patients with blood cancers

| Variable   | Univariate       |         | Multivariate     |         |
|--|------------------|---------|------------------|---------|
|  | OR (95% CI)      | P value | OR (95% CI)      | P value |
| <b>Predictors of hospitalization, by logistic regression (n = 411<sup>a</sup>)</b> |                  |         |                  |         |
| Age (>65 years)  | 1.81 (1.20-2.72) | 0.004   | 1.53 (0.96-2.43) | 0.072   |
| Sex (female)   | 0.89 (0.60-1.32) | 0.575   |                  |         |
| Race (non-white)   | 1.36 (0.91-2.04) | 0.135   | 1.62 (1.05-2.51) | 0.029   |
| BMI ( $\geq 30$ kg/m <sup>2</sup> )  | 0.89 (0.58-1.36) | 0.585   |                  |         |
| Smoking (current/former)   | 1.60 (1.07-2.40) | 0.022   | 1.37 (0.88-2.13) | 0.169   |
| Asthma/COPD  | 1.39 (0.81-2.37) | 0.226   | 1.07 (0.59-1.92) | 0.828   |
| Cancer (non-metastatic solid)  | 1.00 (Ref)       | -       | 1.00 (Ref)       |         |
| Cancer (metastatic solid)  | 0.89 (0.53-1.50) | 0.647   | 0.76 (0.43-1.34) | 0.338   |
| Cancer (hematologic)   | 2.24 (1.25-4.06) | 0.007   | 2.49 (1.35-4.67) | 0.003   |
| Major surgery (within 30 d)  | 1.24 (0.53-2.84) | 0.612   |                  |         |
| Diabetes   | 1.20 (0.73-1.96) | 0.467   |                  |         |
| Cardiac disorder   | 1.86 (1.13-3.07) | 0.015   | 1.35 (0.77-2.36) | 0.297   |
| HTN/chronic kidney disease   | 1.84 (1.24-2.75) | 0.003   | 1.51 (0.96-2.39) | 0.077   |
| Systemic chemotherapy (within 30 d)  | 1.04 (0.70-1.54) | 0.845   |                  |         |
| Chronic lymphopenia or corticosteroids   | 1.86 (1.11-3.15) | 0.019   | 1.85 (1.06-3.24) | 0.030   |
| ICI  | 2.53 (1.18-5.67) | 0.017   | 2.84 (1.24-6.72) | 0.013   |

# Favorable clinical outcomes after COVID-19 in transplant and CAR T patients

VIRTUAL SALON SERIES

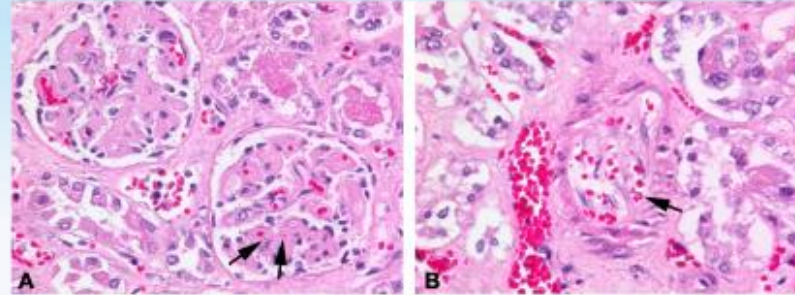


- **14 Deaths (18%)**
  - 41% of admitted
  - 21% if admitted & malignancy in remission
- No new or worsening of **GVHD**
- No new **dialysis** requirements
- No **CVA**
- DVT PPx if Plt adequate
  - 2 **DVTs**

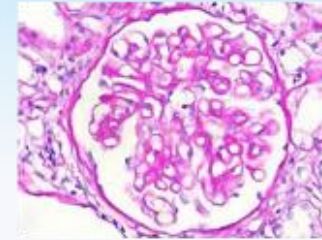
# Transplant associated TMA Is a multivisceral disease

VIRTUAL SALON SERIES

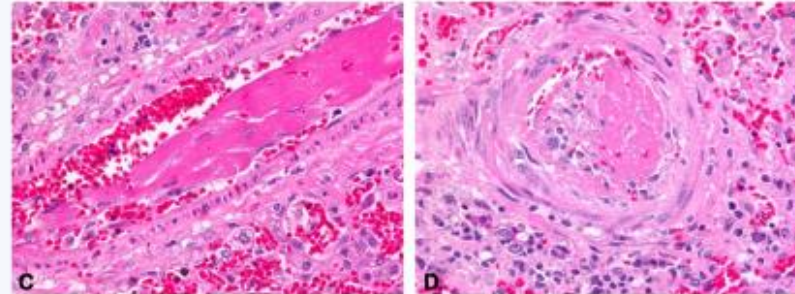
Kidney TMA



Normal kidney



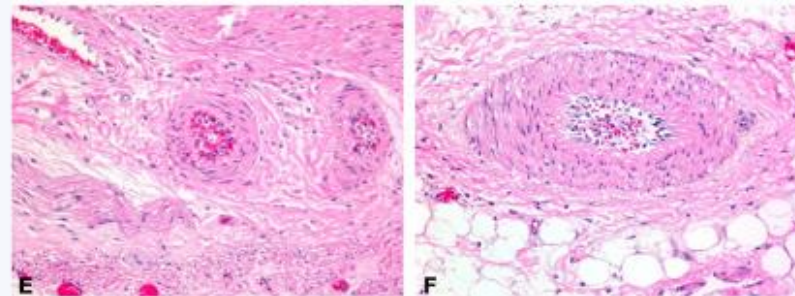
Lung TMA



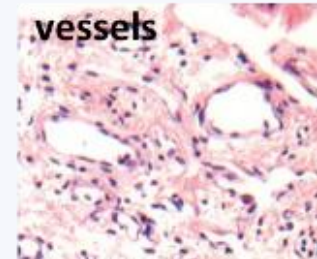
Normal lung



Intestinal TMA

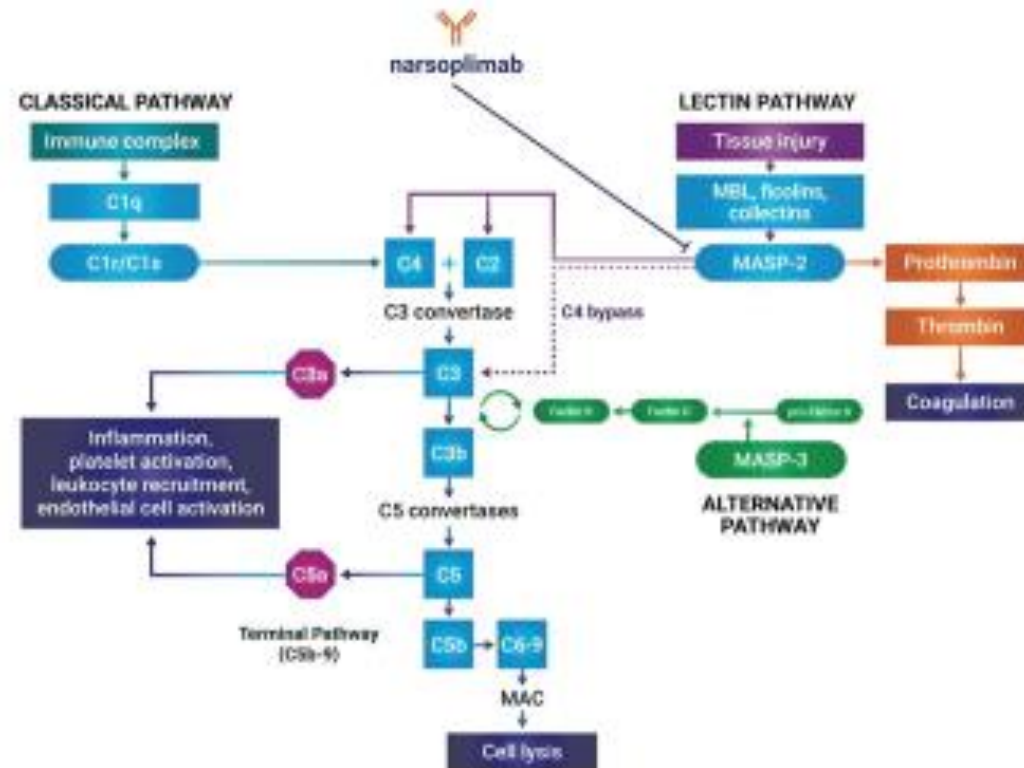


Normal mesenteric vessels



# Narsoplimab

- Narsoplimab (OMS721) is an investigational fully human IgG4 MAb
- It binds to mannan-binding lectin-associated serine protease-2 (MASP-2)
- MASP-2 is the effector enzyme of lectin pathway of complement
- Narsoplimab leaves the classical pathway function fully intact
- It blocks MASP-2-mediated coagulation (conversion of prothrombin to thrombin, activation of Factor XII to XIIa and activation of kallikrein)





# HSCT-TMA Pivotal Trial: Design

 VIRTUAL SALON SERIES

- Single-arm, open-label design
- Initiated as a Phase 2 trial; following receipt of breakthrough therapy designation and discussion with FDA, converted to a pivotal trial.
- Protocol specified that patients receive narsoplimab once weekly for  $\geq 4$  weeks.

# Primary Endpoint

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Response as assessed by clinically meaningful **improvement in laboratory markers** and **improvement in organ function and transfusion freedom**

## Laboratory Markers

**LDH <1.5 UL**

AND

### Platelet Count

- Baseline  $\leq 20,000/\mu\text{L}$ :
  - Triple baseline and absolute count  $>30,000/\mu\text{L}$  and freedom from platelet transfusion
- Baseline  $>20,000/\mu\text{L}$ :
  - Increase by at least 50% and absolute count  $>75,000/\mu\text{L}$  and freedom from platelet transfusion



## Organ Function

### Renal

- Reduction of creatinine  $>40\%$
- OR
- Normalization of creatinine and reduction of creatinine  $>20\%$
- OR
- Discontinuation of renal replacement therapy

### Pulmonary

- Extubation and discontinuation of ventilator support
- OR
- Discontinuation of non-invasive mechanical ventilation (continuous positive pressure ventilation)

### Gastrointestinal (tissue diagnosis)

- Improvement measured by improvement in gastrointestinal measures in the Mount Sinai Acute GVHD International Consortium (MAGIC) criteria

### Neurological

- Limited to stroke, PRES, seizures, weakness

# Response

| Population   | Complete Response Rate (%)  |
|--|-----------------------------|
| All treated patients (N=28)<br>(95% CI)                                      | 54% (15/28)<br>(34% to 72%) |
| Patients treated per protocol ( $\geq 4$ weeks of dosing) (n=23)<br>(95% CI) | 65% (15/23)<br>(43% to 84%) |

# 100-day survival following HSCT-TMA diagnosis

 VIRTUAL SALON SERIES

| Population   | 100-Day Survival |
|--|------------------|
| All treated patients (N=28)                                      | 68% (19/28)      |
| Patients treated per protocol ( $\geq 4$ weeks of dosing) (n=23) | 83% (19/23)      |
| Treatment responders (n=15)                                      | 93% (14/15)      |