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Omeros Corporate Presentation

March 2021

Safe Harbor

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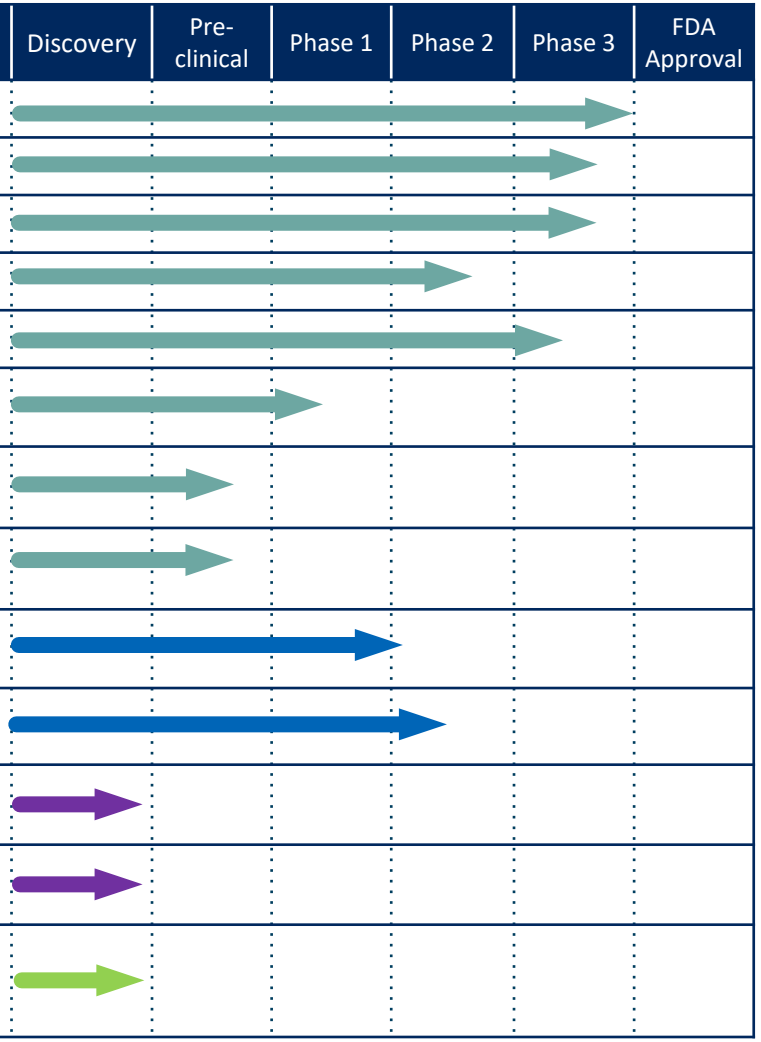
Highly Diversified Pipeline to Drive Sustainable Growth

Omeros Controls All Economic Rights Across Its Programs and Platforms

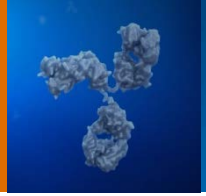
	Program / (Candidate)	Molecule	Targeted Disease
Complement Franchise (iCAB)	MASP-2, lectin pathway (narsoplimab (OMS721))	Ab	Stem Cell Transplant-Associated TMA
			IgA Nephropathy
			Atypical Hemolytic Uremic Syndrome
			Lupus Nephritis & Other Renal Diseases
			COVID-19
	MASP-3, alternative pathway (OMS906)	Ab	PNH and a Wide Range of Other Alternative Pathway Disorders
	MASP-2 (OMS1029)	Ab	Long-Acting 2nd Generation Antibody Targeting Lectin Pathway Disorders
	MASP-2, MASP-3, MASP-2/3	SM	Disorders of the Lectin and Alternative Pathways of Complement
Addiction	PDE7 (OMS527)	SM	Addictions and Compulsive Disorders; Movement Disorders
	PPARγ (OMS405)	SM	Opioid and Nicotine Addiction
Immuno-oncology	GPR174	SM	Cancer
	GPR161	SM	Cancer
Other	GPCR Platform	SM	Immunologic, immuno-oncologic, CNS, Metabolic, CV, Musculoskeletal & Other Disorders



Experienced Management with Deep Industry Experience

	Position	Background
Gregory Demopulos, MD	*Chairman, President & CEO*	Stanford and Duke Departments of Orthopedic Surgery
Chris Bral, PhD, DABT	*VP, Nonclinical Development*	Arrowhead Research, Vertex, Schering-Plough Research Institute
Peter Cancelmo, JD	*VP, General Counsel and Secretary*	Garvey Schubert Barer, Choate Hall
Nadia Dac	*Chief Commercial Officer*	Alder BioPharmaceuticals, AbbVie, Novartis, Biogen
Tim Duffy	*Head of Business Development*	MDRNA, Prometheus, Procter & Gamble
George Gaitanaris, MD, PhD	*Chief Scientific Officer*	Nura, Primal, NCI
Michael Jacobsen	*Chief Accounting Officer & Treasurer*	Sarepta, ZymoGenetics, ICOS, Onvia, Mosaix
Bruce Meiklejohn, PhD	*VP, CMC*	Eli Lilly
Catherine Melfi, PhD	*Chief Regulatory Officer*	Eli Lilly, Indiana University
Narinder Nangia, PhD	*VP, Biostatistics, Data Management & Programming*	Alkermes, PPD, Abbvie, Pfizer, Burroughs Wellcome, Procter & Gamble
Tina Quinton, MS, JD	*VP, Patents*	Christensen O'Connor Johnson Kindness
J. Steven Whitaker, MD, JD	*Chief Medical Officer*	Allon Therapeutics, ICOS
Pete Williams	*VP, Human Resources*	Redbox, Outerwall, Coinstar, Washington Mutual, Expedia

Narsoplimab – MASP-2 Inhibitor



Narsoplimab and Regulatory Status

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- 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)
- BLA for HSCT-TMA under priority review by FDA with PDUFA date of July 17, 2021
- Enrolling 2 additional Phase 3 clinical programs – IgA nephropathy (IgAN) and atypical hemolytic uremic syndrome (aHUS)
- Narsoplimab being evaluated for severe COVID-19 as part of the I-SPY COVID-19 adaptive platform trial sponsored by Quantum Leap Healthcare Collaborative
- ~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

Potential Advantages of Narsoplimab Over Other Complement Inhibitors

- Narsoplimab designed to leave classical and alternative pathways fully functional
  - Leaves fully intact the adaptive immune effector function of complement
  - Maintains antigen-antibody complex-mediated lytic response and killing of virus-infected cells
  - No evidence of increased infection risk

- In addition to lectin pathway inhibition, narsoplimab observed to have anticoagulation effects, potentially beneficial in COVID-19 patients
  - Inhibits MASP-2-mediated cleavage of prothrombin to thrombin and activation of factor XII to XIIa, blocking thrombus formation; also blocks MASP-2-mediated activation of kallikrein
  - No prolongation of PT, aPTT or bleeding time

Benefit:risk ratio heavily weighted toward benefit

Narsoplimab in HSCT-TMA

HSCT-TMA – Serious and Potentially Fatal Complication of HSCT Caused by Endothelial Injury

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25,000 – 30,000
annual allogeneic HSCT in the US and EU

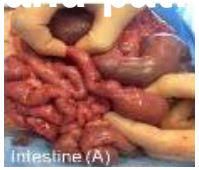
No approved therapies in HSCT-TMA

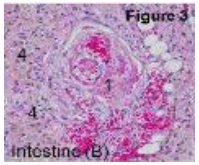
incidence
of TMA in allogeneic HSCT

of patients with HSCT-TMA display at least one **high-risk** feature

of severe cases of HSCT-TMA can be **fatal**

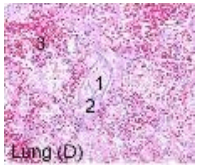
HSCT-TMA Can Lead to Extended Hospitalizations, Intensive Care Unit Stays and Patient Death





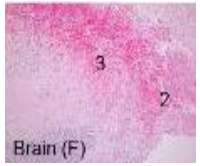
Intestinal HSCT-TMA (iTMA)

- Ischemic colitis (severe pain)
- Intestinal bleeding
- Histologic TMA features
- Bowel strictures



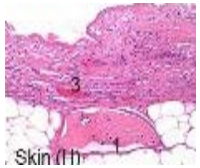
Pulmonary HSCT-TMA

- Acute hypoxemia (ARDS)
- Interstitial bleeding
- Pulmonary hypertension
- Heart failure



CNS HSCT-TMA

- Seizures associated with PRES
- CNS bleed
- Hypertension induced
- Endothelial injury



Skin HSCT-TMA

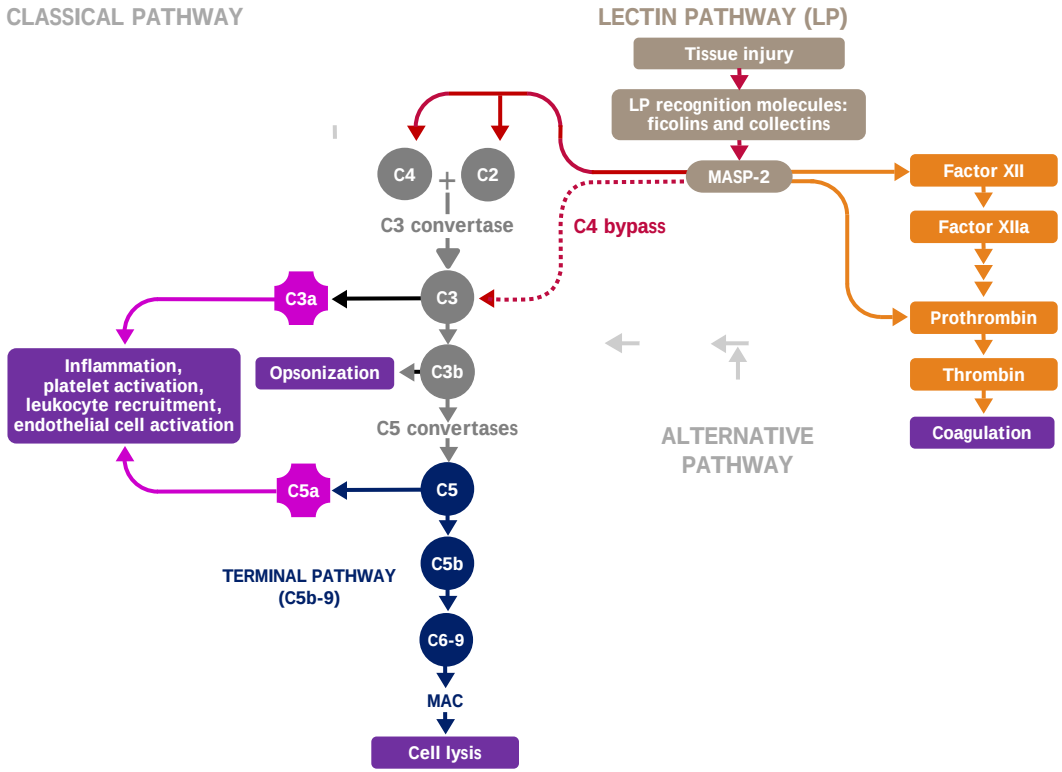
- Vasculitis
- Purpura
- Vessel thrombosis
- Complement deposits

1. Fibrinoid debris or intravascular thrombus, 2. Denuded endothelial cells, 3. Interstitial hemorrhage, 4. Hemosiderin deposits

Slide used with permission from Sonata Jodele, MD. Jodele S et al. *Blood* Rev. 2015;29(3):191-204. Jodele S et al. *Transfus Apher Sci*. 2016;54(2):181-90.

Dandoy, C et al. Biol Blood Marrow Transplant. 2020. 26(S92); Elfeky, R et al. Blood Adv. 3 June 2020; Vaughn, J et al. Bone Marrow Transplant. 9 November 2018; Li, A et al. Biol Blood Marrow Transplant 2019. 25 (570-576); Roque, A et al. EHA Library May 2019. 268219.

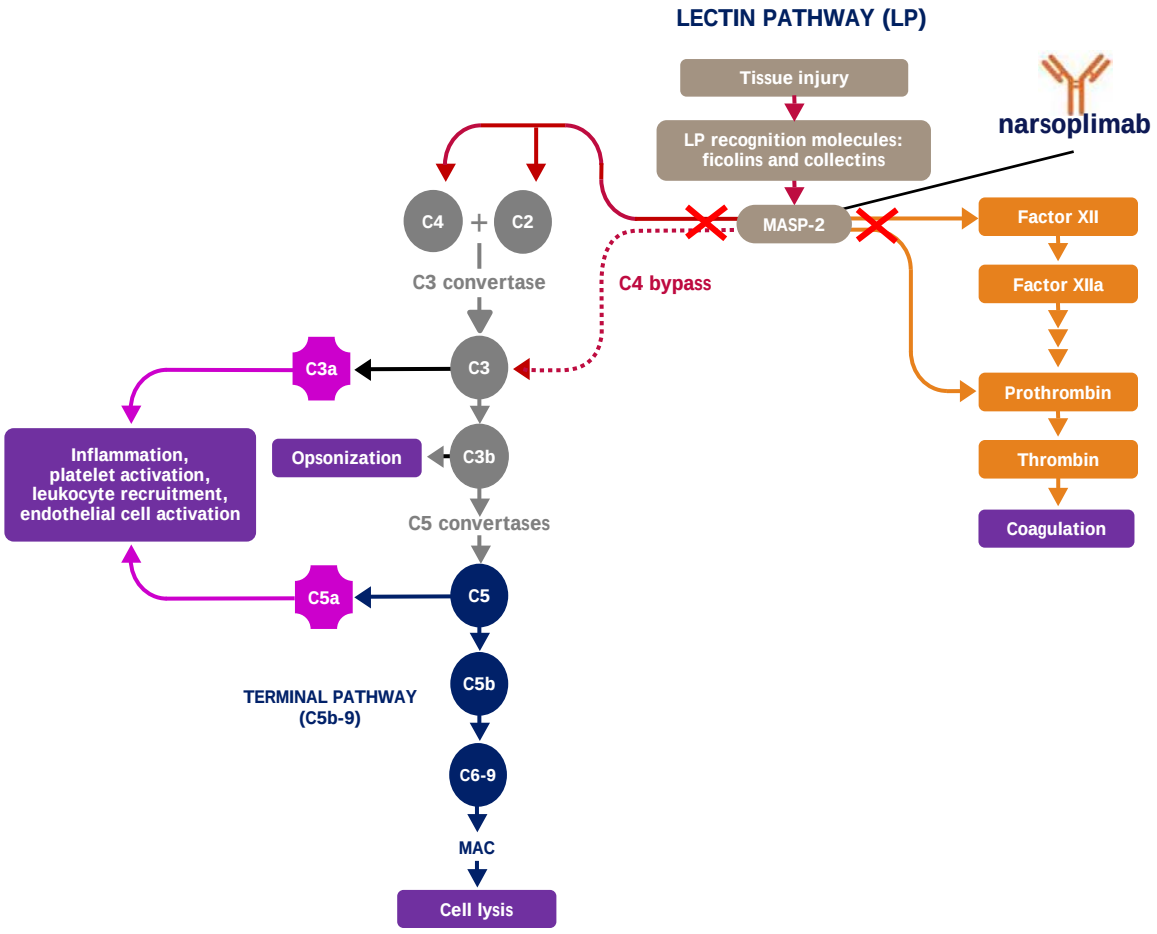
Endothelial Injury Activates the Lectin Pathway of Complement



- Endothelial tissue injury releases damage activated molecular patterns (DAMPS) on the cell surface
- Mannan-binding lectin-associated serine protease-2 (MASP-2) is an enzyme that interacts with those patterns, activating the lectin pathway of complement
- The lectin pathway then triggers an immune response that results in inflammation, hypercoagulation, and further cellular damage
- This can lead to multi-organ damage and death

Khosla J et al. *Bone Marrow Transplant*. 2018;53(2):129-137. doi:10.1038/bmt.2017.207; Collard CD et al. *Am J Pathol*. 2000;156(5); Jodele S et al. *Transfus Apher Sci*. Published April 2016. 2016;54(2):181-190. doi:10.1016/j.transci.2016.04.007

Narsoplimab Targets MASP-2 and the Lectin Pathway of Complement



Narsoplimab

- Fully human monoclonal antibody
- Binds to mannan-binding lectin-associated serine protease-2 (MASP-2), the effector enzyme of the lectin pathway of complement
- Leaves intact the effector function of the adaptive immune response, important for fighting infection
- Blocks MASP-2-mediated coagulation (conversion of prothrombin to thrombin and activation of Factor XII to XIIa) and activation of kallikrein
- Only agent that targets MASP-2 and blocks the lectin pathway

Krarup A et al. 2007. PLoS ONE 2)7): e623; Gulla KC et al. Immunology 2009; 129, 482-495; Demopoulos G et al. W02019246367 (US20200140570A1). World International Property Organization. 26 Dec 2019; Kozarcanin H et al. Journal of Thrombosis and Haemostasis 2016. 14: 531-545.

Narsoplimab In HSCT-TMA: Pivotal Study

Study Population

- Single-arm, open-label study of high-risk HSCT-TMA patients
- Protocol specified that patients receive narsoplimab once weekly for ≥ 4 weeks
- 93% of the trial population had multiple risk factors for poor outcomes

Demographics	N=28
Mean & median age (years)	48
Male Gender, n (%)	20 (71.4%)
Malignant underlying disease	27 (96.4%)
Risk factors:	
Presence of GVHD, n (%)	19 (67.9%)
Significant infection, n (%)	24 (85.7%)
Pulmonary dysfunction (%)	5 (17.9%)
Neurological dysfunction, n (%)	16 (57.1%)
Renal dysfunction	21 (75.0%)
Multi-organ involvement, n (%)	14 (50.0%)

Efficacy Measures

- **Primary Endpoint:** Response as assessed by clinically meaningful improvement in TMA laboratory markers and organ function
  - ***15% complete response rate is the pre-specified threshold for primary endpoint***
- **Secondary Endpoints:** 100-day survival and change from baseline in TMA lab measures

Key Findings

- Most narsoplimab-treated patients achieved a complete response, exceeding the targeted threshold for the primary efficacy endpoint
- 100-day survival was similarly impressive across all groups (responders, per-protocol, and intent-to-treat)
- Narsoplimab was well tolerated in this very sick population with multiple comorbidities
- No safety signal observed: observed adverse events were comparable to those typically seen in post-transplant population
- 21% of patients died during the trial due to causes common in HSCT

Narsoplimab In HSCT-TMA: Pivotal Study Endpoints

Primary Endpoints

- Efficacy (response-based):
  - Improvement in TMA laboratory markers of platelet count and LDH and
  - Safety and tolerability

Secondary Endpoints

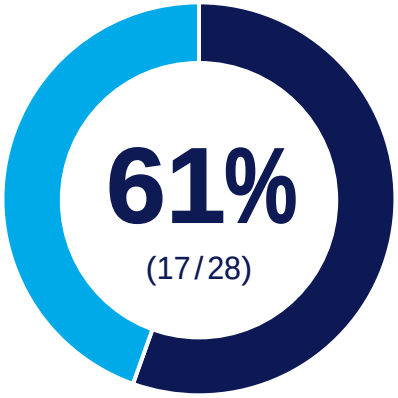
- Survival (100-day and overall)
- Change from baseline in laboratory markers

Organ	Criteria for Improvement in Clinical Status (any of the following)
Blood	• Transfusion freedom
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 assessed using gastrointestinal measures in the Mount Sinai Acute GVHD International Consortium criteria
Neurological	• Limited to stroke, PRES, seizures, weakness

Complete Response Rates (%)

All treated patients (N=28)

(95% CI)

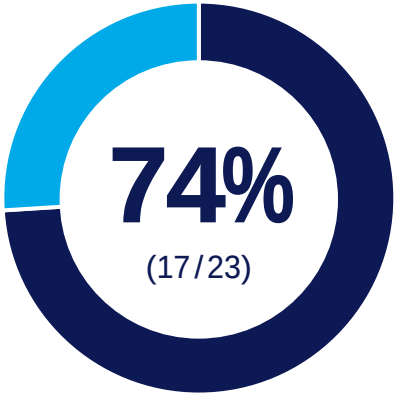


(40.6% to 78.5%)

p<0.0001*

Patients treated per protocol (≥ 4 weeks of dosing) (n=23)

(95% CI)



(51.6% to 89.8%)

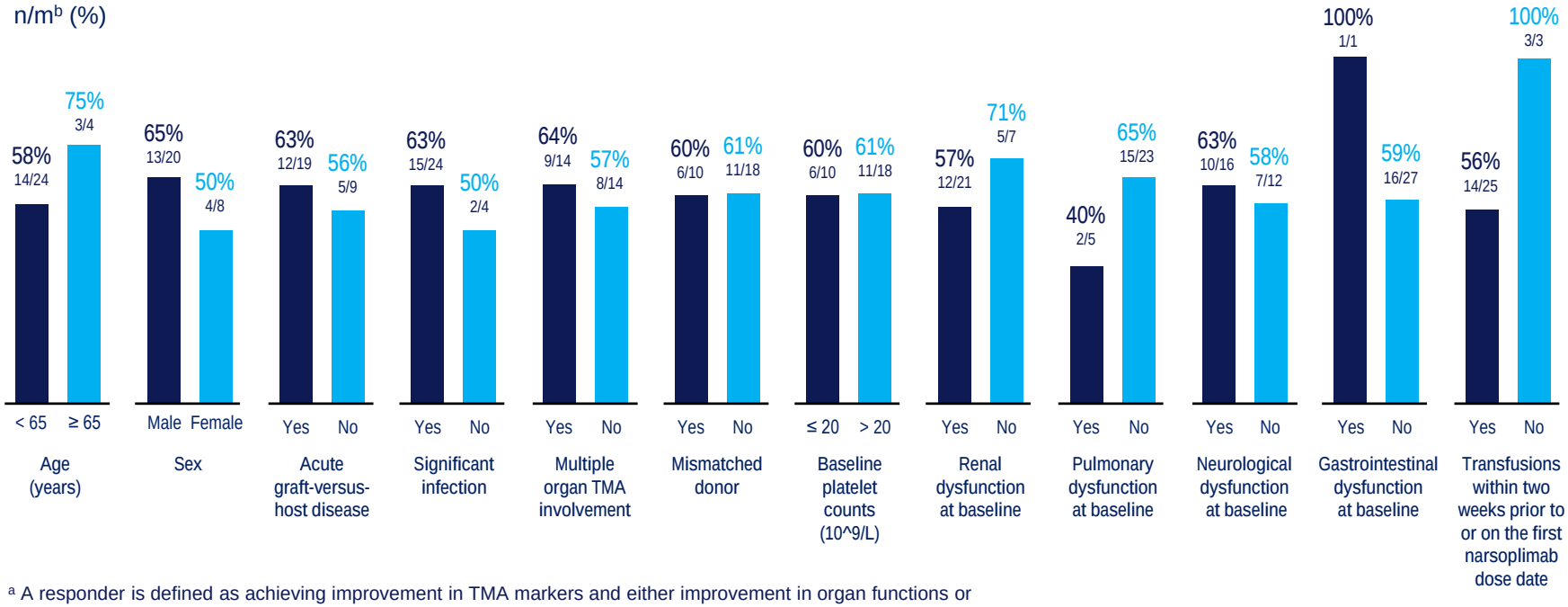
p<0.0001*

- 15% is the pre-specified efficacy threshold for the primary endpoint (i.e., the complete response rate) in the clinical trial

* Exact two-sided p-value for testing response rate equal to 15%

Complete Response by Subgroup (%)

Responders[a]



[a] A responder is defined as achieving improvement in TMA markers and either improvement in organ functions or freedom from transfusion. Patients whose response cannot be determined are considered non-responders.

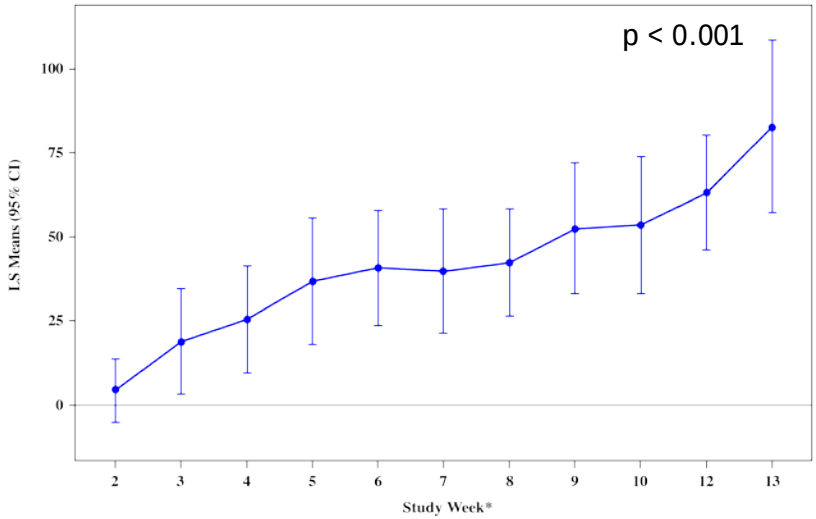
[b] n is the number of responders in the subgroup and m is the total number of patients in the corresponding subgroup.

OMS721-TMA-001. A Phase 2 Trial. Data on file; Rambaldi A et al. EHA Library. June 15, 2018. Abstract nr PF724; Rambaldi, A et al. European Hematology Society. Abstract S262. 2020.

Platelet Count and Hemoglobin Change from Baseline Over Time in Full Analysis Set

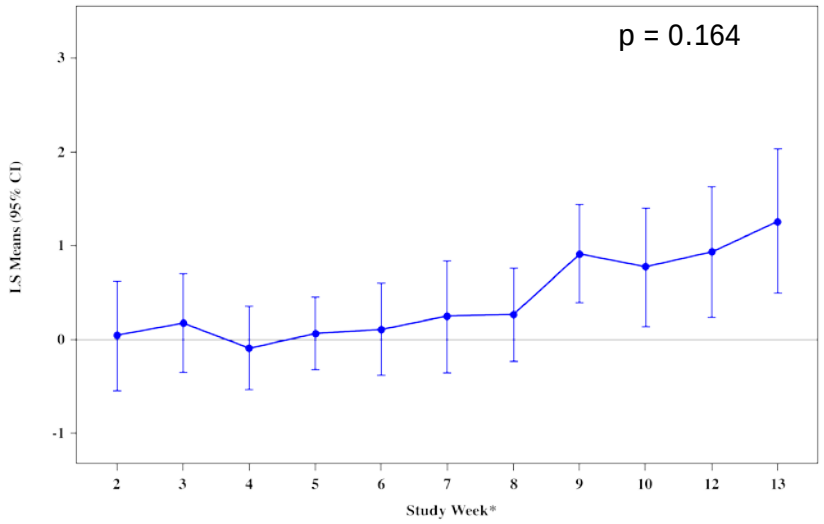
Least Squares Means of Platelet Count (10^9/L) Change from Baseline for HSCT-TMA

Full Analysis Set Population



Least Squares Means of Hemoglobin (g/dL) Change from Baseline for HSCT-TMA

Full Analysis Set Population



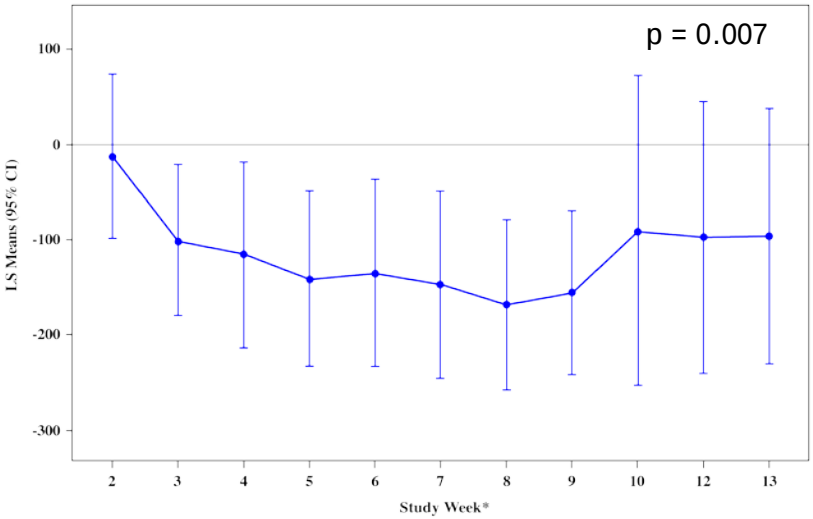
* No patient data were censored; all available data were included

** p-values from time-weighted average change-from-baseline using one-sample t test

LDH and Haptoglobin Change from Baseline Over Time in Full Analysis Set

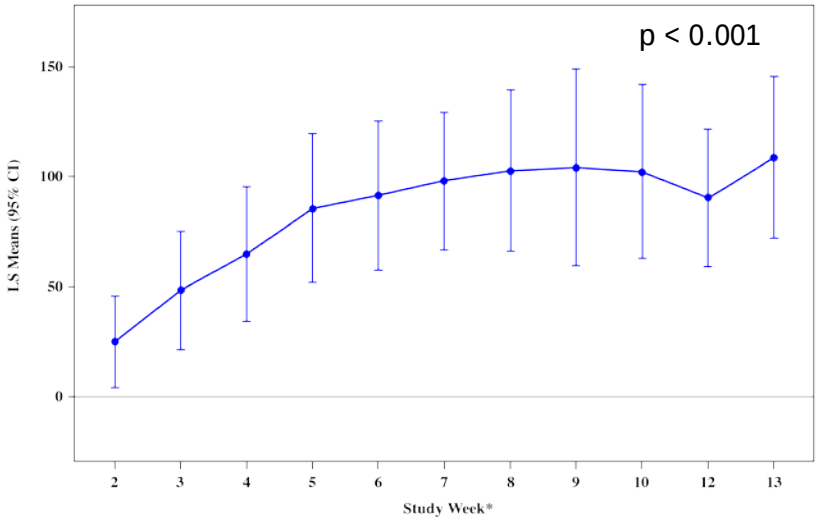
Least Squares Means of LDH (U/L) Change from Baseline for HSCT-TMA

Full Analysis Set Population



Least Squares Means of Haptoglobin (mg/dL) Change from Baseline for HSCT-TMA

Full Analysis Set Population

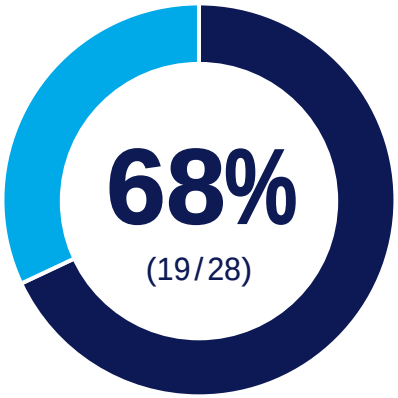


* No patient data were censored; all available data were included

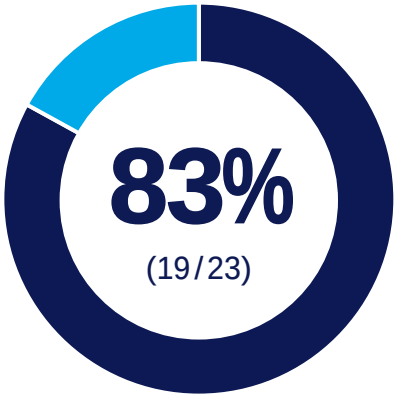
** p-values from time-weighted average change-from-baseline using one-sample t test

100-Day Survival Following HSCT-TMA Diagnosis

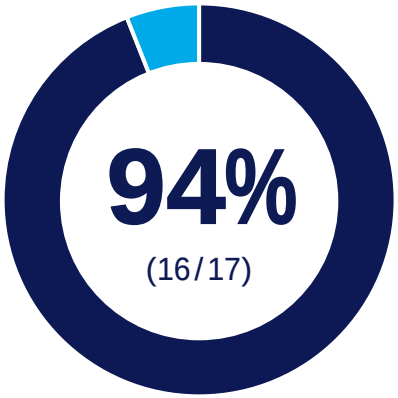
All treated patients (N=28)



Patients treated per protocol (≥ 4 weeks of dosing) (n=23)



Complete responders (n=17)



Patient Survival with Narsoplimab

Kaplan-Meier Plot of Overall Survival for HSCT-TMA

Median survival for the full analysis population was 274 days

(95% CI: 103, NE)

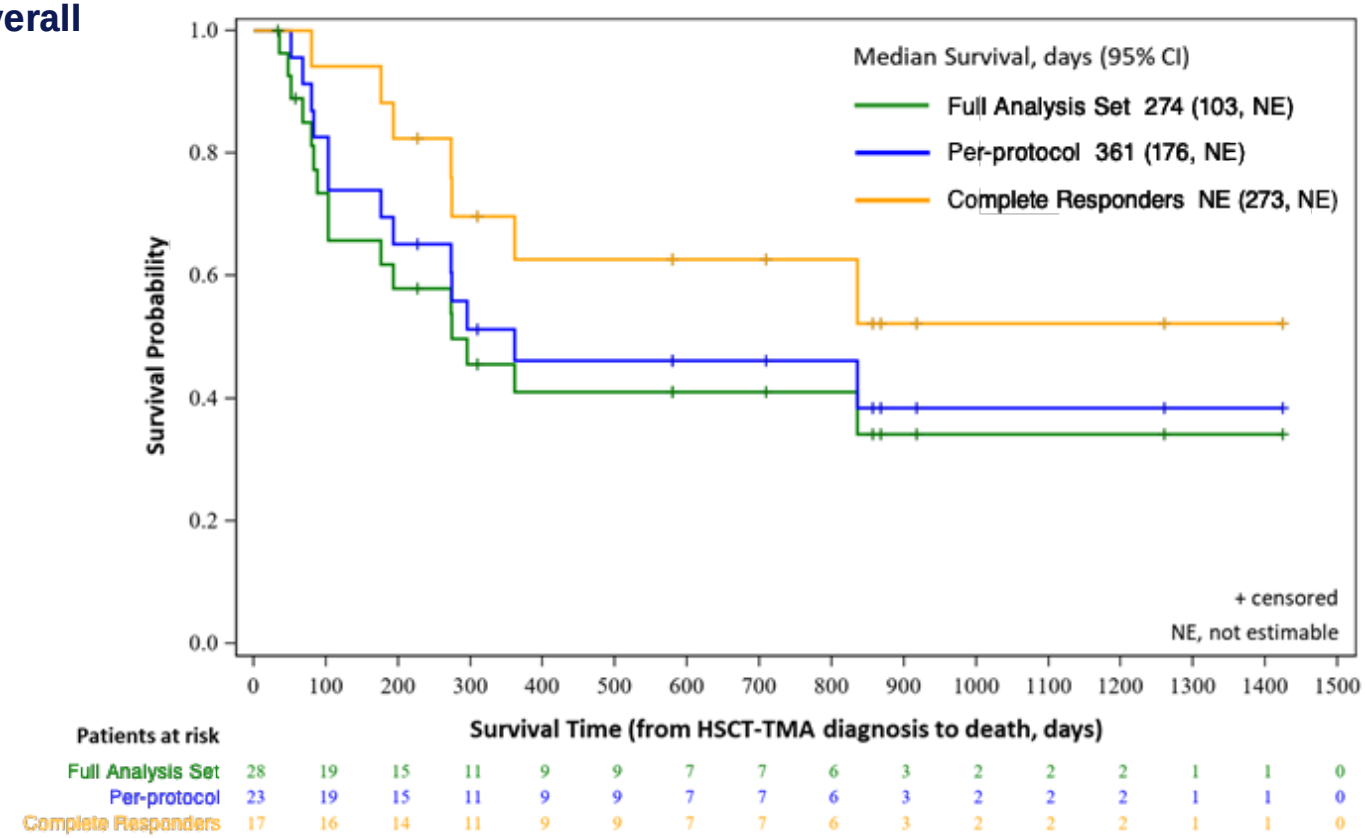
Median survival for the per-protocol population was 361 days

(95% CI: 176, NE)

Median survival for the responder population was not estimable

(95% CI: 273, NE)

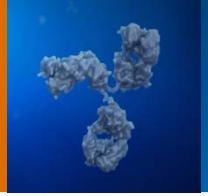
Median survival is estimated by Kaplan-Meier method. 95% confidence interval for median survival is calculated using complementary log-log transformation.



Safety and Tolerability: Most Common Adverse Events in >15% of Patients

- Narsoplimab was well tolerated in this very sick population with multiple comorbidities
- The most commonly reported adverse events were nausea, vomiting, diarrhea, hypokalemia, neutropenia and fever
- The observed adverse events are comparable to those typically seen in the post-transplant population
- 6 patients died during the trial due to causes common in HSCT

Preferred Term, n (%)	(N = 28)
Any Event	27 (96.4)
Pyrexia	10 (35.7)
Diarrhea	9 (32.1)
Vomiting	9 (32.1)
Nausea	7 (25.0)
Neutropenia	7 (25.0)
Fatigue	6 (21.4)
Hypokalemia	6 (21.4)
Back pain	5 (17.9)



Regulatory and CMC Milestones for Narsoplimab in HSCT-TMA

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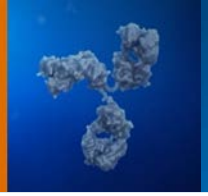
Narsoplimab in HSCT-TMA: Moving Rapidly Toward Global Regulatory Approvals

- Breakthrough therapy designation from FDA
- Orphan Drug designation from FDA and from EMA
- BLA under priority review by FDA – PDUFA date of July 17, 2021
- MAA submission is in preparation for submission to EMA; targeting 1H 2021 for completion
- Drug substance and drug product process validation lots successfully completed
- More than sufficient supply of drug product for launch



Narsoplimab in HSCT-TMA
Launch Readiness Milestones

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Engagement	Comprehensive engagement plan with top leaders from US and international transplant centers ✓ Introduce Omeros as a potential new partner in the transplant market ✓ Increase awareness of HSCT-TMA ✓ External steering committee establishing guidelines for diagnosis and treatment
Education	✓ Initiation of educational disease awareness campaign focusing on HSCT-TMA pathogenesis and unmet need ✓ International digital and print campaign ✓ Significant 2020 presence at US/EU hematology and transplant congresses
Value	Robust value framework to demonstrate clinical and financial value to global payers and providers ✓ Pricing strategy to ensure broad access across provider segments ✓ HEOR/RWE plan – reduction in post-HSCT complication costs; improved outcomes ✓ Convenient route of administration in inpatient and outpatient settings ✓ Pursuing coding strategy to ensure seamless access to narsoplimab, if approved (ICD-10, NTAP, J-code, etc.)
Operations	Organizational launch readiness ✓ Heads of national sales, medical science liaisons and advocacy already hired ✓ US Sales force hiring process initiated ✓ Long-term commercial manufacturing agreement with Lonza executed ✓ Commercial lots successfully manufactured

Narsoplimab for the Treatment of Severe COVID-19 Requiring Mechanical Ventilation

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
- Diabetes
- Heart disease

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

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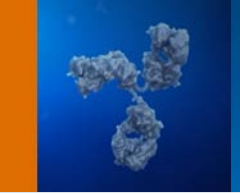
Endothelial Injury with Complement Activation is Central to the Pathophysiology of COVID-19

- Severe acute respiratory syndrome-associated coronavirus-2 (SARS-CoV-2) directly infects endothelial cells, leading to diffuse endothelial damage
- The resulting injury/inflammation specifically activates lectin pathway of complement on the endothelial cell surface
- Complement activation amplifies underlying cellular injury and induces cytokine response (e.g., IL-6)
- Complement activation has been demonstrated to cause lung injury; and complement blockade reduces that injury in models of MERS-CoV, SARS-CoV and SARS-CoV-2
- Complement activation in COVID-19 appears to be through the lectin pathway
- MASP-2, the lectin pathway's effector enzyme, binds the nucleocapsid protein of SARS-CoV-2, resulting in complement activation and lung injury

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



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References

COVID-19 as a cardiovascular disease: the potential role of chronic endothelial dysfunction

Clinical & Experimental Immunology

The Journal of Translational Immunology

British Society for immunology

Original Article | Free Access

MASP2 levels are elevated in thrombotic micro association with microvascular endothelial cell suppression by anti-MASP2 antibody narsoplir

S. Elhadad, J. Chapin, D. Copertino, K. Van Besien, J. Ahamed, J. Laurence

First published: 18 July 2020 | https://doi.org/10.1111/cei.13497 | Citatic

nature reviews immunology

Comment | Published: 21 May 2020

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 | Metrics

An Author Correction to this article was published on 04 June 2020

This article has been updated

THE LANCET Haematology

ARTICLES | ONLINE FIRST

Endotheliopathy in COVID-19-associated coagulopathy: evidence from a single-centre, cross-sectional study

PDF [498 KB] Figures

Is COVID-19 an Endothelial Disease? Clinical and Basic Evidence

Celestino Sardu, Jessica Gambardella, Marco Bruno Morelli, Xujun Wang, Raffaele Marfella, Gaetz Santulli

Version 1 : Received: 9 April 2020 / Approved: 13 April 2020 / Online: 13 April 2020 (02:23:33 CEST)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ticagrelor and Aspirin or Aspirin Alone in Acute Ischemic Stroke or TIA

NEJM Catalyst eBook: The Clinician Role in Health Care Delivery and Innovation

ORIGINAL ARTICLE

Timing of Initiation of Ren Replacement Therapy in Acu Kidney Injury

Editor's Note: This article was published on May 21, 2020, at NEJM.org.

Mount Sinai Study Indicates COVID-19 May be Driven by Pulmonary Thrombi & Pulmonary Endothelial Dysfunction

APR 18, 2020 | COVID-19, ENDOTHELIAL DYSFUNCTION, ICAHN SCHOOL OF MEDICINE, MOUNT SINAI, THROMBOLYSIS, THROMBOSIS

Medscape Friday, July 17, 2020

NEWS & PERSPECTIVE DRUGS & DISEASES CME & EDUCATION ACADEMY

Perspective > Medscape Oncology > EHA 2020

Endothelial Injury May Play a Major Role in COVID-19-Associated Coagulopathy

Alan P. Lyss, MD

DISCLOSURES | June 29, 2020

ORIGINAL ARTICLE

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
Lectin-Pathway Activation from Endothelial Damage	✓	✓
Cause of Endothelial Injury	Viral	Conditioning regimen, Immunosuppressants, GVHD, infection
MASP-2 Activation	✓	✓
Multi-Organ TMA	✓	✓

- **~70 patients have been dosed with narsoplimab across the two endothelial injury syndromes**

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

- 6 patients, each included for presence of ARDS requiring mechanical ventilation (4 on CPAP, 2 intubated) have been treated with narsoplimab
- Narsoplimab was administered through IV twice weekly for 2 to 4 weeks
- All patients fully recovered, survived and were discharged
- 2 patients also had massive bilateral pulmonary thromboses that resolved following 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 journal *Immunobiology*

Data from the COVID-19 Study in Italy

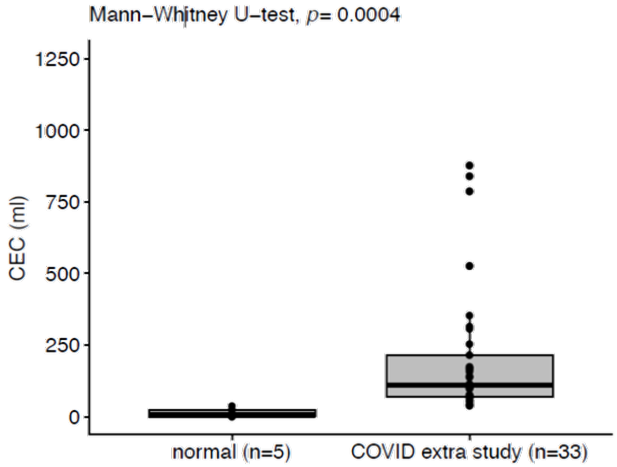
Demographics and Treatment Summary

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

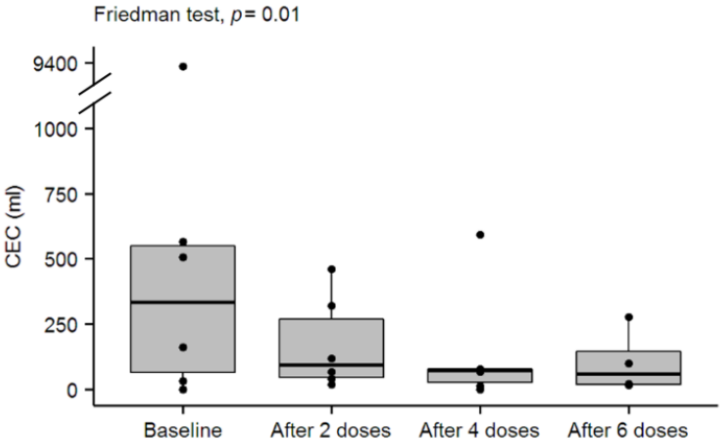
Treatment Summary	n (%) or Median (range)
Timing of narsoplimab treatment from start of CPAP oxygen support	
Within 24 hours	4 (67%)
Within 48 hours	2 (33%)
Time from hospital admission to treatment	2 days (1-4)
Duration of follow-up (to date) after first dose	27 days (16-90)

Data from the COVID-19 Study in Italy

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

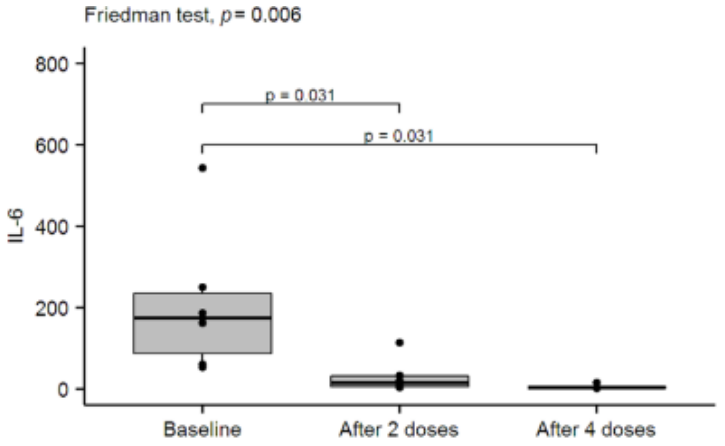


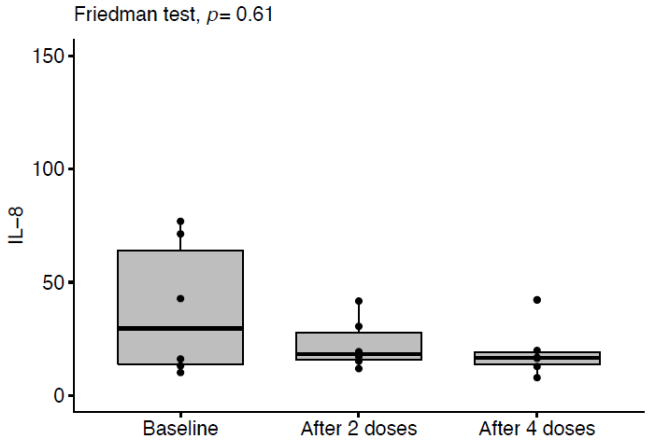
5 normal (uninfected) and 33 infected patients without Narsoplimab



6 infected patients treated with Narsoplimab

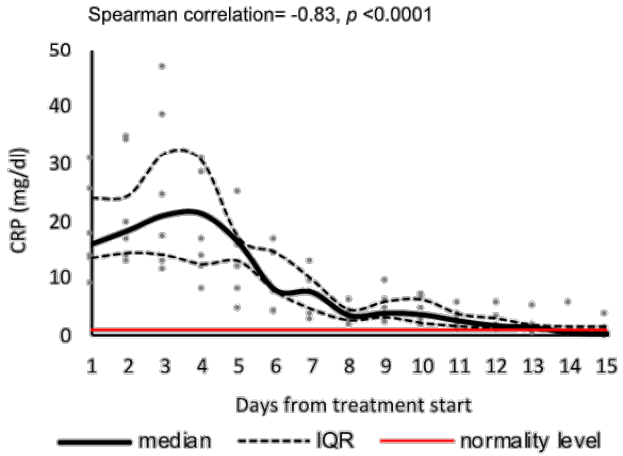
IL-6 / IL-8 Levels Improved in 6 Patients Treated with Narsoplimab



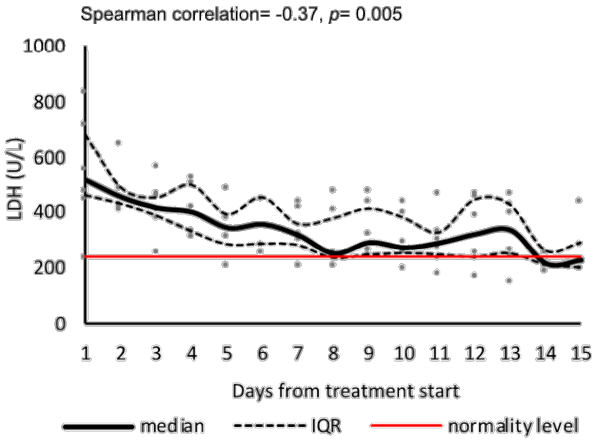


Data from Narsoplimab-treated COVID-19 Patients

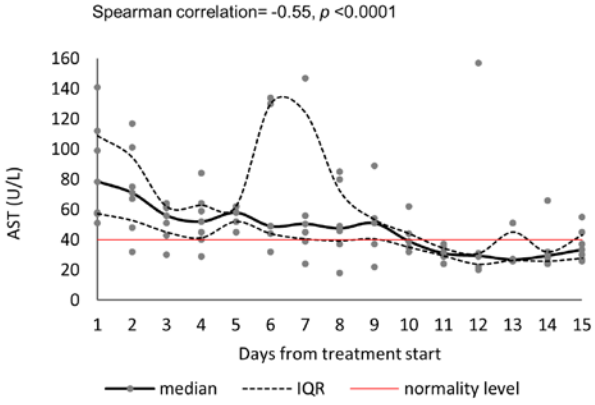
C-Reactive Protein
Improved in all 6 Patients



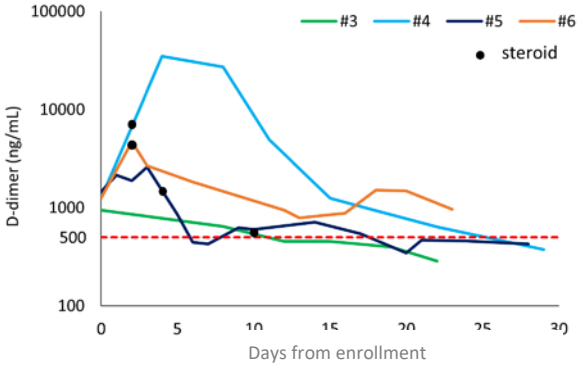
Lactate Dehydrogenase
Improved in all 6 Patients



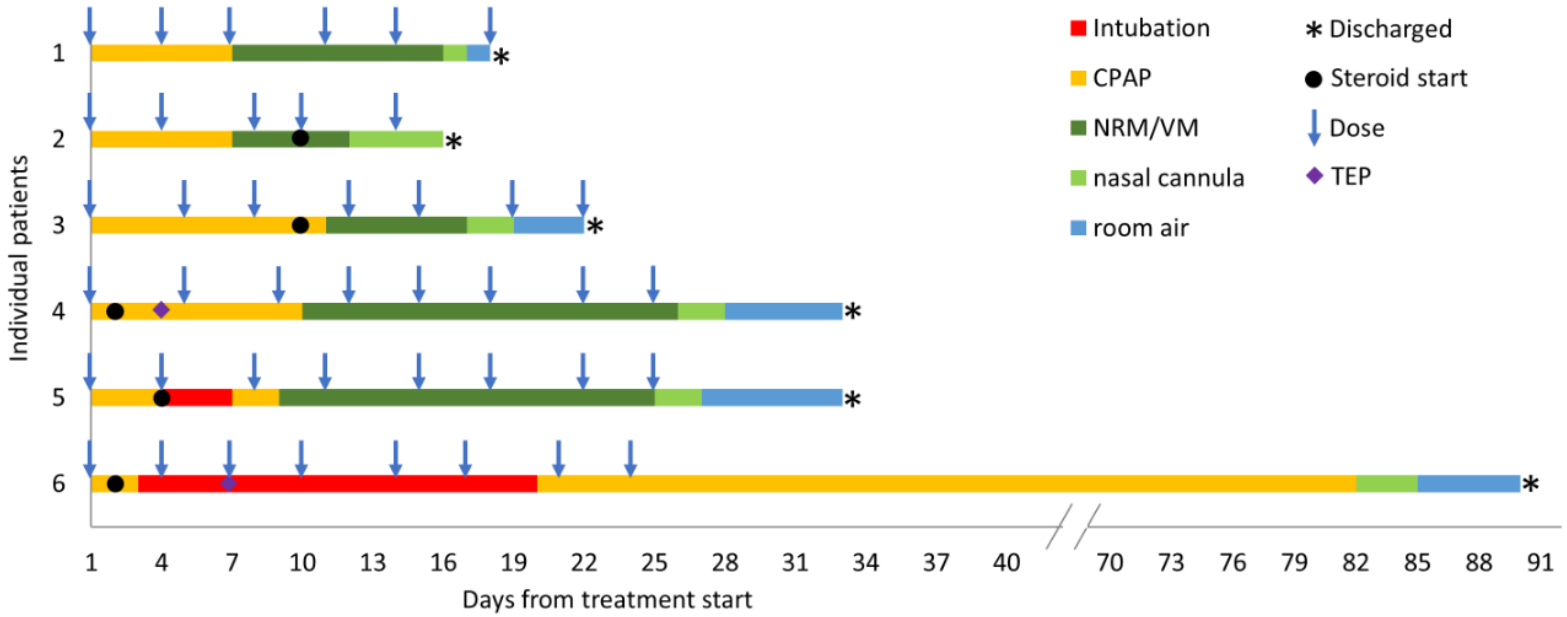
Aspartate Aminotransferase (AST)
Improved in all 6 Patients



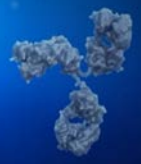
D-Dimer
Improved in all Assessed Patients



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



Narsoplimab Could Have a Role in Treatment of "Long-Hauler" COVID-19 Patients

OMEROS

- Published studies from multiple international research groups now show that "recovered" COVID-19 patients have high incidence of longer-term sequelae – e.g., cognitive impairment/CNS, cardiac, pulmonary, multi-organ disorders

- COVID-19 patients treated with narsoplimab show no observed clinical or laboratory evidence of sequelae at 5-6 months after treatment

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

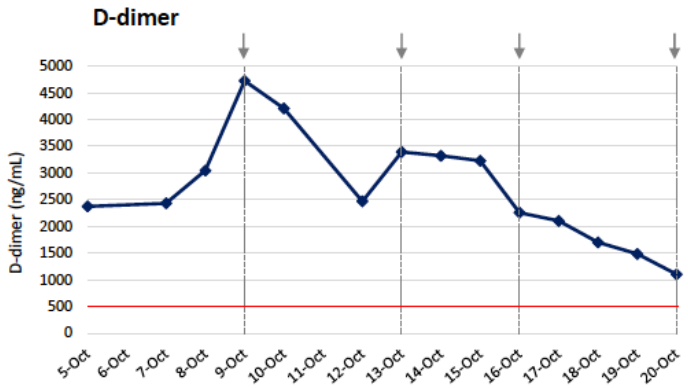
OMEROS

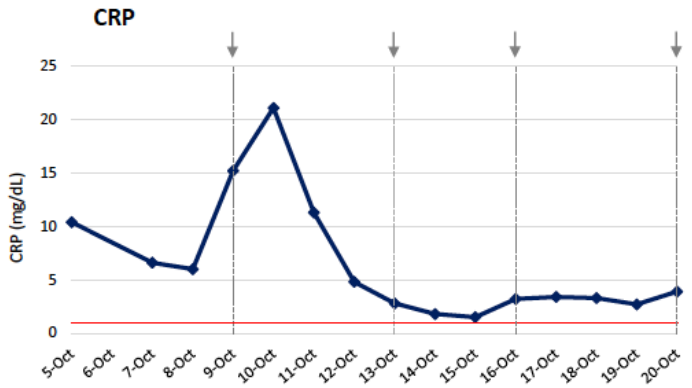
Laboratory Findings	Baseline	Last Evaluation (5-6 Mos. Post-Discharge)
White cell count - per mm^3, median (range)	8335 (6420-10,120)	7320 (3200-8770)
> 10,000 per mm^3 - no. (%)	2 (33)	0 (0)
< 4000 per mm^3 - no. (%)	0 (0)	1 (17)
Lymphocyte count - per mm^3, median (range)	875 (410-1290)	2815 (810-3780)
Platelet count - x 10^3 per mm^3, 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)

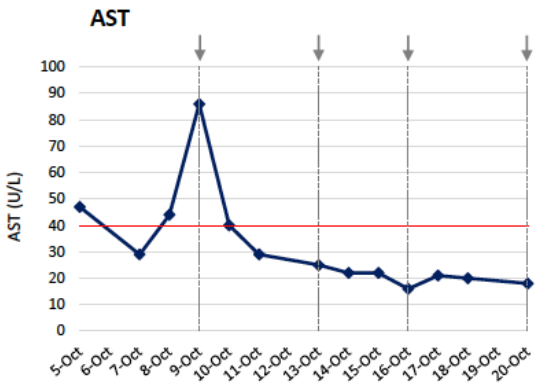
- Clinical status at last evaluation of all 6 patients – no evidence of post-COVID sequelae

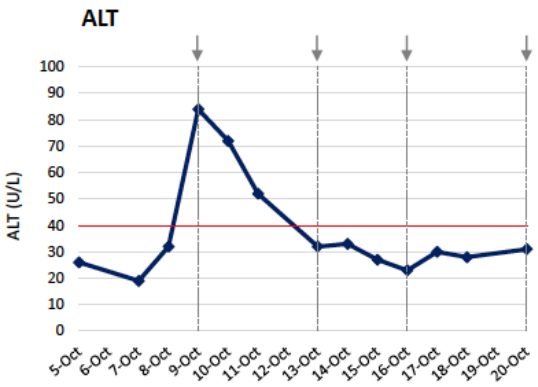
Bergamo Patient #7 Undergoing Narsoplimab Treatment

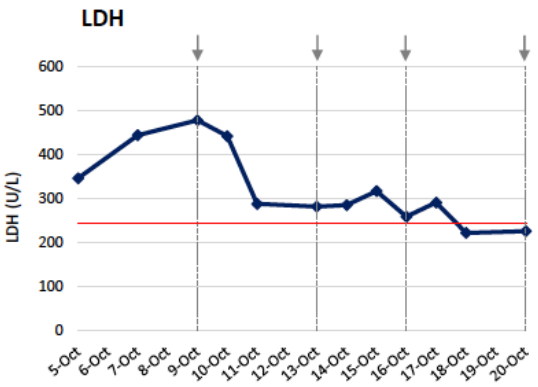
- 74-year-old man
- High-risk: diabetic, obese, long history of smoking/COPD, prostate cancer
- Rapidly deteriorating pulmonary status: nasal cannulae → mask → CPAP → intubation
- Began treatment with narsoplimab following intubation; extubated around the 2nd dose



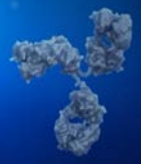








* Gray arrows denote dosing; Red lines denote normal value threshold



Experience with Narsoplimab Following Initial Cohort of Bergamo Patients

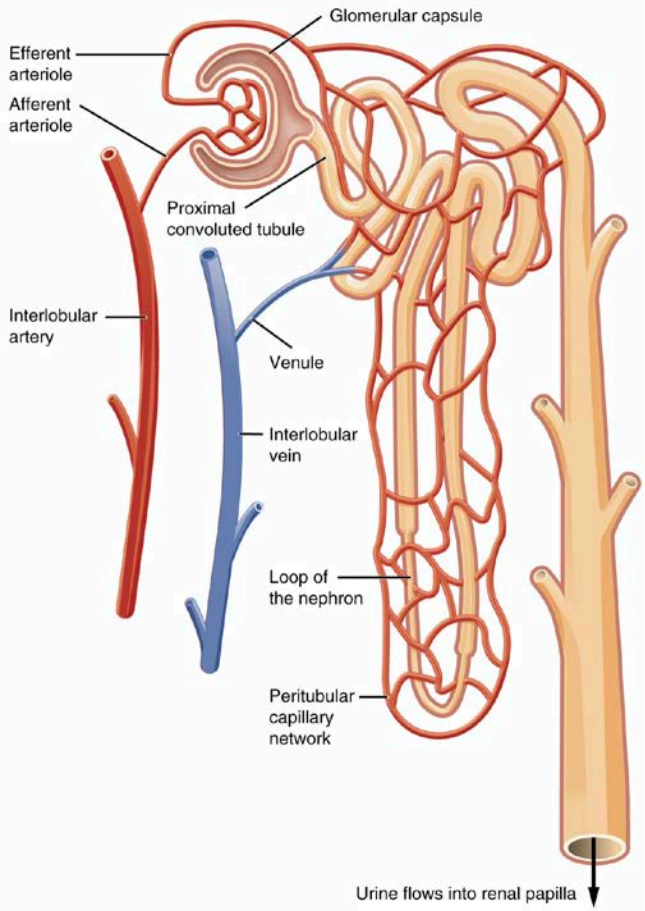
OMEROS

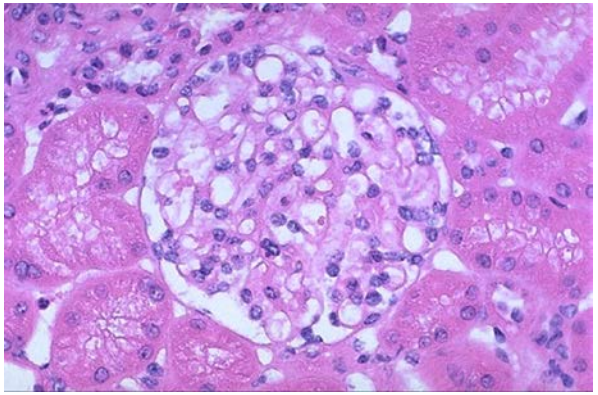
- Have continued treating patients in the US and in Bergamo under compassionate use
  - All additional patients have been severely ill prior to treatment with narsoplimab
    - All intubated with majority initiating narsoplimab multiple days after intubation
    - All had failed other therapies prior to initiating narsoplimab
  - Similarly striking outcomes to those in the initial Bergamo study

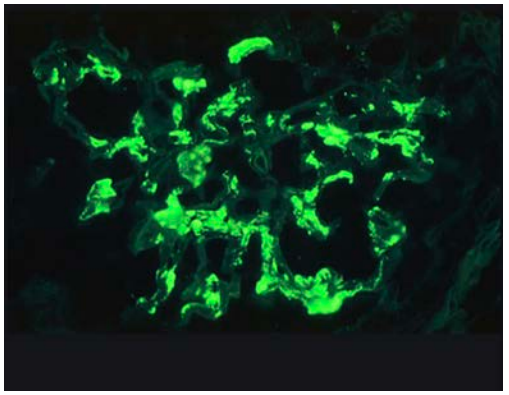
- COVID-19 patients treated with narsoplimab develop appropriately high anti-SARS-CoV-2 antibodies
- Advancing discussions with BARDA, NIAID, NCATS and the Biden Task Force
- In discussions with international regulatory authorities and global healthcare organizations regarding narsoplimab for COVID-19
- Narsoplimab is the only complement inhibitor included in the I-SPY COVID-19 TRIAL: An Adaptive Platform Trial for Critically Ill Patients

Narsoplimab in IgA Nephropathy

Role of Lectin Pathway in IgAN







Nephrol Dial Transplant (1999) 14: 881–886

Nephrology Dialysis Transplantation

Original Article

Glomerular deposition of mannose-binding lectin in human glomerulonephritis

Karl Lhotta[1], Reinhard Würzner[2] and Paul König[1]

Nephrol Dial Transplant (1998) 13: 1984–1990

Nephrology Dialysis Transplantation

Original Article

Glomerular deposition of mannose-binding lectin (MBL) indicates a novel mechanism of complement activation in IgA nephropathy

Morito Endo[1], Hiroyuki Ohi[1], Isao Ohsawa[1], Takayuki Fujita[1], Misao Matsushita[2] and Teizo Fujita[2]

Mesangial IgA2 Deposits and Lectin Pathway–Mediated Complement Activation in IgA Glomerulonephritis

Satoshi Hisano, MD, Misao Matsushita, PhD, Teizo Fujita, MD, Yuzo Endo, MD, and Shigeo Takebayashi, MD

Article

Mesangial C4d Deposits in Early IgA Nephropathy

Alfons Segarra,[1] Katheryne Romero,[1] Irene Agraz,[1] Natalia Ramos,[1] Alvaro Madrid,[2] Clara Carnicer,[3] Elias Jatem,[4] Ramón Vilalta,[2] Luis Enrique Lara,[2] Elena Ostos,[4] Naiara Valtierra,[4] Juliana Jaramillo,[1] Karla V. Arredondo,[1] Gema Ariceta,[5] and Cristina Martínez[5]

NEPHRON

Original Paper

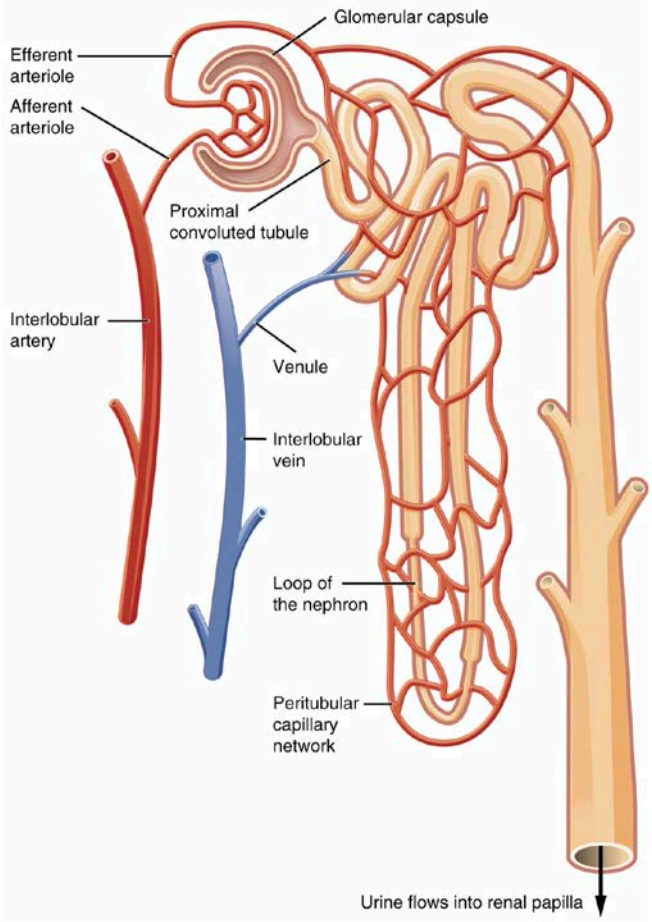
Nephron 1998;80:408–413

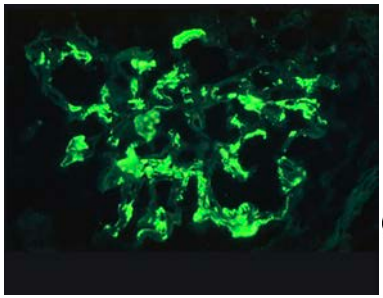
Deposition of Mannan Binding Protein and Mannan Binding Protein-Mediated Complement Activation in the Glomeruli of Patients with IgA Nephropathy

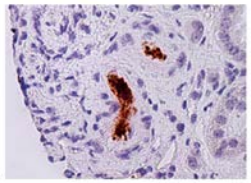
Mitsuhiro Matsuda[a] Kenichi Shikata[a] Jun Wada[a] Hikaru Sugimoto[a] Yasushi Shikata[a] Toshisuke Kawasaki[b] Hirofumi Makino[a]

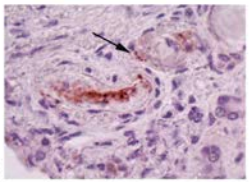
[a] Department of Medicine III, Okayama University Medical School, Okayama, and [b] Department of Biological Chemistry, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan

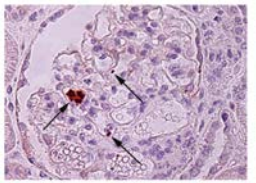
Thrombotic Microangiopathy and IgAN

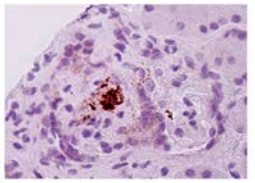












CLINICAL RESEARCH www.jasn.org

A Clinicopathologic Study of Thrombotic Microangiopathy in IgA Nephropathy

Khalil El Karoui,*† Gary S. Hill,* Alexandre Karras,‡ Christian Jacquot,‡ Luc Moulonguet,§ Olivier Kourilsky,‖ Véronique Frémeaux-Bacchi,¶ Michel Delahousse,** Jean-Paul Duong Van Huyen,* Alexandre Loupy,* Patrick Bruneval,* and Dominique Nochy*

*Department of Pathology, Hôpital Européen Georges Pompidou, Paris, France; †Institut National de la Santé et de la Recherche Médicale INSERM U845, Hôpital Necker-Enfants Malades, Paris, France; ‡Department of Nephrology, Hôpital Européen Georges Pompidou, Paris, France; §Department of Nephrology, Hôpital Ambroise Paré, Boulogne Billancourt, France; ‖Department of Nephrology, Hôpital Sud Francilien, Evry, France; ¶Department of Immunology, Hôpital Européen Georges Pompidou, Paris, France; and **Department of Nephrology, Hôpital Foch, Suresnes, France

Nephrol Dial Transplant (2019) 1–6
doi: 10.1093/ndt/gfz241

ndt Nephrology Dialysis Transplantation

Glomerular endothelial activation, C4d deposits and microangiopathy in immunoglobulin A nephropathy

Hernán Trimarchi[1] and Rosanna Coppo[2]

[1]Nephrology Service, Hospital Británico de Buenos Aires, Buenos Aires, Argentina and [2]Fondazione Ricerca Molinette, Regina Margherita Hospital, Turin, Italy

REVIEW

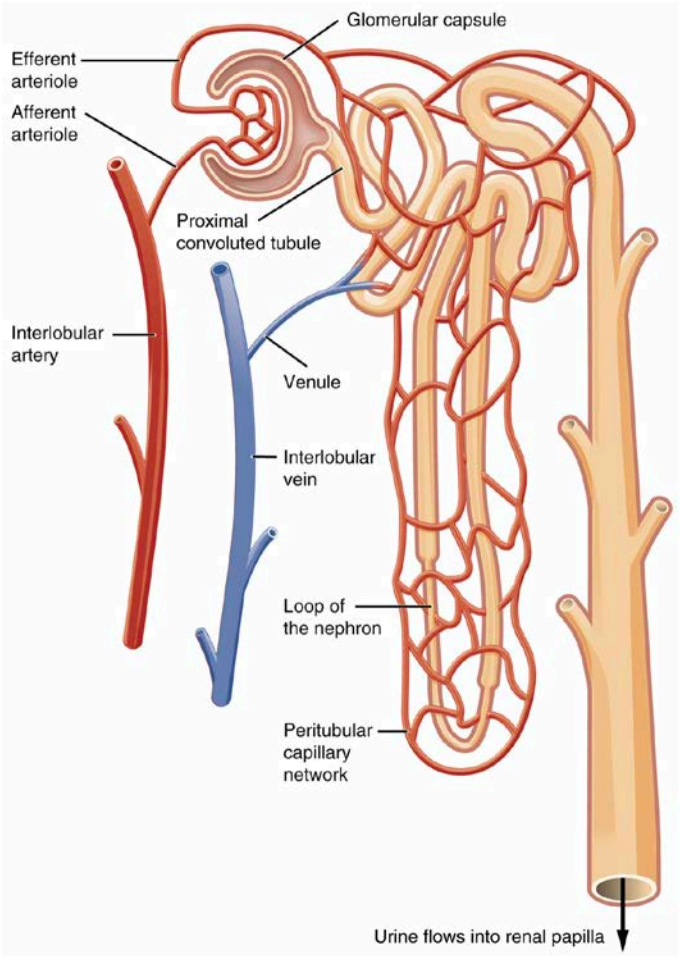
KI REPORTS KIReports.org CLINICAL RESEARCH

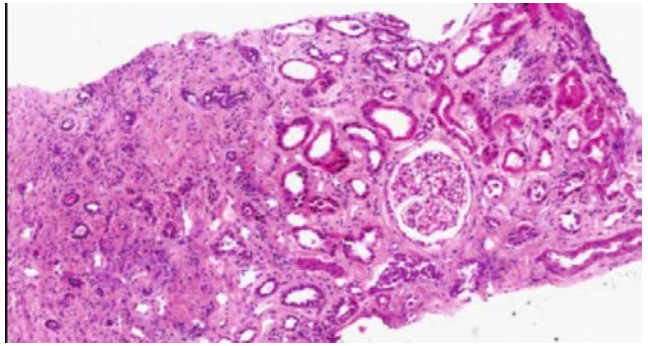
Epidemiology and Pathophysiology of Glomerular C4d Staining in Native Kidney Biopsies

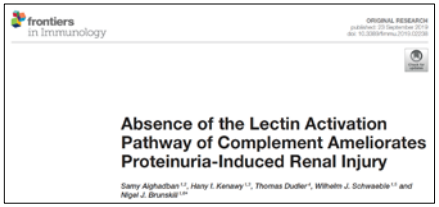
Cinthia B. Drachenberg[1], John C. Papadimitriou[1], Preeti Chandra[2], Abdolreza Haririan[2], Susan Mendley[3], Matthew R. Weir[2] and Mario F. Rubin[2]

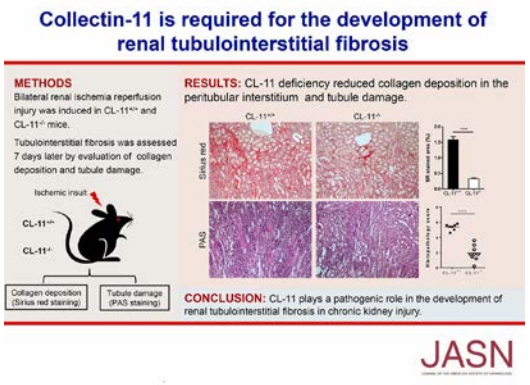
[1]Department of Pathology, University of Maryland School of Medicine, Baltimore, Maryland, USA, [2]Department of Medicine, Division of Nephrology, University of Maryland School of Medicine, Baltimore, Maryland, USA; and [3]Department of Pediatrics, Division of Nephrology, University of Maryland School of Medicine, Baltimore, Maryland, USA

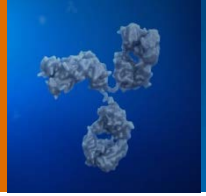
Tubulointerstitial Fibrosis in IgAN











Narsoplimab Clinical Program in IgAN

OMEROS

Phase 2 Clinical Trial

- Substudy 1: Narsoplimab in patients with IgAN, lupus nephritis, C3 glomerulopathy and membranous nephritis, all who were receiving treatment with corticosteroids
- Substudy 2: Narsoplimab in patients with IgAN who were not receiving corticosteroids

Phase 2 Trial Results

- Across the 2 studies, median proteinuria reduction was 60-70% and eGFR stabilized
- 4 of 5 lupus nephritis patients showed ~70% decrease in 24-hour urine protein
- No treatment-related serious adverse events (SAEs) were observed
- Manuscripts published
  - J. Barratt and R. Lafayette, *MASP-2 inhibition as a potential strategy for the management of IgA nephropathy,* Drugs of the Future 2020, 45(6): 389-396
  - R. Lafayette, et. al., *Safety, Tolerability, and Effect of Narsoplimab (OMS721), a Novel MASP-2 Inhibitor for the Treatment of IgA Nephropathy,* Kidney International Reports 2020, 5(11), 2032-2041

Summary of ARTEMIS-IGAN Phase 3 Trial – Enrolling at over 120 Sites Globally

Overview	• Phase 3 randomized, double-blind, placebo-controlled trial of narsoplimab in patients with IgA nephropathy • Planned enrollment primary endpoint = 280 patients (140/arm) ➢ High-Risk Subset (≥2g UPE) = 156 patients (78/arm)
Inclusion Criteria	• Biopsy-confirmed diagnosis of IgAN within 8 years prior to screening • Proteinuria of >1 g/day within 6 months prior to screening or uPCR >0.75 by spot urine at screening • Mean of two proteinuria measurements >1 g/day at baseline • eGFR of ≥ 30mL/min/1.73 m^2 at screening and baseline
Efficacy Measures	• Primary efficacy endpoint: Change from baseline 24-hour urine protein excretion (UPE g/day) at 36 weeks from baseline for **EITHER** the entire population or the subset of "high-protein" spillers • Secondary efficacy endpoints include rate of change from baseline in eGFR

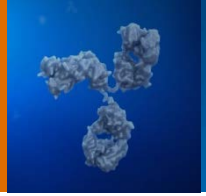
Regulatory Milestones for Narsoplimab in IgAN

Narsoplimab: Advancing Toward Global Regulatory Submissions in IgAN

- Breakthrough Therapy designation from FDA
- Orphan Drug designation from FDA and from EMA
- First and only IgAN investigational treatment to receive breakthrough therapy designation
- Potential to seek full or accelerated approval on proteinuria alone in either of the overall or high-protein-spiller populations
- Over 120 trial sites activated and enrolling for Phase 3 trial in US, EU, Australia, Canada and Asia; additional sites being activated
- Enrollment challenging due, in good part, to COVID-19 – working to expand to additional geographies, including China
- Data read-out expected in 2022

OMEROS

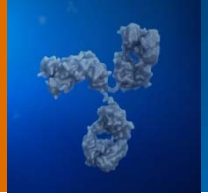
Narsoplimab in Atypical Hemolytic Uremic Syndrome (aHUS)



Narsoplimab
Summary of aHUS Phase 2 Results

OMEROS

- Improvements in TMA markers (platelets, LDH and haptoglobin)
- 3 aHUS patients were able to discontinue dialysis
- 3 others on chronic dialysis were deemed eligible for renal transplant, with one successfully transplanted to date
- Narsoplimab was well tolerated with predictable safety profile



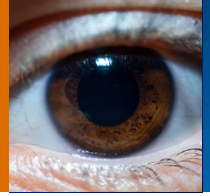
Narsoplimab
Phase 3 Clinical Program in aHUS

OMEROS

- Fast track and orphan designations from FDA
- Phase 3 trial in newly diagnosed or ongoing aHUS
- Agreement with FDA and EMA on one single-arm (i.e., no control group), open-label trial to satisfy both agencies
  - ~40 patients for EMA full and US accelerated approvals
  - ~80 patients for US full approval
- Clinical package for biologics license application (BLA) similar to that which formed basis of approval for Soliris® in aHUS
- Safety can be demonstrated across range of diseases
- FDA and EMA agreement on CMC and nonclinical safety/tox plans
- Pursuing US accelerated approval and European full approval
- Enrollment ongoing at sites in US, Europe and Asia

OMEROS

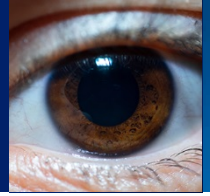
OMIDRIA® (phenylephrine and ketorolac intraocular solution) 1% / 0.3%



OMIDRIA®
Ophthalmological Surgery

OMEROS

- First and only FDA-approved intraocular product to prevent miosis and to reduce postoperative ocular pain in both adult and pediatric patients
- Used in over 1 million cataract procedures without any safety concerns
- Strong post-launch (“real-world”) clinical data
- On VA National Formulary and continuing to expand reimbursement across commercial and Medicare Advantage payers
- Issued patents through 2033 (2035 if pending patents issue)
- Nearly 4 million cataract procedures performed annually in US
- Permanent J-code
- Separate payment in ASCs
- NOPAIN Act introduced in House and Senate with broad and growing bipartisan co-sponsorship and leadership/committee-member support



Real-World Evidence — OMIDRIA® Improves Outcomes

OMEROS

Peer-reviewed publications detailing post-launch studies demonstrate that the use of OMIDRIA statistically significantly:

- ✓ Prevented IFIS[1]
- ✓ Prevented iris prolapse[1]

Compared to steroids:*

- ✓ Reduced cystoid macular edema[2,3]
- ✓ Decreased breakthrough iritis[3]
- ✓ Reduced pain[3]

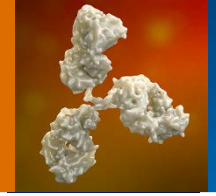
Compared to epinephrine:

- ✓ Decreased complication rates[4]
- ✓ Decreased use of pupil-expanding devices[4–8]
- ✓ Enabled performance of surgery and postoperative care without the use of steroids[2,3,9]
- ✓ Shortened surgical times[4,6,8]
- ✓ Reduced need for opioids (*i.e.*, fentanyl) during surgery while decreasing VAS pain scores[10]
- ✓ Prevented miosis during femtosecond laser-assisted surgery[7]
- ✓ Improved uncorrected visual acuity on day after surgery[4]

*OMIDRIA used intraoperatively with postoperative NSAIDs (no steroids) when compared to postoperative steroids with or without NSAIDs (no OMIDRIA)

1. Silverstein SM, et al. J Cataract Refract Surg. 2018;44(9):1103–1108. 2. Walter K, et al. J Cataract Refract Surg. 2020;46:350–354. 3. Visco DM, et al. Effect of intracameral phenylephrine and ketorolac 1.0%/0.3% on postoperative cystoid macular edema, iritis, pain, and photophobia following cataract surgery. J Cataract Refract Surg. In press. 2020. 4. Rosenberg ED, et al. Clin Ophthalmology. 2018;12:21–28. 5. Bucci FA, et al. Clin Ophthalmology. 2017;11:1039–1043. 6. Visco D. Clin Ophthalmol. 2018;12:301–305. 7. Walter K, et al. J Cataract Refract Surg. 2019;45(4):465-469. 8. Data on file. Clinical outcomes of phenylephrine/ketorolac intraocular solution versus epinephrine in cataract surgery in a real-world setting. 9. Al-Hashimi S, et al. J Cataract Refract Surg. 2018;44:1032–1041. 10. Donnenfeld, E et al. Clin Ophthalmol. 2019;13:2143-2150.

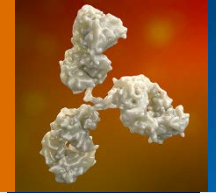
MASP-3 Development Program



OMS906: MASP-3 Inhibitor Targeting the Alternative Complement Pathway

OMEROS

- Omeros' lead MASP-3 inhibitor, OMS906, an investigational, fully-human monoclonal antibody designed to have high potency and selectivity for MASP-3 and potential to treat multiple alternative pathway-driven diseases with infrequent subcutaneous delivery
- By inhibiting MASP-3, OMS906 blocks conversion of pro-Factor D to mature Factor D
- Phase 1 SAD/MAD clinical trial began dosing in September
- Broad application in conditions involving inflammation and tissue damage as well as disorders associated with dysregulation of the alternative pathway
- The initial targeted indication is paroxysmal nocturnal hemoglobinuria (PNH), a rare, acquired, life-threatening disease of the blood
- Targeting monthly subcutaneous dosing



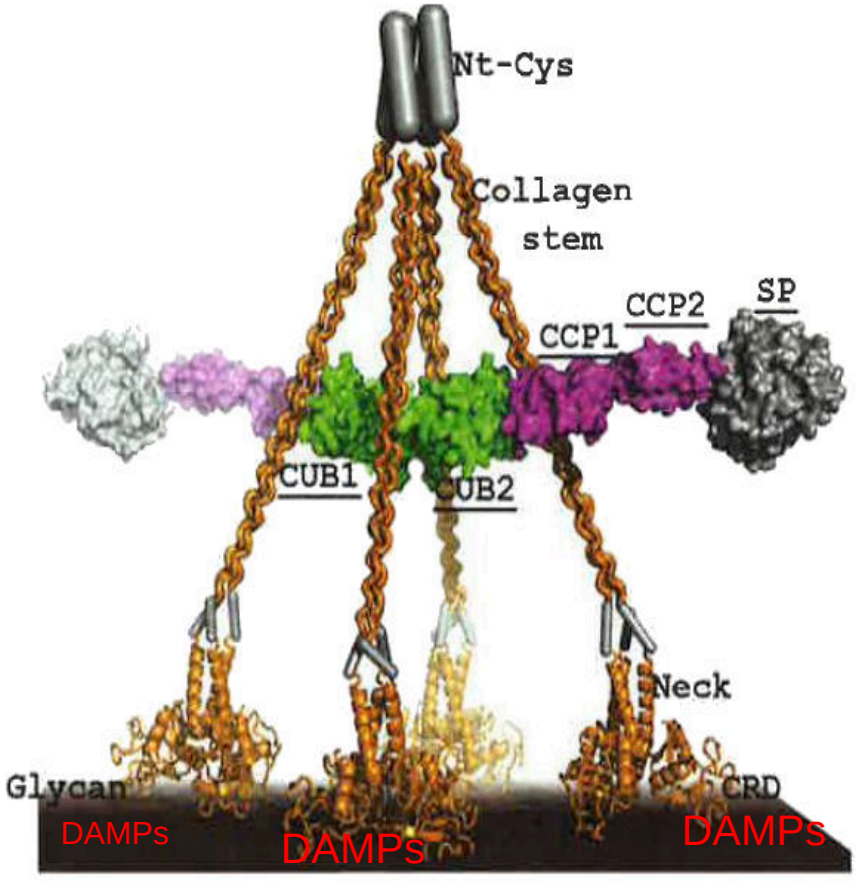
OMS906 Inhibits MASP-3, Considered the Premier Target in the Alternative Pathway

OMEROS

- MASP-3 is the key activator of the alternative pathway ("AP")
- MASP-3 is the premier target within the AP
  - Has the lowest concentration of all AP proteins
  - Has low relative clearance of AP targets
    - Example: ~50% of systemic CFD is cleared per hour
  - Unlike C5 and C3 blockers, leaves intact the lytic arm of the classical pathway, important in fighting infection

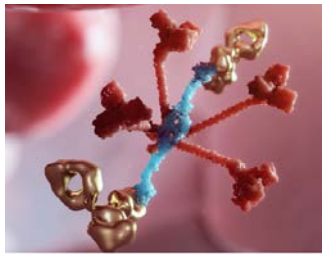
Lectin and Alternative Pathway Activation

- "MBL-associated serine proteases"
- Three MASPs can form complexes with five possible pattern recognition molecules
- Serine protease with pattern binding potential
- Lectins, via carbohydrate recognition domains (CRD), bind molecular patterns on microbes or damaged/altered host tissue
- Inhibitors expected to have broad applications in conditions involving inflammation and tissue damage



Targeting MASP Proteins

MASP Inhibitory MAb Programs



MASP-2 Inhibitor

- Narsoplimab

MASP-3 Inhibitor

- OMS906

LECTIN PATHWAY

Blocked Upstream

ALTERNATIVE PATHWAY

Blocked Upstream

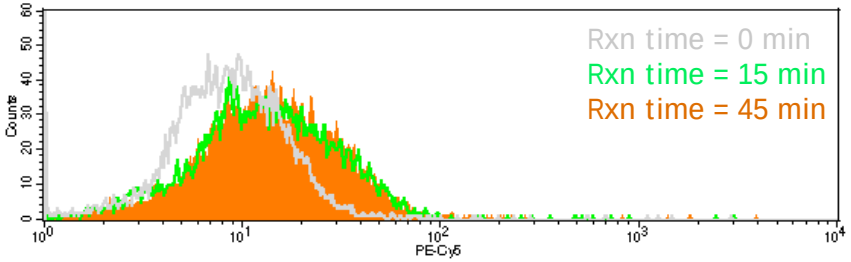
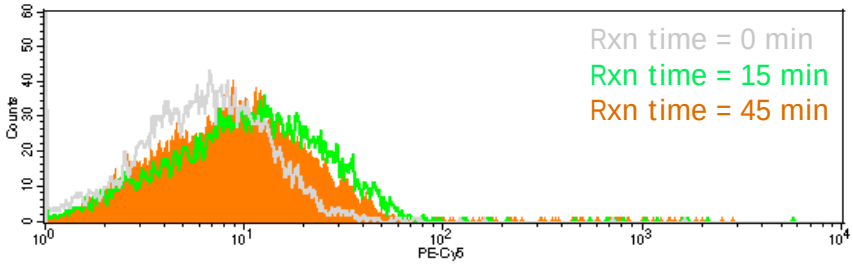
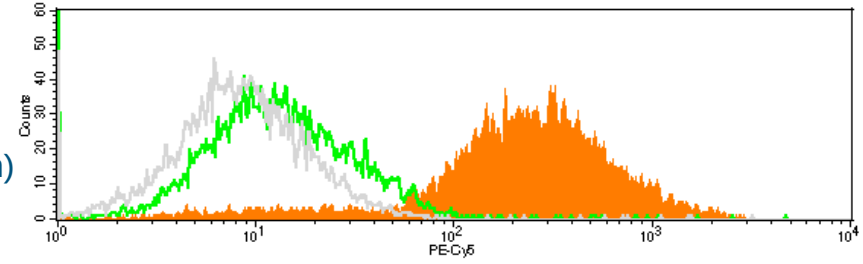
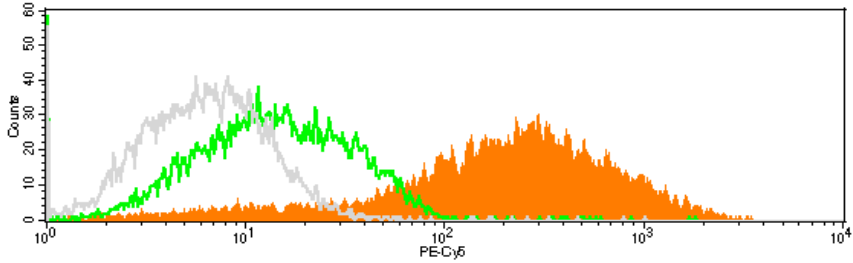
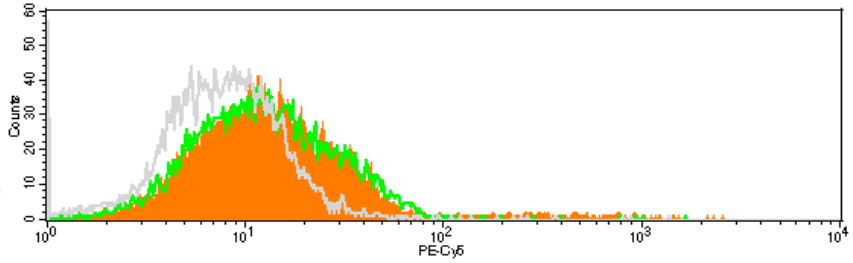
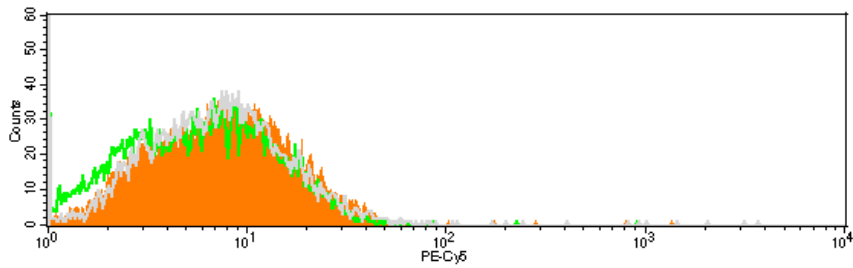
The MASP inhibitor approach preserves classical pathway function

CLASSICAL PATHWAY

Intact

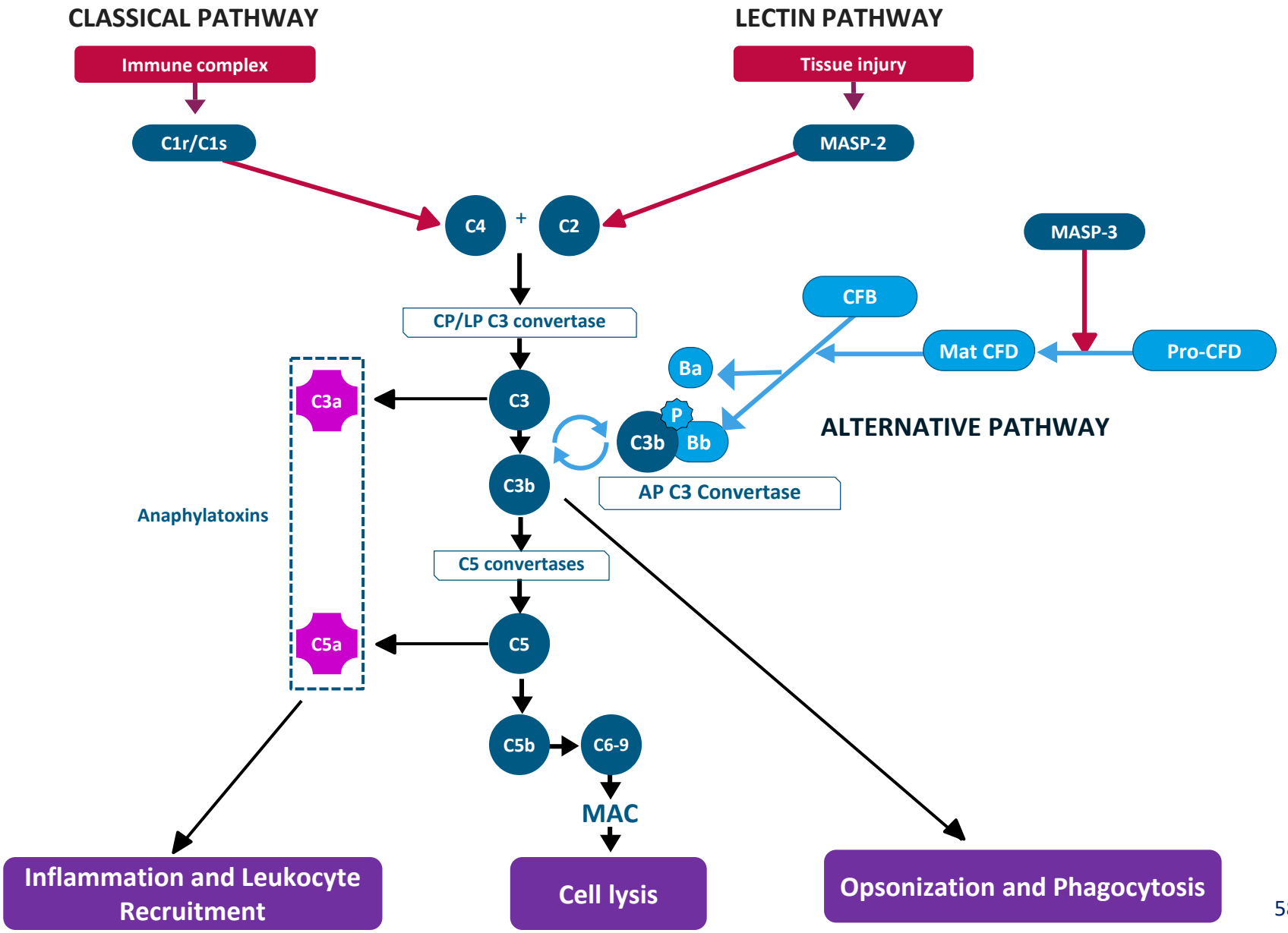
Role of MASP-3 in AP Activity of Human Serum

OMEROS

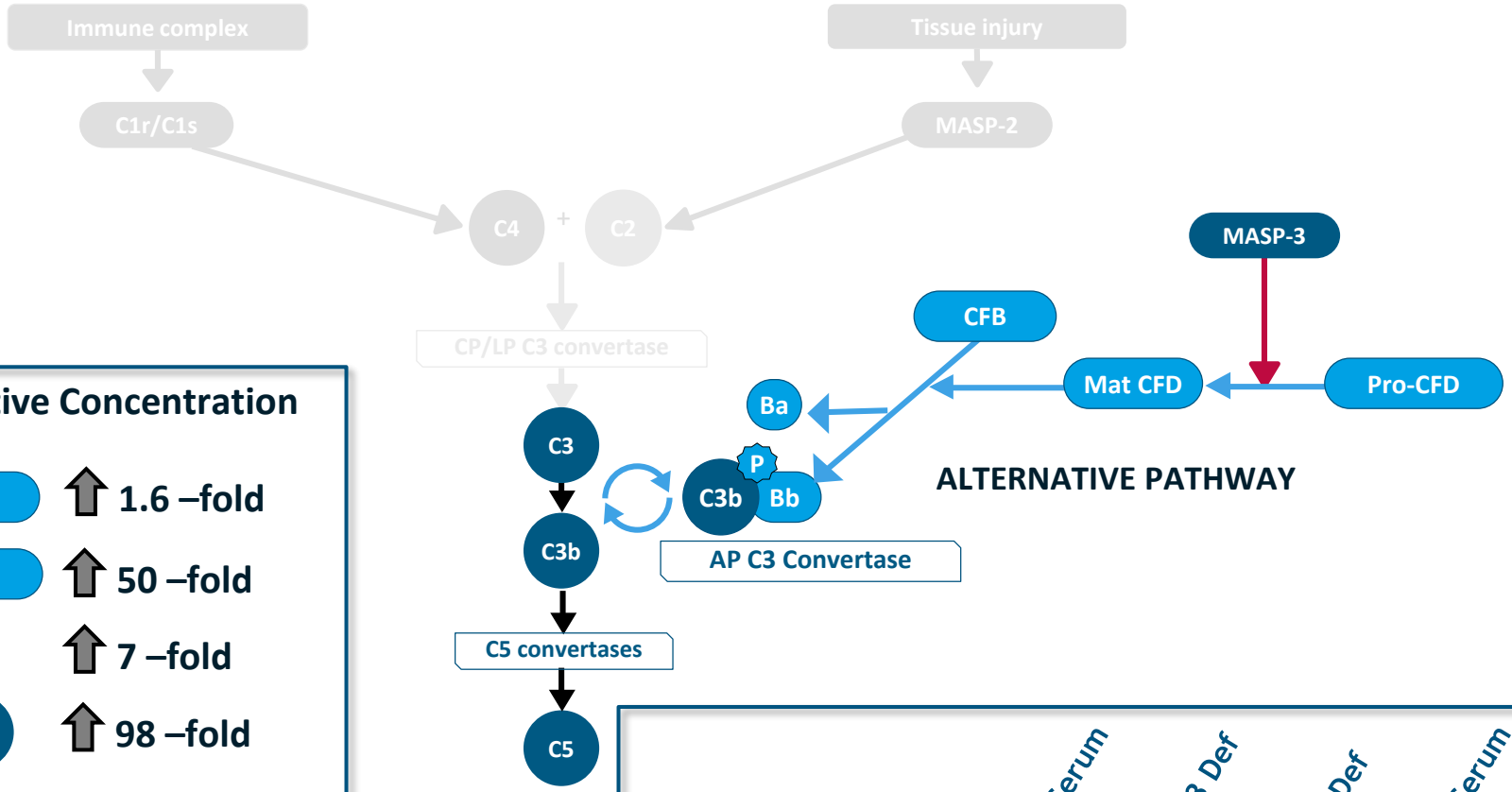
	MASP-3 Deficient Individual	MASP-1/3 Deficient Individual
No protein		
+ rMASP-3 (full-length)		
+ rMASP-3A (catalytic mutant; full-length)		

Presence of MASP-3 is required to drive AP in human serum

Three Pathways of Complement

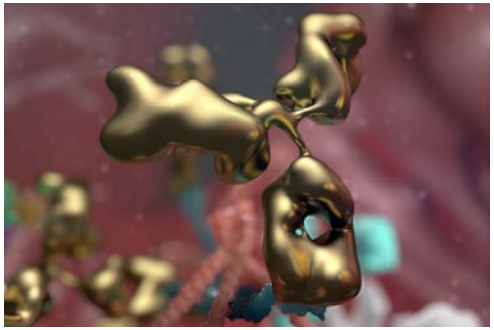


Three Pathways of Complement



Properties of OMS906

OMS906



Humanized monoclonal antibody **highly potent** and **selective** for MASP-3

Infrequent SubQ Administration

Convenient dosing regimen allows self-administration in an **outpatient setting**

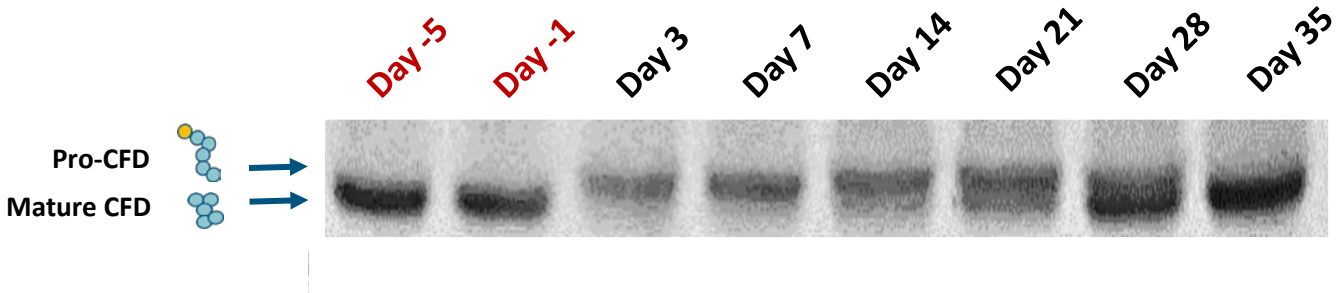
OMS906
is designed to treat multiple alternative pathway-driven diseases with infrequent, SubQ delivery

Initial Phase 1 clinical data expected later this year

Analysis of CFD Status in a Treated Monkey

CFD is matured by cleavage and release of activation peptide on the N-terminus of the protein

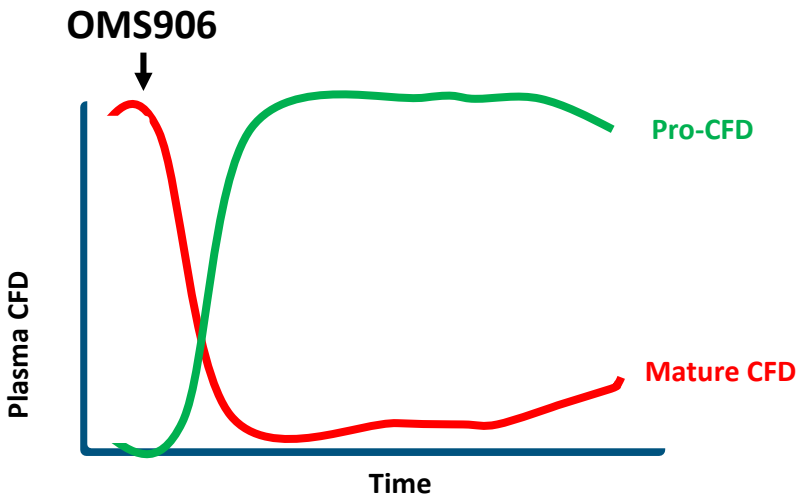
IP Ab: αCFD > Western Blot



CFD is present in plasma as pro-CFD following single dose of OMS906

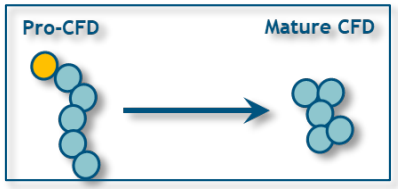
Measurement of CFD Status

CFD is matured by cleavage and release of activation peptide on the N-terminus of the protein

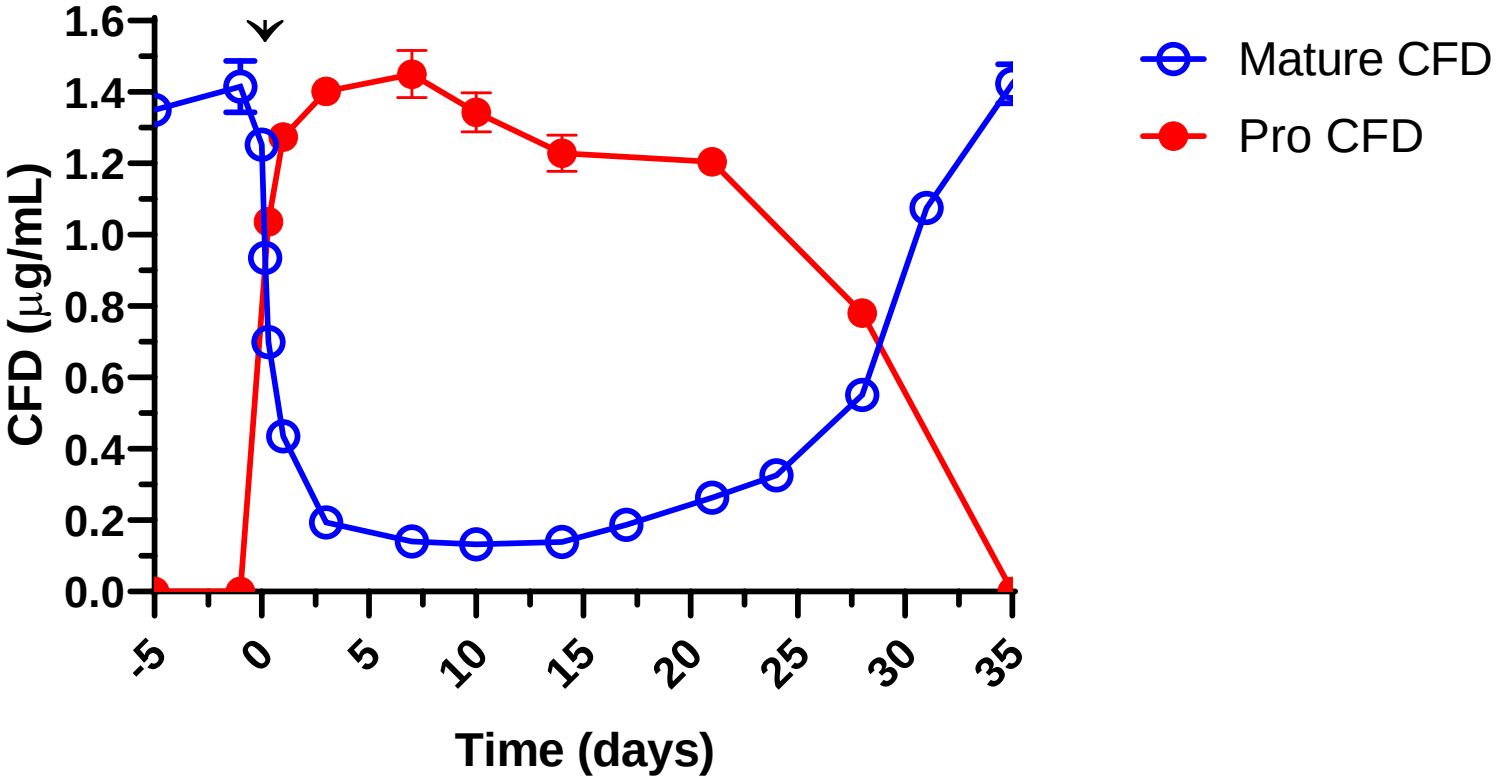


CFD status (pro vs. mature) can be used as direct measurement of MASP-3 inhibition

Measurement of CFD Status

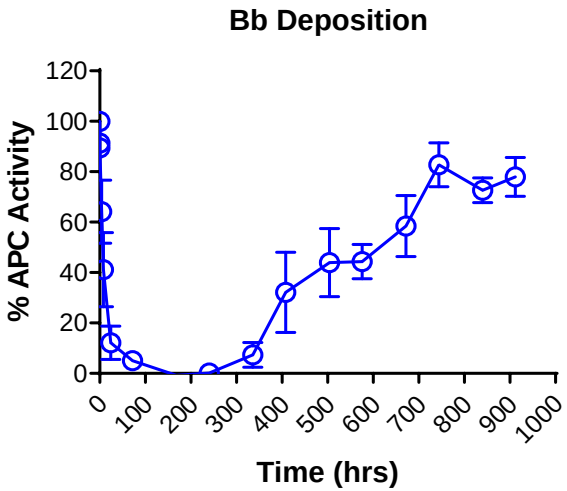


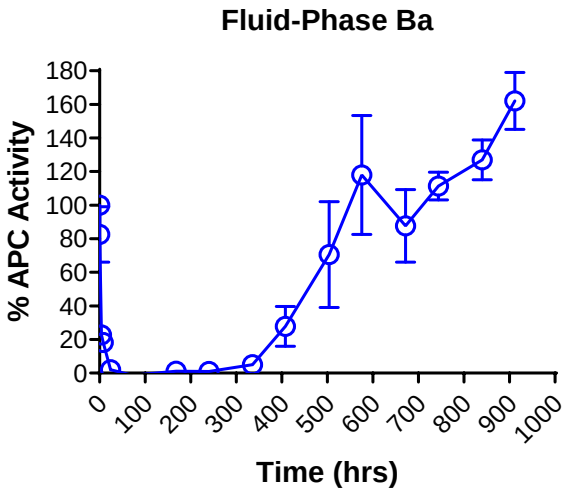
Single-Dose Monkey Study

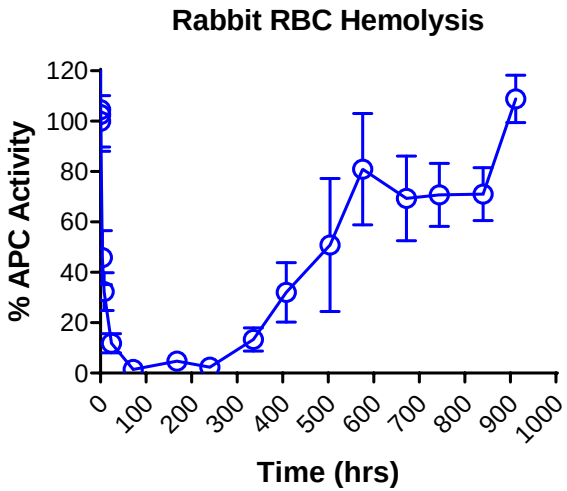


OMS906 blocks systemic maturation of CFD and results in accumulation of Pro-CFD

Inhibition of the Alternative Pathway in Monkey



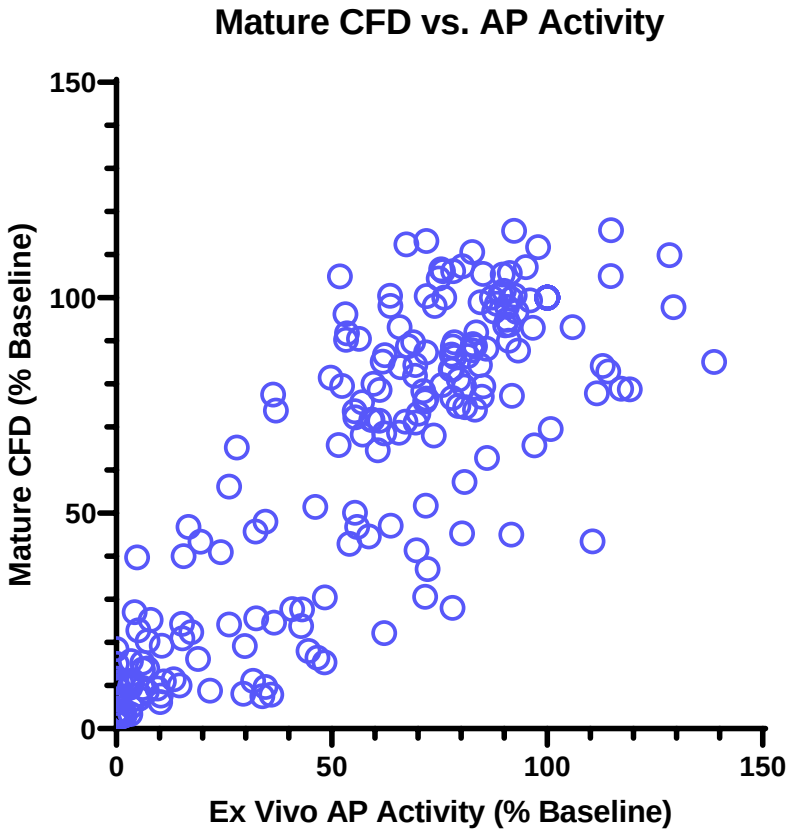




Number of Days of ≥ 90% Alternative Pathway Inhibition		
Bb Deposition on Zymosan	Fluid-Phase Ba	Hemolysis of Rabbit RBCs
13	14	12

Single dose is sufficient for sustained inhibition of the Alternative Pathway in monkey

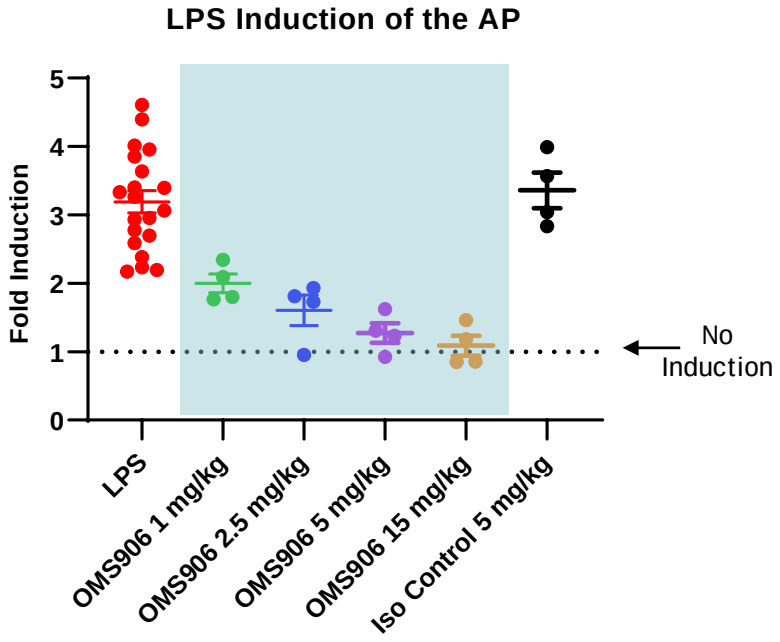
Relationship of CFD Status with Activity



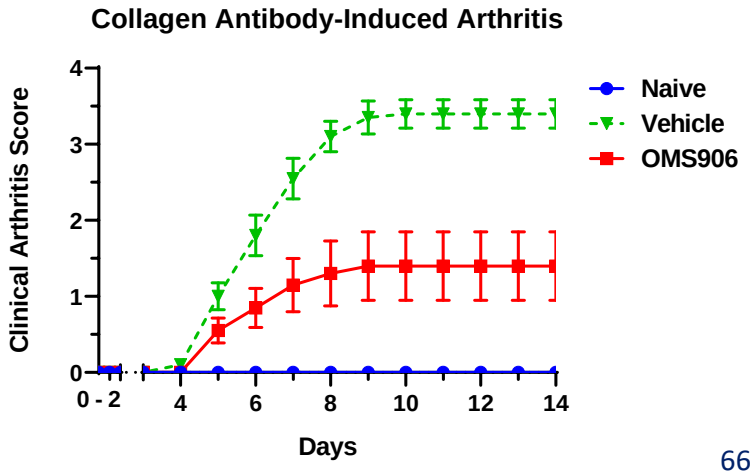
Lowest levels of detectable mature CFD correlate with complete inactivation of the AP

Demonstration of Efficacy in Mouse Disease Models

- In vivo induction of AP with LPS
  - OMS906 decreases systemic Ba levels caused by LPS injection into mice



- Collagen antibody-induced arthritis (CAIA) model
  - OMS906 decreases severity (and incidence) of arthritis



Systemic inhibition of CFD maturation is sufficient to block in vivo AP

OMS906 Potential in Paroxysmal Nocturnal Hemoglobinuria

PNH is a Rare, Chronic, Life-Threatening Complement-Mediated Blood Disorder

OMEROS

PNH is characterized by intravascular and extravascular hemolysis

Unmet Need Persists

~70%

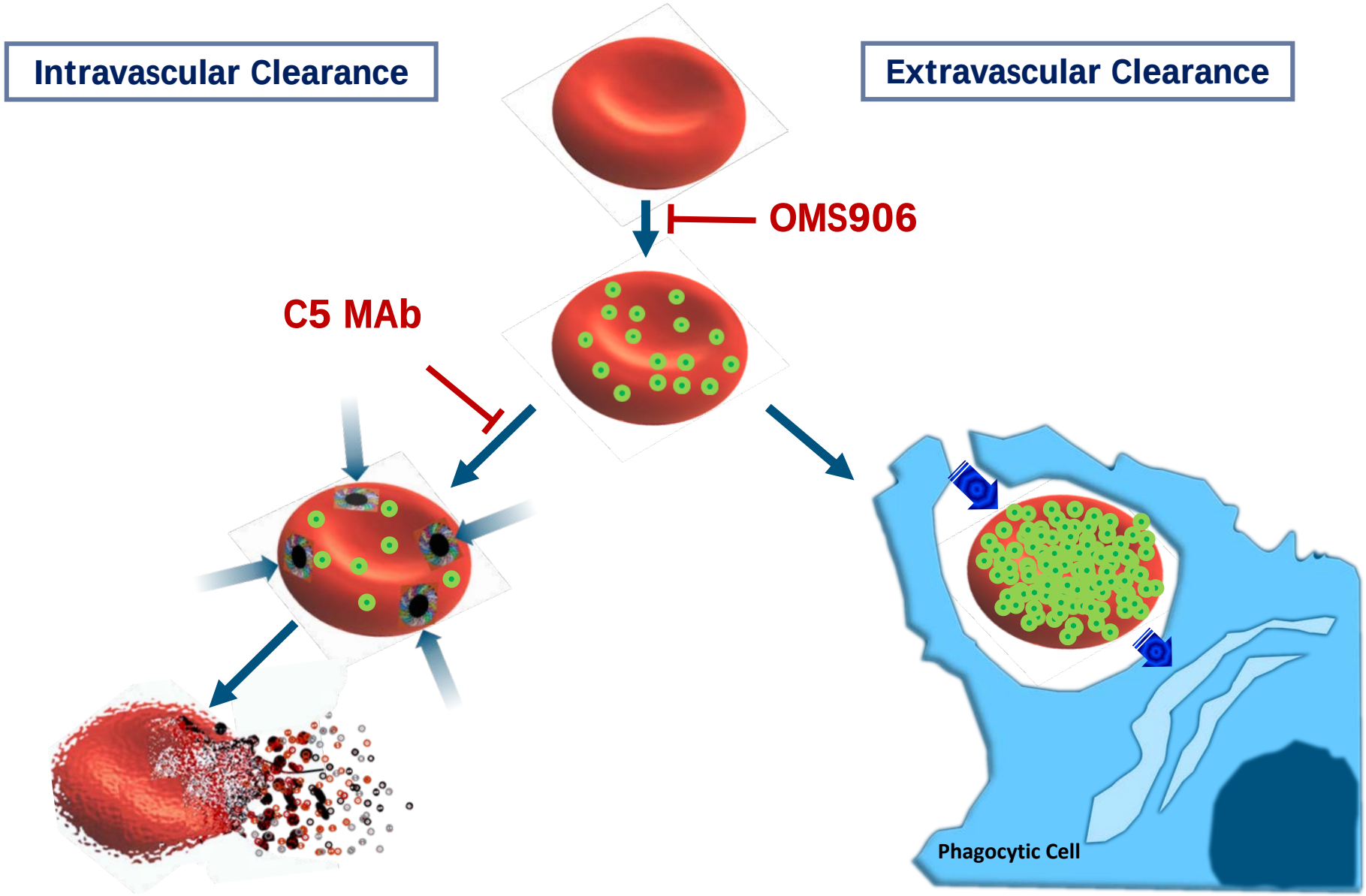
of PNH patients continue to have
low hemoglobin levels while on a C5 inhibitor[1,2]

~1/3

of PNH patients require
one or more transfusions a year while on a C5 inhibitor[3]

1. Risitano AM, Marotta S, Ricci P, et al. (2019) Anti-complement Treatment for Paroxysmal Nocturnal Hemoglobinuria: Time for Proximal Complement Inhibition? A Position Paper From the SAAWP of the EBMT. Front. Immunol. 10:1157. doi: 10.3389/fimmu.2019.01157. 2. Risitano AM, Notaro R, Marando L, et al. (2009) Complement fraction 3 binding on erythrocytes as additional mechanism of disease in paroxysmal nocturnal hemoglobinuria patients treated by eculizumab. Blood. 2009 Apr 23;113(17):4094-100. 3. McKinley C. Extravascular Hemolysis Due to C3-Loading in Patients with PNH Treated with Eculizumab: Defining the Clinical Syndrome. Blood. 2017;130:3471.

Red Blood Cell Clearance in PNH



Demonstration of Efficacy in PNH Models

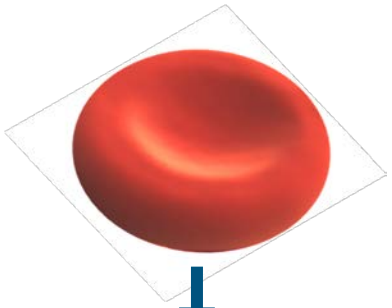
- In vitro destruction of human “PNH-like RBCs” (sensitized with αCD55/59 Abs)
  - Hemolysis
  - Opsonization (C3b/iC3b and C3d deposition)

- In vivo clearance of RBCs (Crry-/- mouse RBCs)
  - Primarily model of extravascular pathway of clearance

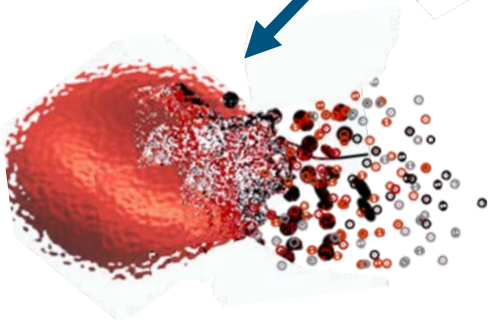
Red Blood Cell Clearance in PNH

Intravascular Clearance

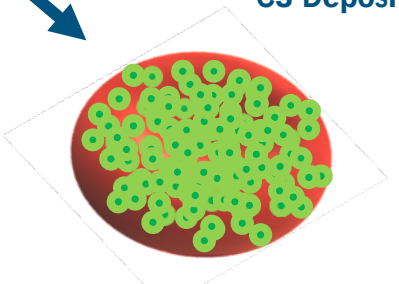
Extravascular Clearance



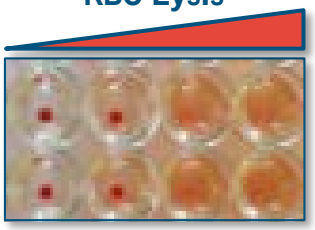
Hemolysis

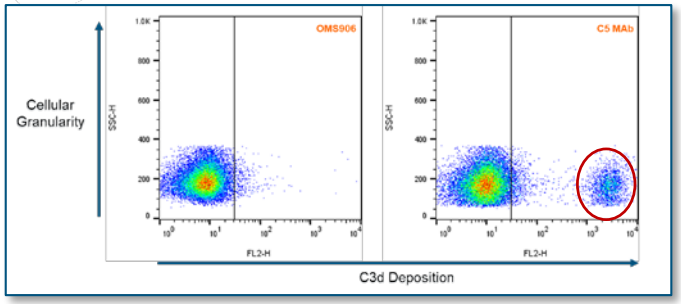


C3 Deposition

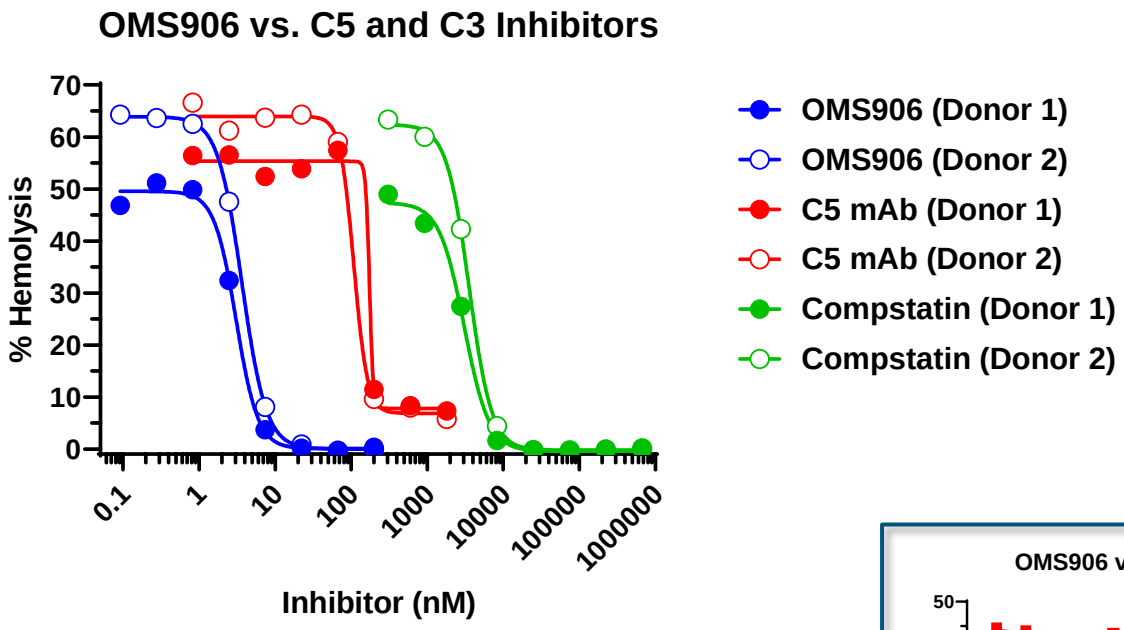


RBC Lysis

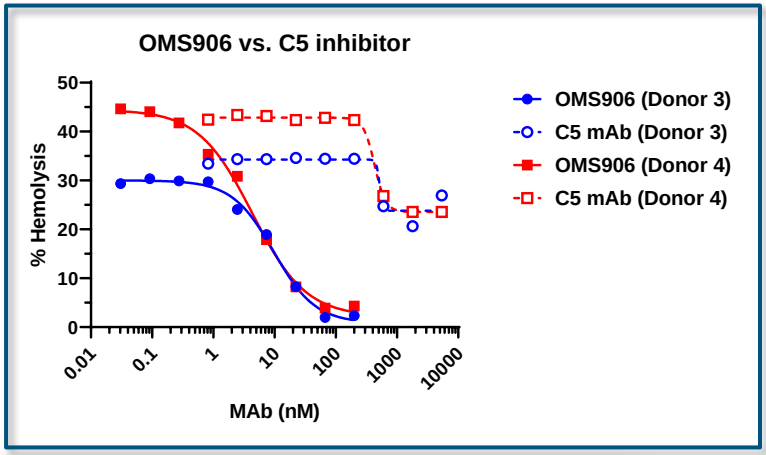




Model of Intravascular Lysis of PNH RBCs: Comparison with C3 and C5 Inhibitor

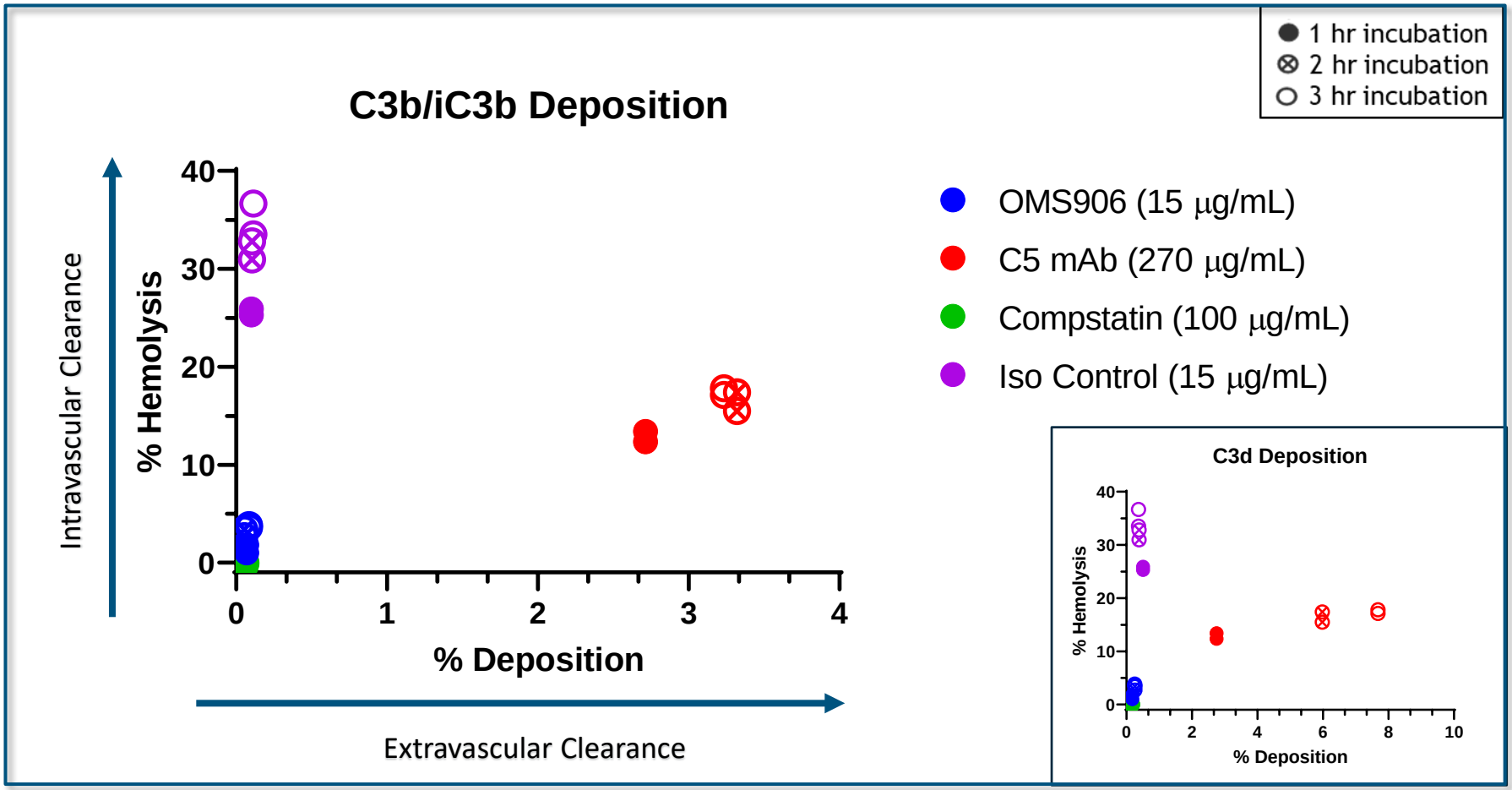


	C5 MAb	Compstatin
Relative OMS906 Potency	~30-fold	~1000-fold



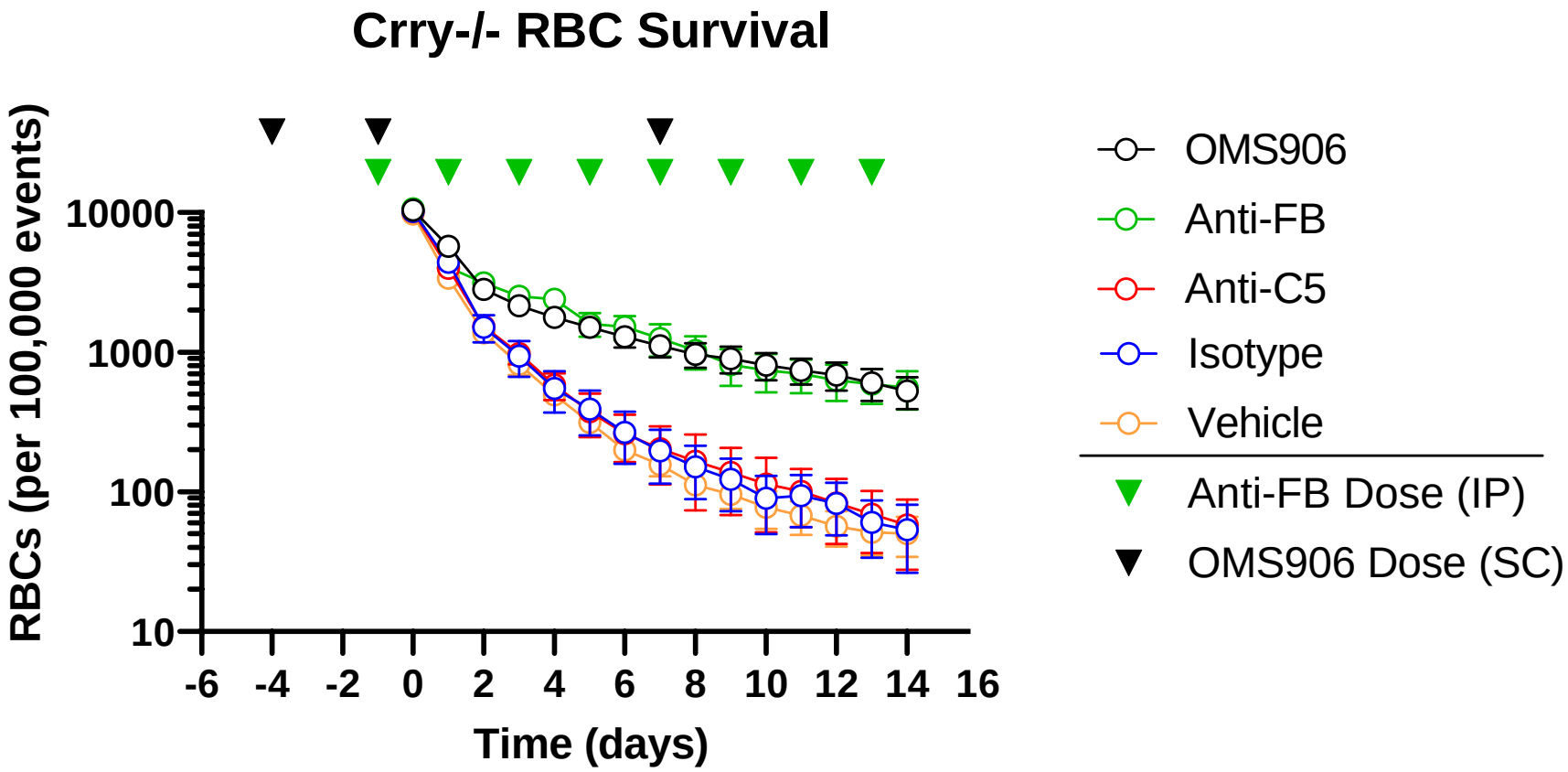
OMS906 demonstrates greater potency and greater degree of pathway inhibition than C5 mAb

Comparison to C3 and C5 Inhibition for PNH



OMS906 blocks a shared step in both pathways of PNH RBC clearance.

Donor RBCs Survival



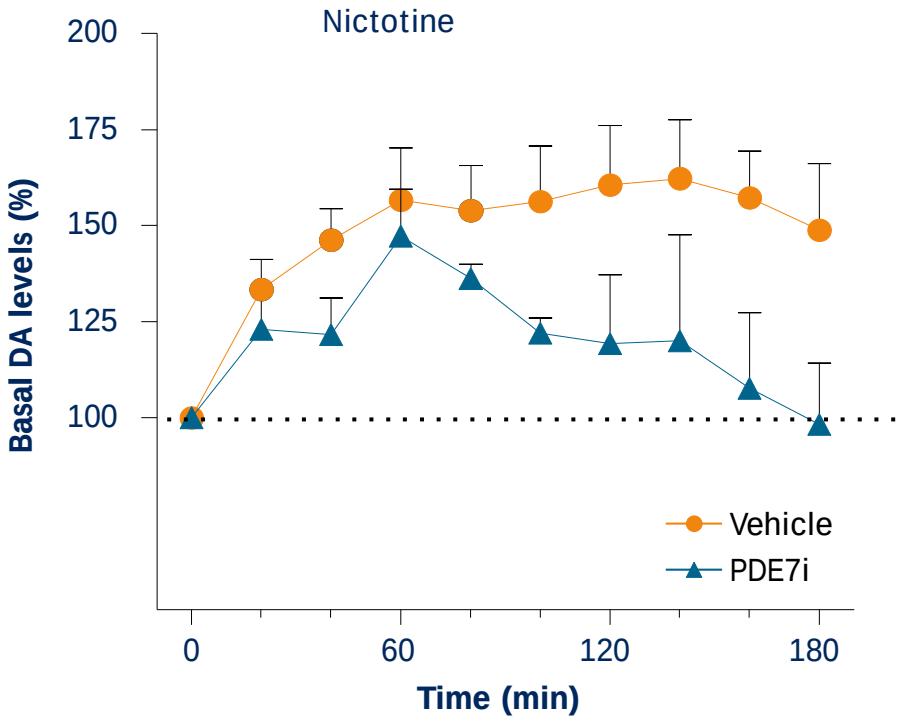
Addiction: OMS527

OMS527
PDE7 Inhibitor

OMEROS

- Novel target and novel mechanism for treating addiction
- Mechanism is highly conserved between humans and rodents
- Works through the dopamine system
- PDE7 inhibitors in animal models:
  - Have not appeared to alter reward system (no interference with other pleasurable activities)
  - Reduced both craving and relapse
  - Did not exhibit addictive properties
- Significant effects observed in animal models of:
  - Nicotine, cocaine, alcohol, and opioid addiction
  - Binge eating
- Broad issued and pending patents internationally cover any PDE7 inhibitor for treatment of any addiction or compulsive behavior
- Nicotine addiction selected as initial indication
- Manuscript detailing OMS527 data and PDE7 mechanism of action submitted for peer-reviewed publication

OMS527
Dopamine Levels in the “Liking” (or Craving) Phase



PDE7 inhibition reduced nicotine-induced increase of extracellular dopamine levels in the rat nucleus accumbens

OMS527
Clinical Development

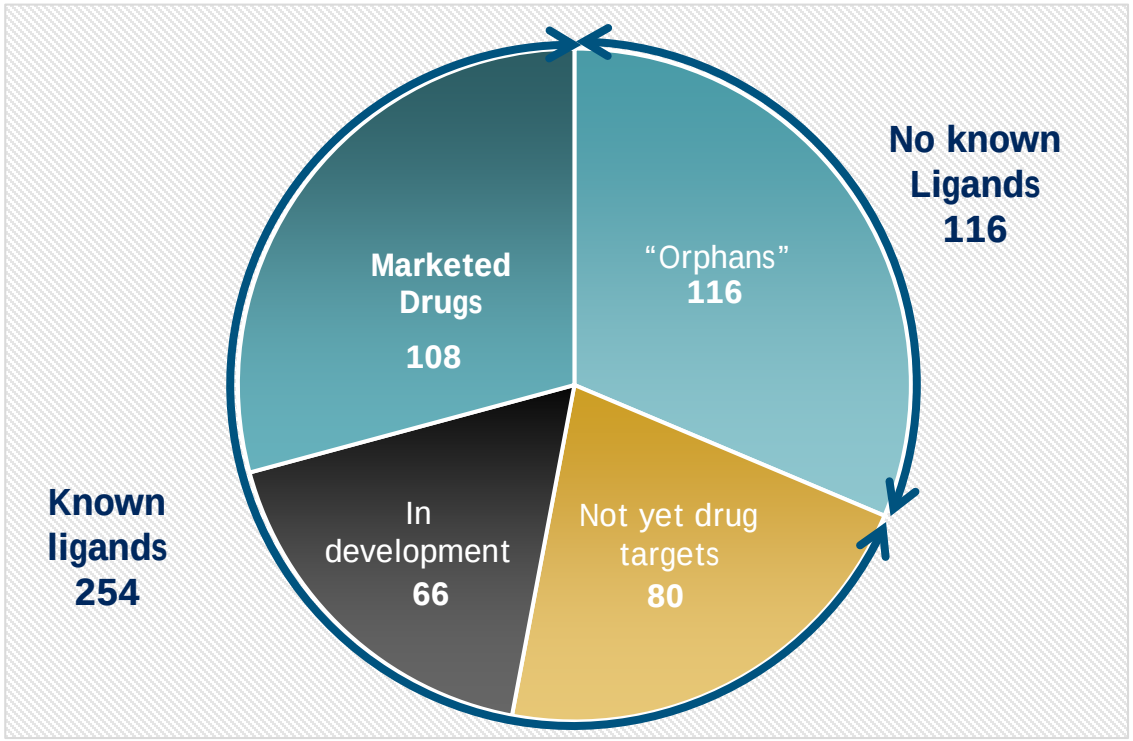
- Phase 1 trial assessed the safety and pharmacokinetics of the study drug (OMS182399)
- Double-blind, randomized, placebo-controlled trial evaluated 6 single-ascending-dose and 3 multiple-ascending-dose cohorts
- Met primary safety and tolerability endpoints
  - No significant adverse events were reported and OMS182399 was generally well-tolerated over the dose ranges tested – no meaningful difference from placebo
- Data showed a favorable and dose-proportional pharmacokinetic profile supporting once-daily dosing

G-Protein Coupled Receptors (GPCR) Platform

GPCRs - Attractive Drug Targets

GPCRs are promising drug targets, but there are challenges in drug discovery

370 Non-Sensory GPCRs

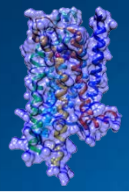


Challenges

- Ligand required for assay development
- Signaling pathway not known
- Laborious fractionation for natural ligand identification
- Current technologies limited only to agonist screening

Opportunities

Over 100 new drug targets

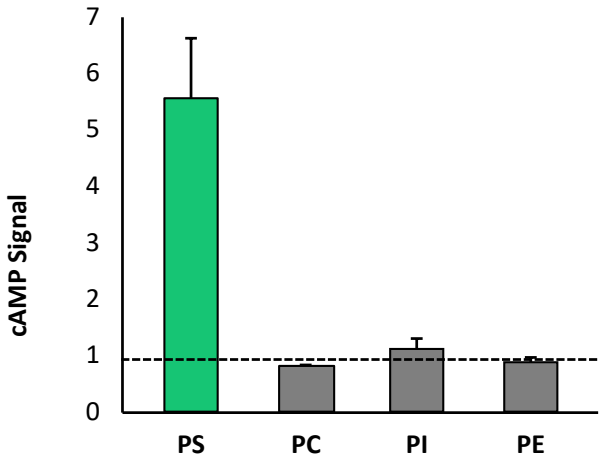


Immuno-Oncology: GPR174

- GPR174 inhibition amplifies tumor-killing properties of T and NK cells
- GPR174 is activated by phosphatidylserine (PS) and lyso PS, which are produced by the tumor microenvironment, especially following chemo- or radiation therapy
- GPR174 inhibitors have the potential to address non-responders to current therapies
  - Combined inhibition of GPR174 and the adenosine pathway synergistically enhanced anticancer phenotypes
  - GPR174 inhibition may be amenable to combination with checkpoint inhibitors, cellular therapies and cytotoxic therapies
- GPR174 is expressed almost exclusively in the immune system

GPR174 Is Activated by Phosphatidylserine (PS), a Product of Cell Death and Stress

GPR174 Signaling



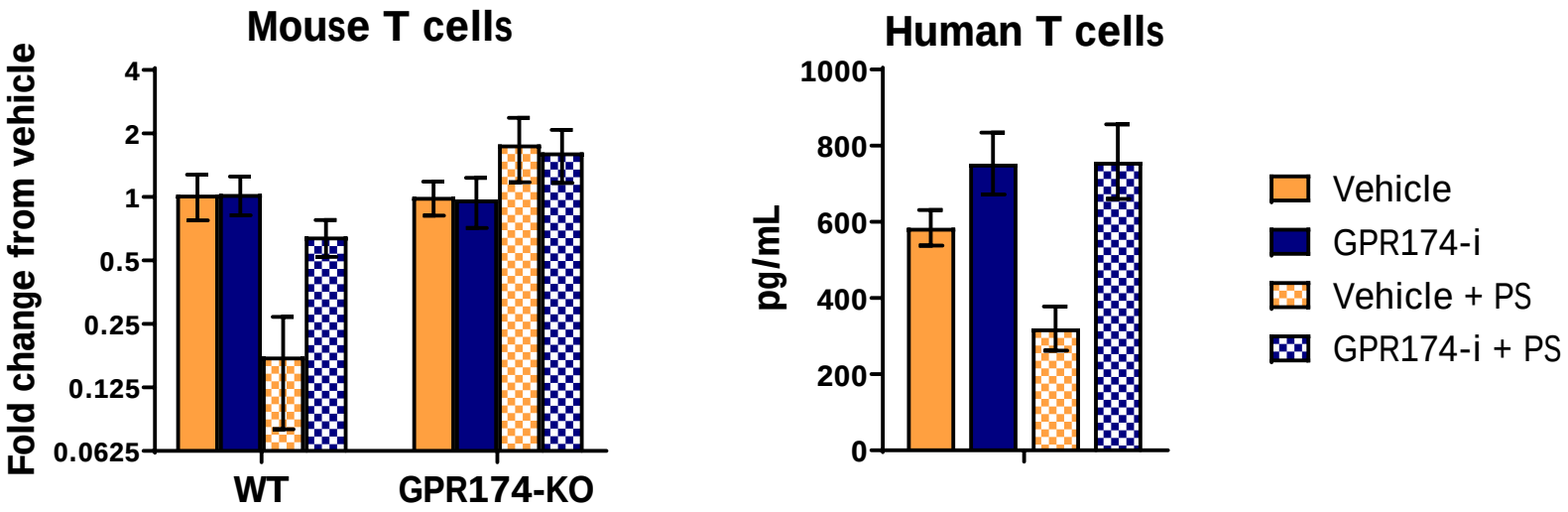
Liposomes made with:

- Phosphatidylserine (PS)
- Phosphatidylcholine (PC)
- Phosphatidylinositol (PI)
- Phosphatidylethanolamine (PE)

PS is a global immunosuppressive signal in cancer

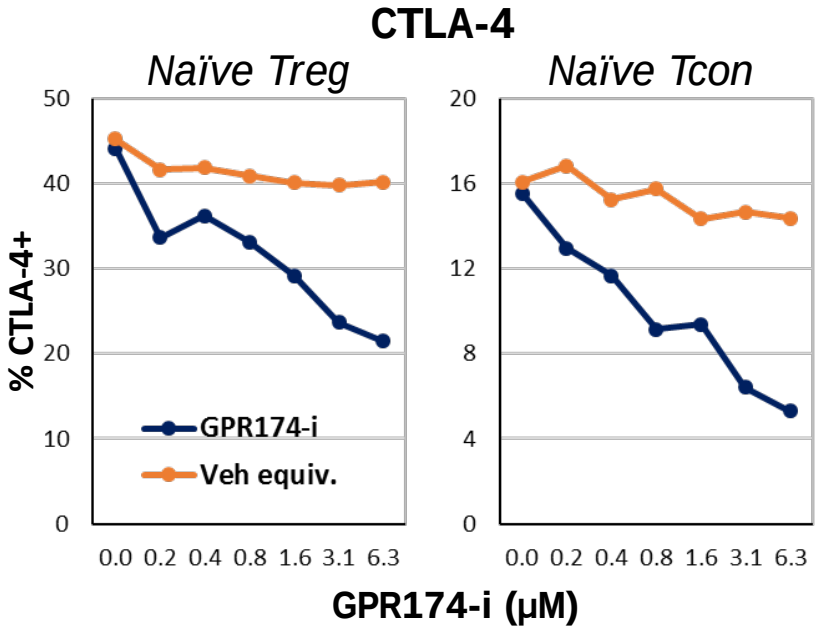
PS Activity on Purified T Cells Is GPR174-Dependent and Is Inhibited by GPR174-i

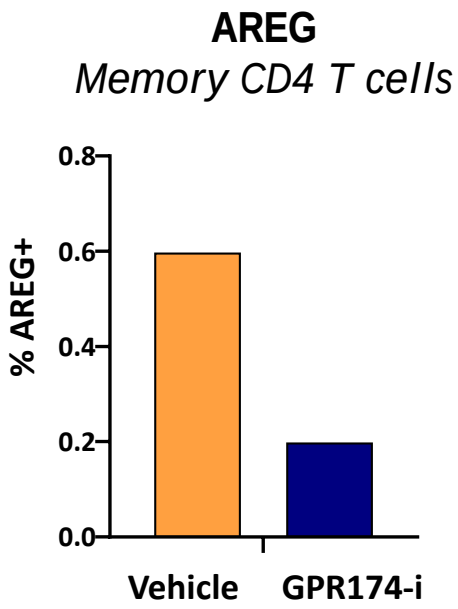
IL-2



- IFN-γ and TNF are also induced
- Tumor-promoting immune regulators are decreased: CTLA-4, Amphiregulin

GPR174 Inhibition Reduced Expression of Tumor Promoting Immunomodulators

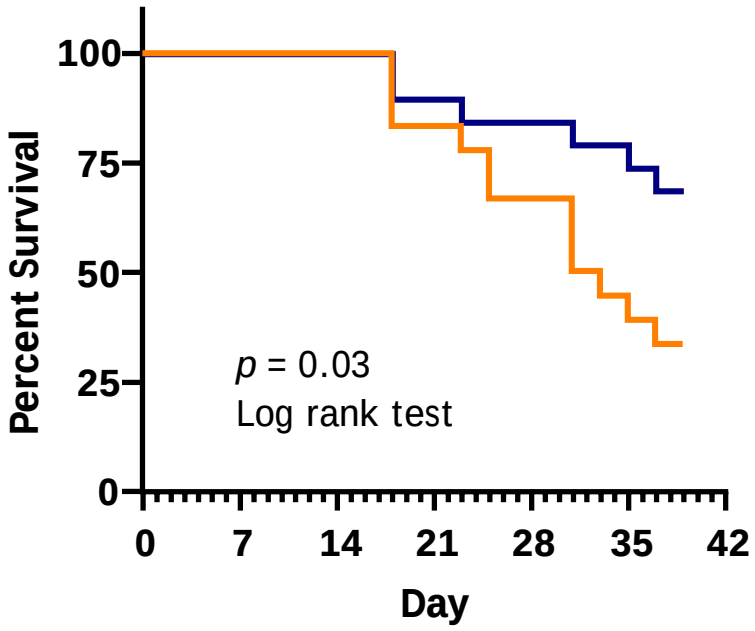




- CTLA-4 is an immune checkpoint targeted by YERVOY®
- Amphiregulin (AREG) is a tumor-promoting growth factor

GPR174 Deficiency Activates Anti-Tumor Immunity

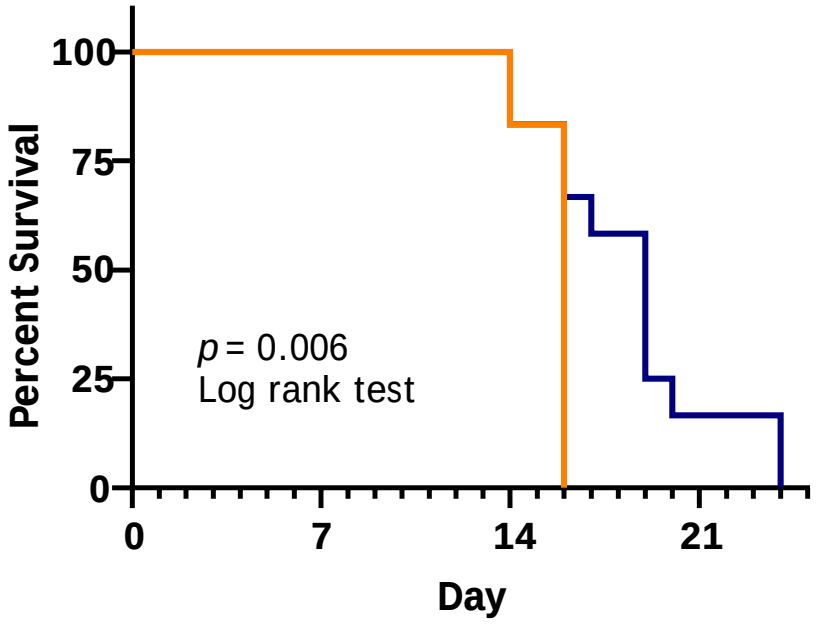
Colon Carcinoma



WT

KO

Melanoma



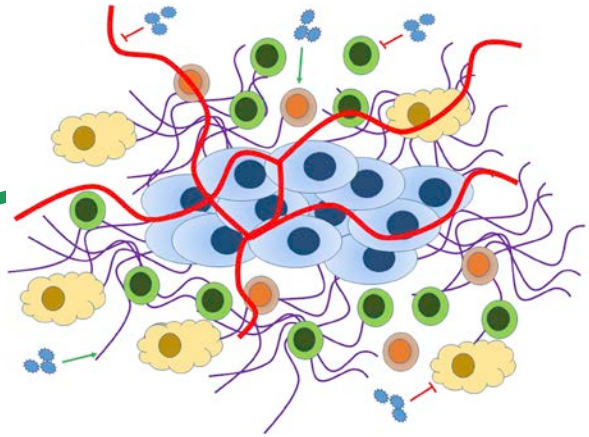
*Anti-GITR co-therapy was used to attenuate Treg dominance in these models

Activating Ligands for GPR174 and Adenosine Receptors A2A/A2B Are Products of the Tumor Microenvironment

OMEROS

Cell stress and death in the tumor microenvironment

PS & lysoPS are abundant in tumors
- From tumor cells, exosomes & extracellular vesicles, immune cells, platelets, vascular endothelium
- Further enriched by chemo- and radiation-therapy



ATP → CD39 → CD73 → Adenosine

PS & LysoPS → GPR174 → Gαs → cAMP

Adenosine → A2A/A2B → Gαs → cAMP

T cell

cAMP → *Immune suppression*

cAMP → *Immune suppression*

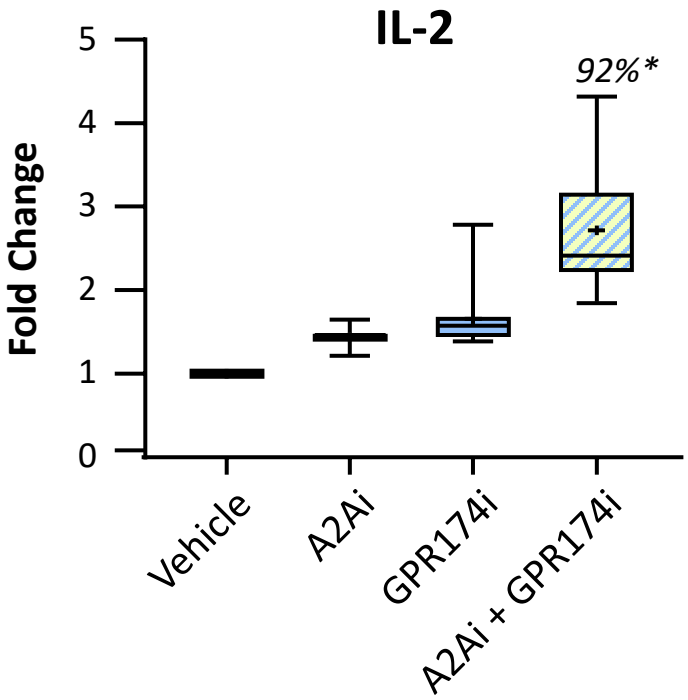
GPR174 and A2A/A2B adenosine receptors suppress T and NK cells through the cAMP pathway

Image: Journal of Cellular Immunotherapy, 2:2, 2016.

Inhibition of GPR174 and A2A Receptors Synergistically Activates Human T Cells

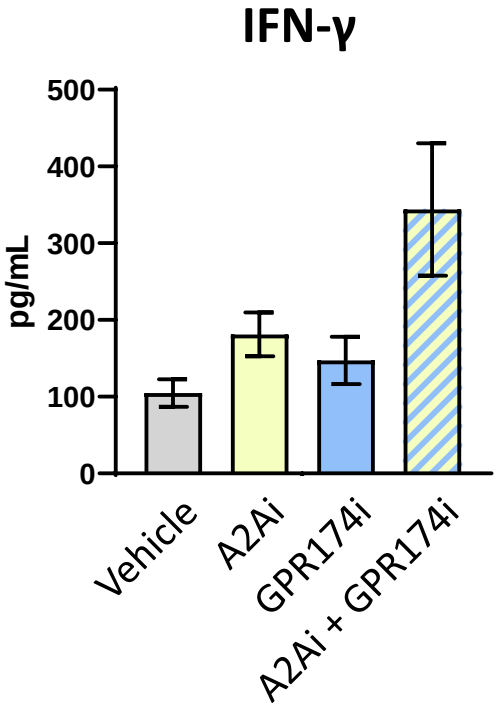
Total PBMC culture

High cell density, rich in PS and adenosine



CD8 T cell culture

Low cell density, with supplemented PS and adenosine (NECA)



Normalized Data from 12 Human Donors

**Percent of donors exhibiting GPR174i/A2Ai synergy*