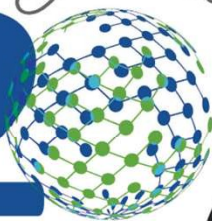




Reimagined
2020 
NOVEMBER 9-14 



Society for Immunotherapy of Cancer



Immunotherapy with B cell activating antibody CPI-006 in patients with mild to moderate COVID-19 stimulates anti-SARS-CoV-2 antibody response, memory B cells, and memory/effector T cells.

Presenting Author: Dr. Gerard Criner
Abstract/Poster ID: 325



Society for Immunotherapy of Cancer

#SITC2020

DISCLOSURES

Dr. Criner reports grants and personal fees from Galaxo Smith Kline, grants and personal fees from Boehringer Ingelheim, grants and personal fees from Chiesi, grants and personal fees from Mereo, personal fees from Verona, grants and personal fees from Astra Zeneca, grants and personal fees from Pulmonx, grants and personal fees from Pneumrx, personal fees from BTG, grants and personal fees from Olympus, grants and personal fees from Broncus, personal fees from EOLO, personal fees from NGM, grants and personal fees from Lungpacer, grants from Alung, grants and personal fees from Nuvaaira, grants and personal fees from ResMed, grants and personal fees from Respironics, grants from Fisher Paykel, grants and personal fees from Patara, grants from Galapagos, outside the submitted work.

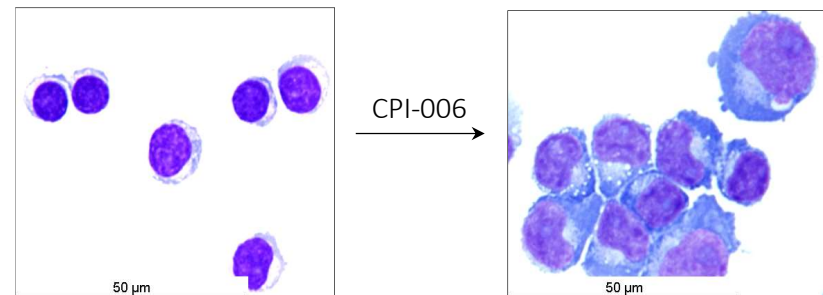
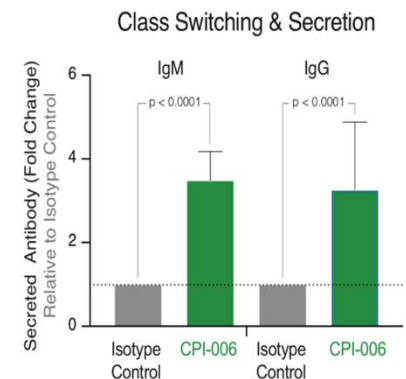
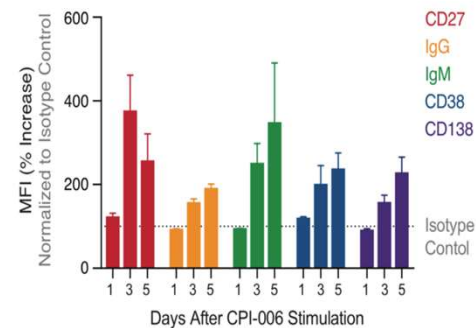
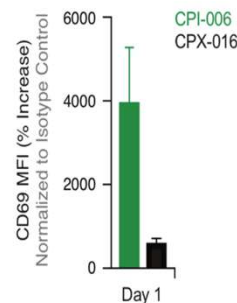
A subset of authors are employees and shareholders of Corvus Pharmaceuticals. SW and RM are inventors on patents owned by Corvus Pharmaceuticals related to this work.

There will be discussion about the use of products for non-FDA approved indications in this presentation

CPI-006 IS AN ANTI-CD73 WITH IMMUNOMODULATORY PROPERTIES

- CD73 is an ectoenzyme present on subsets of B cells (70%) and T cells (CD4 10%, CD8 50%)
 - Costimulatory on T cells¹
 - Activation of B cells²
- CPI-006 is a humanized IgG1 Fcγ receptor deficient anti-CD73 with unique properties^{2,3}
 - Differentiation of B cells into plasmablasts and Ig secretion
 - Increases expression of CD69
 - Induces memory B cells
- Ph 1/2 cancer trial demonstrates lymphocyte activation and effects on trafficking^{2,3}

Initial B Cell Activation → B Cell Surface Marker Expression

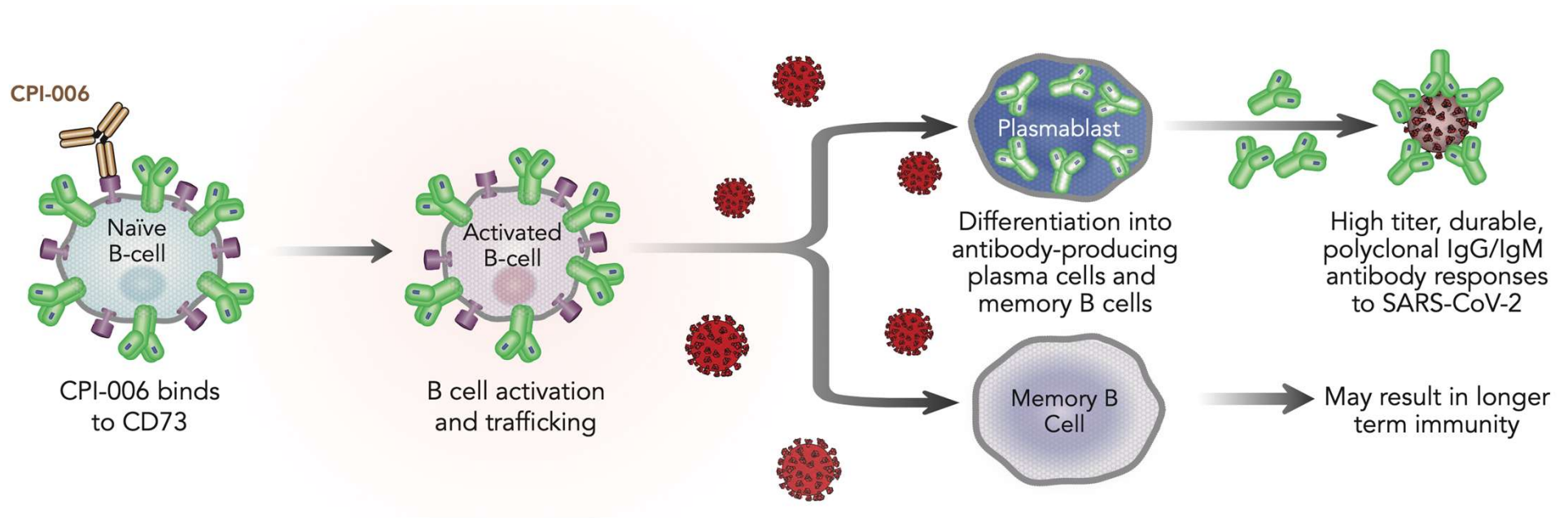


¹Resta & Thompson, Cell Signaling, 1997 ²Luke, ASCO Annual Meeting, 2019

³Willingham et al, medRxiv, 2020

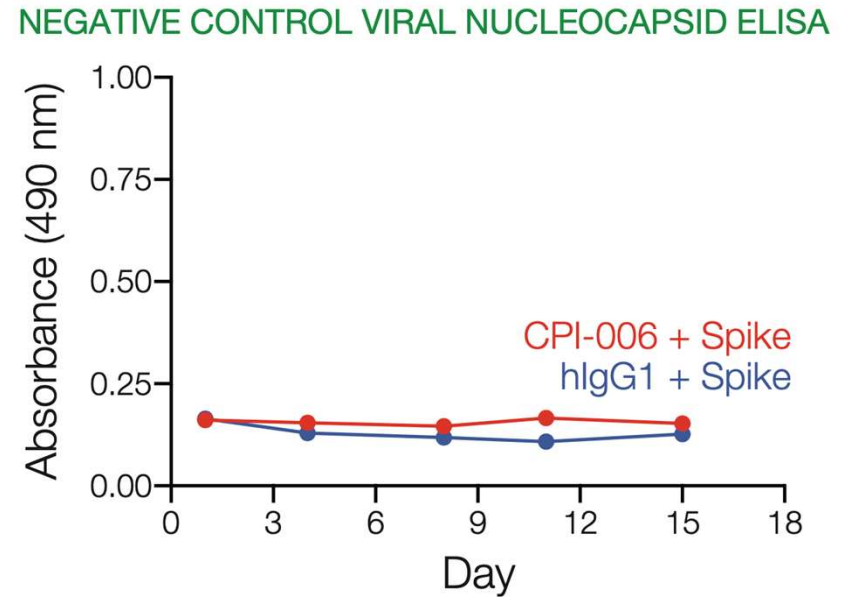
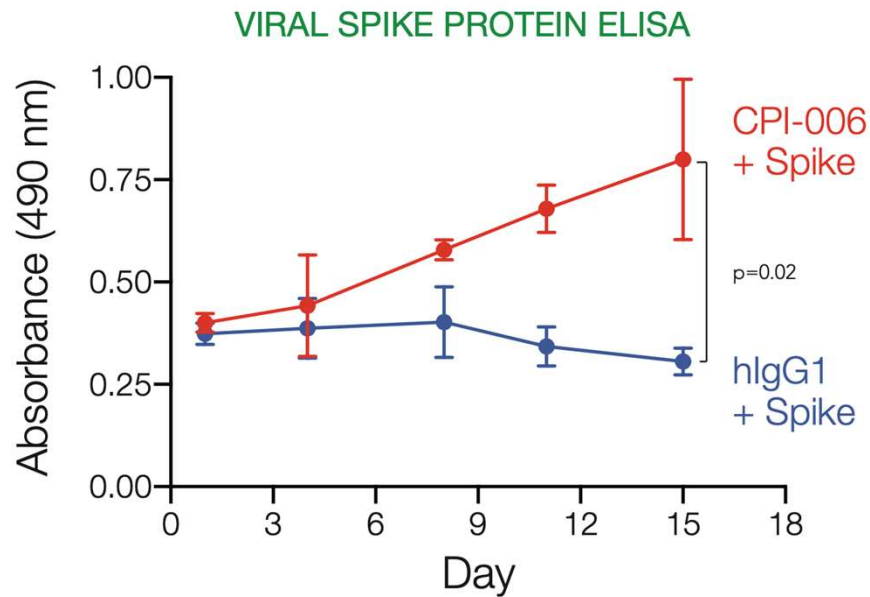
B CELL ACTIVATING CPI-006 IMMUNOTHERAPY OF COVID-19

- Enhance anti-SARS-CoV-2 antibodies to improve clinical outcome
- Improve long term immunity and protection from re-infection
- Accelerate viral clearance/reduce the risk of spreading
- Foundational therapy for treatment or prevention of other infectious diseases



VACCINATION OF HUMANIZED MICE WITH CPI-006 AND SPIKE PROTEIN ELICITS ANTIGEN SPECIFIC IMMUNITY

- NSG-SGM3 mice vaccinated with CPI-006 + SARS-CoV-2 spike protein produce antigen specific antibodies
- Mice receiving spike protein + isotype control antibody do not mount a response.



Mice (n=4/group) were immunized with the recombinant SARS-CoV-2 spike protein in incomplete adjuvant on Day 1 and treated with CPI-006 or human IgG1 control for 15 days.

PHASE 1 COVID-19 TRIAL & PATIENT CHARACTERISTICS

Single dose (IV) escalation study in hospitalized patients with mild to moderate COVID-19

- Patients receive SoC; no patient received convalescent plasma or other antibody therapy
- No drug related adverse events or changes in quantitative serum immunoglobulins
- 95% of patients were from high-risk patient populations

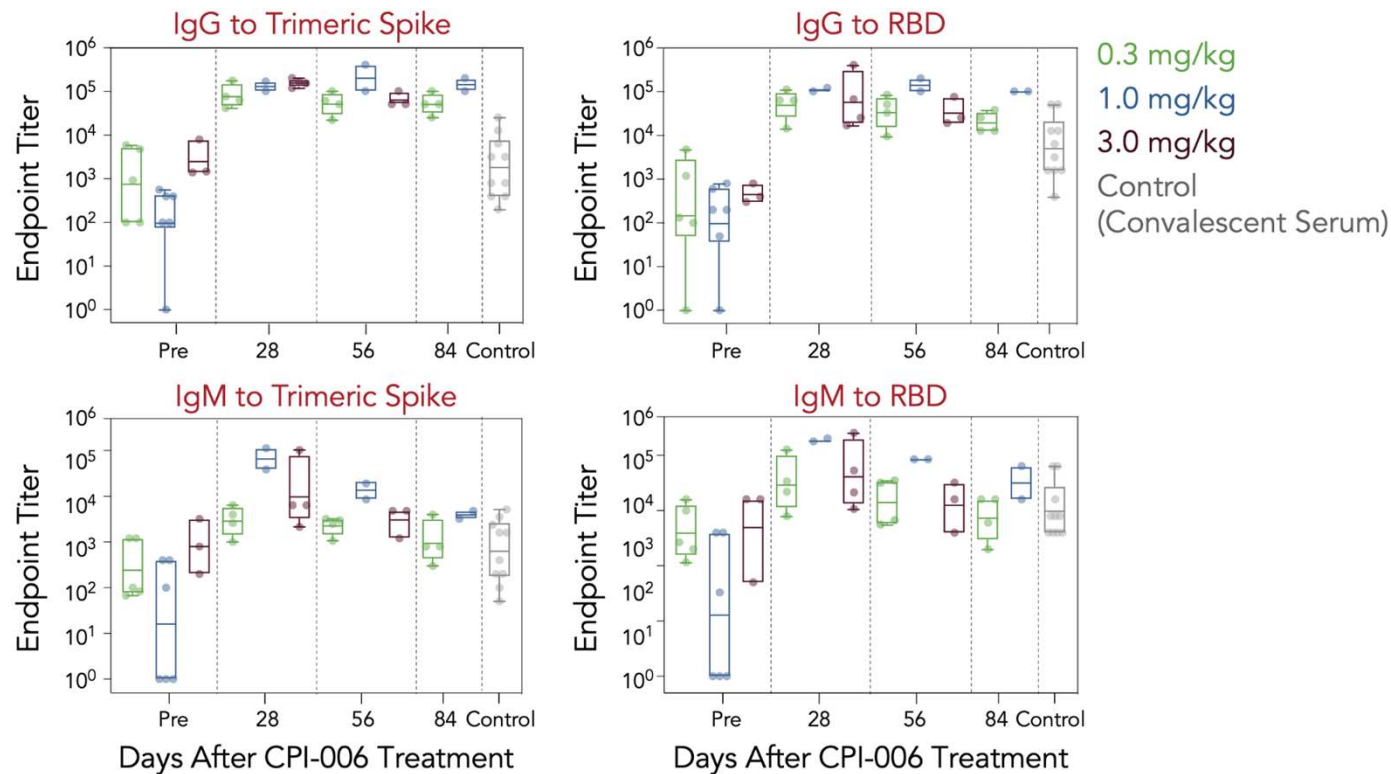
	Median Age Years (Range)	Median Days From POS to CPI-006 (Range)	Comorbidities	Median BMI in kg/m ² (Range)	Median ALC k/mm ³ (Range)	Median Time to Discharge (Range)
Cohort 4 (N=5) 5.0 mg/kg	56 (23-68)	5 (4-8)	DM, HTN, CKD, cancer	33.3 (23.3-47.5)	1.3 (0.7-2)	4.5* (3-8)
Cohort 3 (N=5) 3.0 mg/kg	53 (26-76)	5 (1-9)	DM, HTN, asthma, cancer	30.7 (26.5-33.9)	1.2 (1-2.2)	4 (2-23)
Cohort 2 (N=7) 1 mg/kg	63 (37-76)	7 (3->21)	DM, CAD, HTN, COPD	33.2 (16.5-35.1)	0.9 (0.6-2.3)	4 (2-12)
Cohort 1 (N=5) 0.3 mg/kg	48 (28-72)	4 (1-8)	DM, CAD, HTN asthma, cancer	30.3 (24.6-33.7)	1.3 (0.8-1.5)	3 (3-4)
OVERALL (N=22)	58.5 (23-76)	5 (1->21)		32.2 (16.5-47.5)	1.1 (0.6-2.3)	4* (2-23)

* One patient is still hospitalized

SoC=Standard of Care, DM=diabetes, CAD=coronary artery disease, COPD=chronic lung disease, CKD=chronic kidney disease, HTN=hypertension

MAGNITUDE AND DURATION OF Anti-SARS-CoV2 RESPONSES

Dose-response with sustained titers



Ig responses to Spike and receptor binding domain (RBD) increase out to 28 days and high titers are sustained for 84+ days

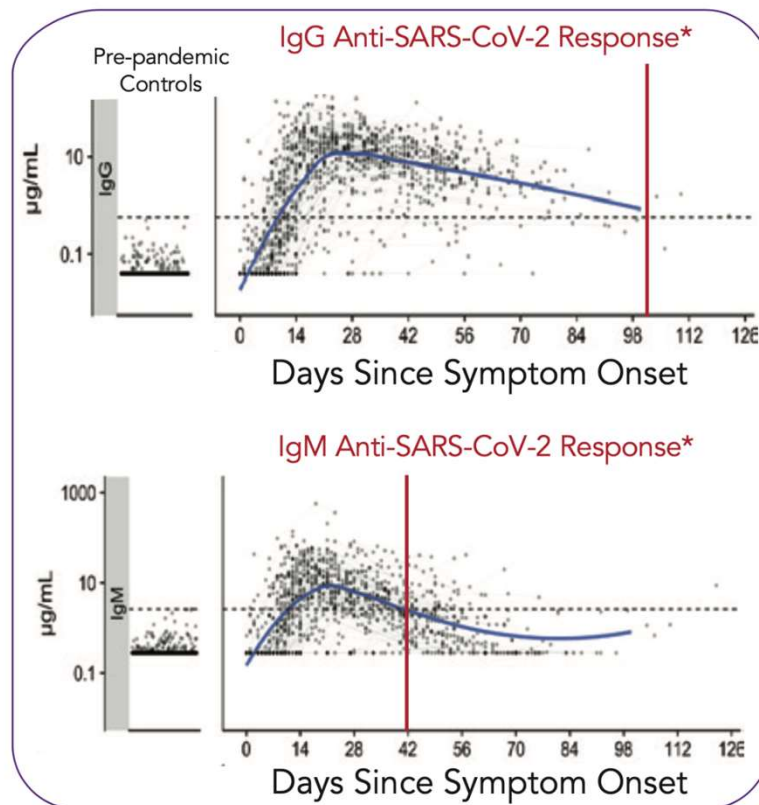
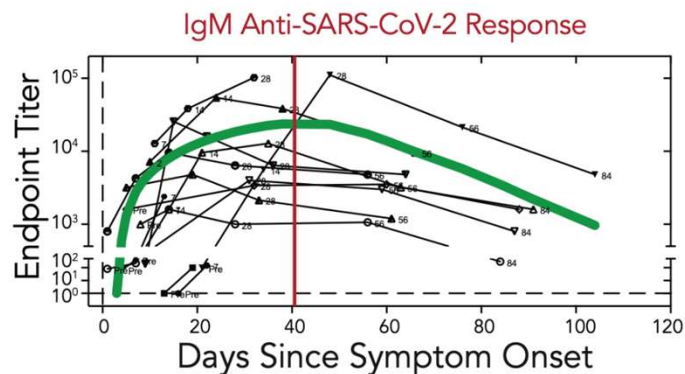
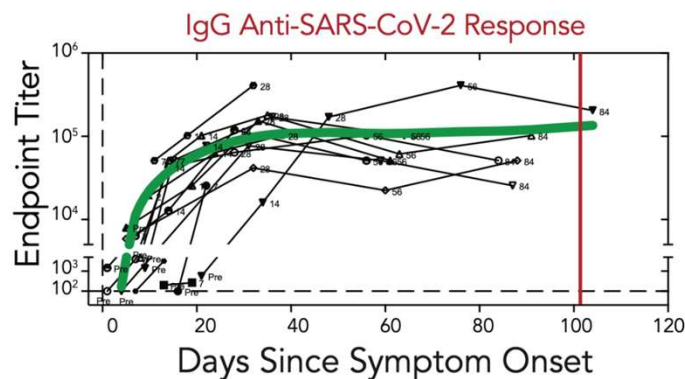
High IgM titers out to 84+ days

Dose response observed, with higher and more prolonged titers at ≥ 1.0 mg/kg

Neutralizing antibodies measured in pseudovirus assay out to 56+ days¹

¹SITC2020 Poster 325

ANTIBODY TITERS REMAIN ELEVATED 84+ DAYS AFTER SYMPTOM ONSET



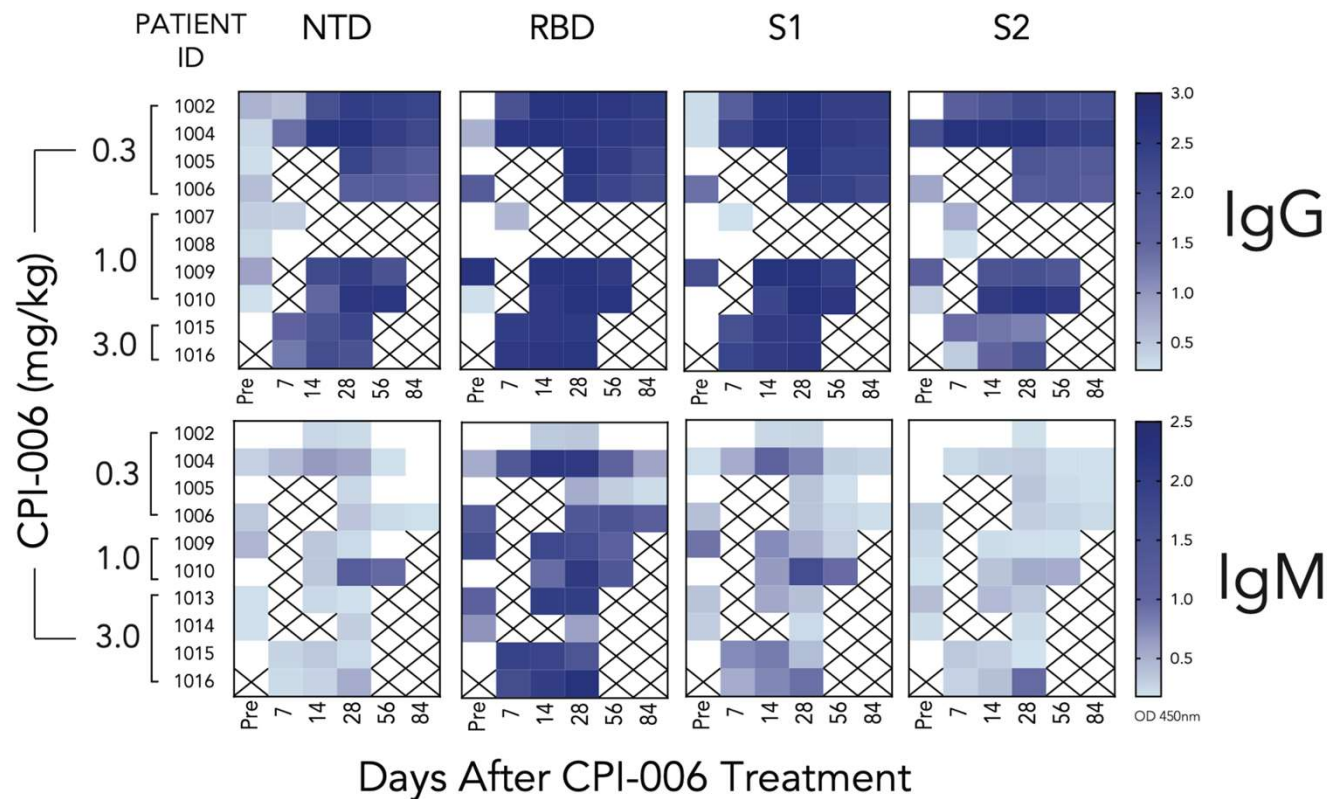
CPI-006 treated patients (left) compared to 343 hospitalized patients (right)¹

Sustained production of virus-specific IgG is associated with short disease duration²

¹Iyer et al, Sci Trans Med, 2020

²Chen et al, Cell, 2020

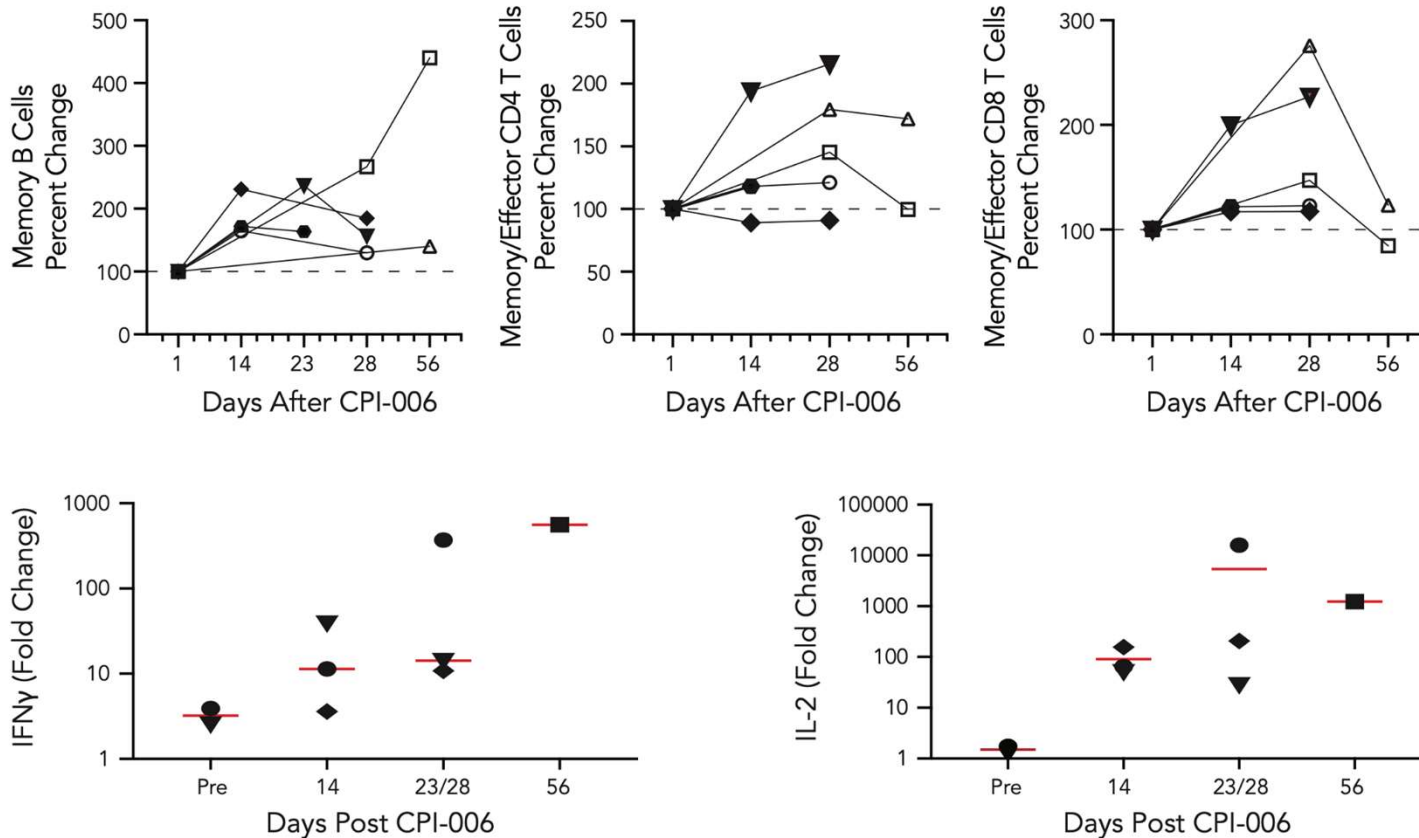
ANTI-VIRAL ANTIBODY RESPONSES ARE POLYCLONAL & POLYSPECIFIC



Serum antibody binding to N-terminal domain (NTD), receptor binding domain (RBD) or the S1 and S2 Spike subunits

Broad spectrum IgG activity to all subdomains, with IgM antibodies preferentially reacting with the RBD

INCREASED MEMORY & ANTIGEN SPECIFIC CELL RESPONSES



Increased frequency of peripheral memory B and memory/effector T cells measured by flow cytometry

- Memory B cells: $CD19^{POS}IgD^{NEG}CD27^{POS}$
- Memory/effector T cells $CD3^{POS}CD45RA^{NEG}$

PBMCs from patients treated with CPI-006 secrete IL-2 and IFN γ in response to SARS-CoV-2 membrane, nucleocapsid, and spike proteins

CONCLUSIONS

- CPI-006 activates B cells, leading to lymphocyte trafficking, plasmablast differentiation, and antigen specific antibody secretion.
- Humanized mice vaccinated with CPI-006 and SARS-CoV-2 spike protein produce antigen specific antibodies.
- Single doses of 0.3 mg/kg - 5 mg/kg CPI-006 are well tolerated in hospitalized COVID-19 patients with no drug related adverse events.
- Dose dependent increases occur in the titers of IgG, IgM to SARS-CoV-2 spike and receptor binding domain.
- IgG and IgM titers to SARS-CoV-2 are sustained over 84+ days beyond onset of symptoms.
- Mapping studies show CPI-006 potentiates polyclonal antibody responses in COVID-19 patients targeting multiple epitopes within the N terminus, RBD, S1, S2 of SARS-CoV-2.
- Increased peripheral memory B cell and memory/effector T cell populations were observed. T cells release IFN γ and IL-2 consistent with antigen specific Th1 immune response.
- CPI-006 may be a foundation for therapy of other infectious diseases. A randomized controlled phase 3 study in COVID-19 is planned.

ACKNOWLEDGMENTS & ADDITIONAL INFORMATION

We thank the patients, their families, and the physicians, nurses, and staff at Temple University Hospital, El Centro, and Mt Sinai for their participation in these clinical studies.

Additional preclinical, translational, and clinical details provided in medRxiv paper

Characterization and Phase I Trial of a B Cell Activating Anti-CD73 Antibody for the Immunotherapy of COVID-19

Stephen B Willingham, Gerard Criner, Craig Hill, Shenshen Hu, Jenny A Rudnick, Barbara Daine-Matsuoka, Jessica Hsieh, Haider Mashhedi, Andrew N Hotson, Joshua Brody, Thomas Marron, Emily Piccione, Joseph J Buggy, Suresh Mahabhashyam, William B Jones, Mehrdad Mobasher, Richard A Miller

doi: <https://doi.org/10.1101/2020.09.10.20191486>

