SARS-COV-2 IMMUNITY IN MODERATE TO SEVERE COVID-19 PATIENTS ENROLLED IN THE PRAGMATIC, ADAPTIVE CO-VIC COVID-19 TREATMENT STUDY

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CO-VIC
COVID VICTORY STUDY

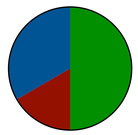
BACKGROUND

- **Clinical COVID-19 outcome is likely dependent on the degree of immune dysregulation, development of effective anti-viral immunity, and limited SARS-CoV-2 induced immunopathology.**
- **Current therapeutic strategies are focused on anti-viral and/or anti-inflammatory treatments. These therapeutics may differentially impact the development of SARS-CoV-2 specific immunity and clinical outcome.**

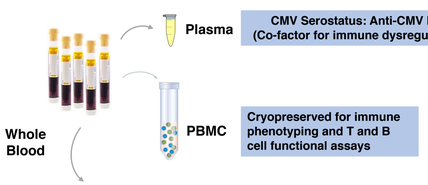
Objective: To describe cellular and humoral immunity in patients with moderate to severe COVID disease before and after COVID-19 treatment to determine correlates of improved clinical outcome.

METHODOLOGY

- **Upon informed consent, hospitalized COVID-19 patients with moderate to severe disease are enrolled in the CO-VIC treatment study and an immunologic substudy.**
  - ***Disease severity determined by 8 point ordinal scale***
- **Study arm assignment is based on eligibility and sequential order of available investigational therapeutics.**



Blood processing and biobanking



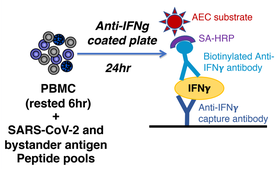
Direct ex vivo immune phenotyping by flow cytometry

T cells			B cells
CD3	CD57	*Activation and*	CD20
CD4	PD-1	*exhaustion markers*	CD19
CD8	Tim-3	*In CD3+CD4+ and*	CD10
CD27	CTLA-4	*CD3+CD8+ T cell subsets*	CD21
CD28			CD27

Boolean gated B cell subsets	CD19	CD20	CD27	CD10	CD21
Immature transitional	+	+	-	+	-/+
Resting memory	+	+	+	-	+
Naïve	+	+	-	-	+
Activated memory	+	+	+	-	-
TLM	+	+	-	-	-
Plasma	+	-	+	-	-

Functional Assays

T Cell ELISPOT



B Cell ELISPOT

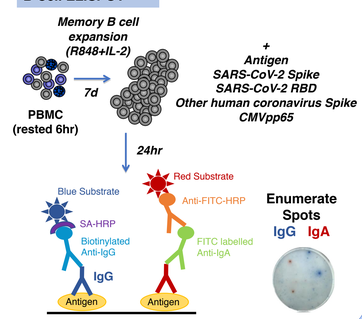


Table 1: CO-VIC participant demographics and disease severity

	Clinical Standard of Care	Baricitinib	Hydroxychloroquine
N	6	4	2
Sex (M/F)	3/3	3/1	1/1
Age in Years, median (IQR)	47 (39-51)	54.5 (54-55)	82 (79-85)
Disease (Moderate/Severe)[a]	5/1	3/1	1/1

[a]Categorized based on WHO defined 8 point ordinal scale. Moderate <=4; Severe 5-7

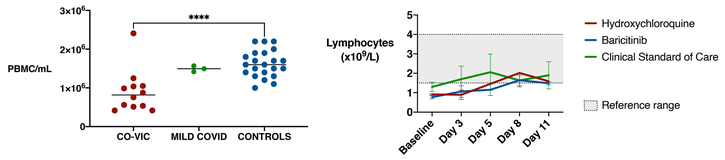


Figure 1: Low PBMC recovery in hospitalized COVID-19 patients is due to marked lymphopenia which is slow to recover

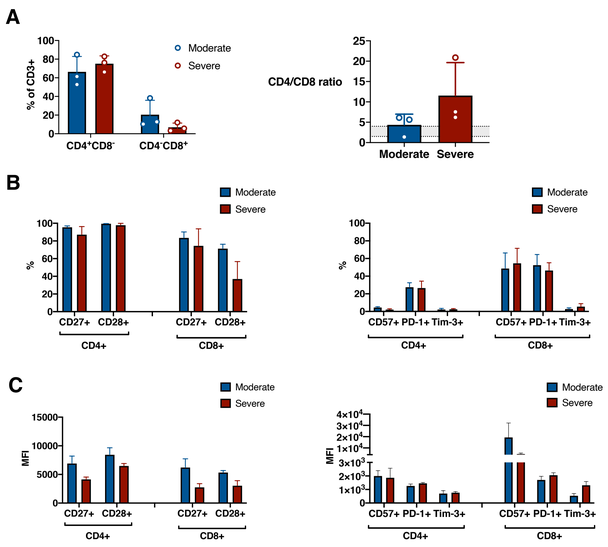


Figure 2: Hospitalized COVID-19 individuals have decreased CD8+ T lymphocytes (A) which frequently express inhibitory PD1 and senescence CD57 markers (B). Severe COVID-19 patients have lower expression levels of activation markers (C).

- **Hospitalized COVID-19 patients have marked lymphopenia at time of hospitalization, largely due to decreased CD8+ T cells**
- **Individuals with severe COVID-19 show increased frequencies of dysfunctional B cells**
- **There is a reversal of T cell exhaustion is with COVID-19 recovery**
- **SARS-CoV-2 specific T cell responses across major structural proteins are present in hospitalized patients and increase with treatment**
- **Ongoing studies aimed at the comprehensive characterization of global and SARS-CoV-2 cellular and humoral immunity in COVID-19 patients and relationship to viral persistence, disease severity and outcome, will provide important information on the immune response to SARS-CoV-2 and immune correlates of disease outcome.**

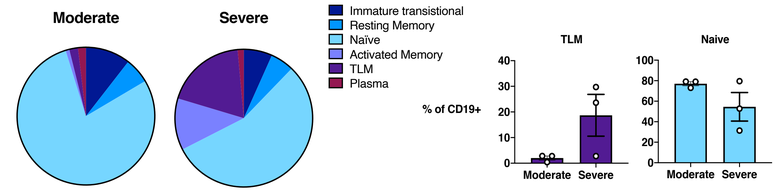


Figure 3: Individuals with severe COVID-19 disease have higher levels of dysfunctional tissue-like memory B cells

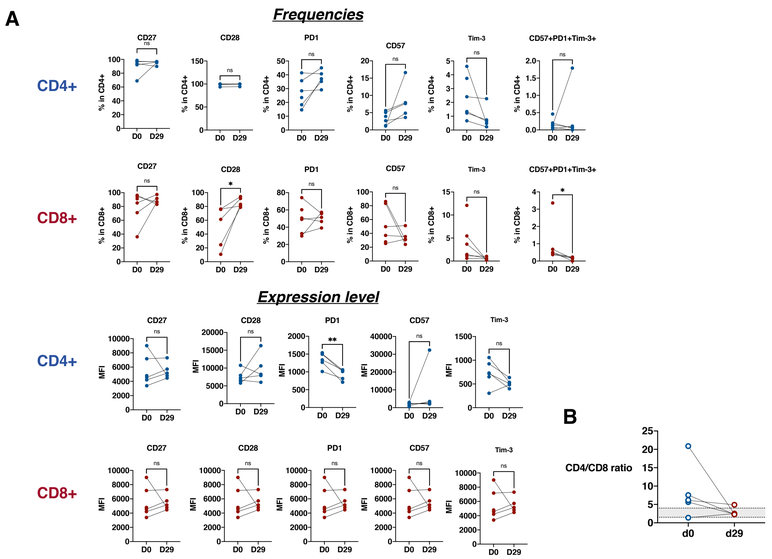


Figure 4: A) COVID-19 recovery is associated with an increased frequency of CD28⁺ and decreased frequency of CD57⁺PD1⁺Tim-3⁺ CD8⁺ T cells and decreased expression of PD-1 on CD4⁺ T cells. B) CD8+ T cells increase with recovery.

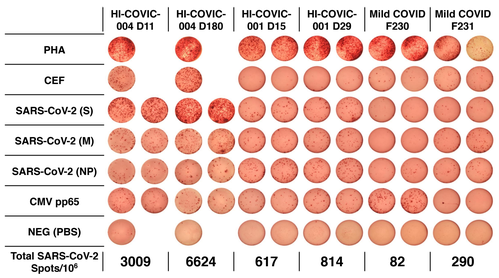


Figure 5: Hospitalized COVID-19 patients have SARS-CoV-2 spike, nucleoprotein and membrane specific IFNγ producing T cells that increase through the course of treatment

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