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ORIGINAL RESEARCH

# Post-Acute SARS-CoV-2 Symptoms are Fewer, Less Intense Over Time in People Treated with Mono-Clonal Antibodies for Acute Infection

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**Introduction:** Many with post-acute SARS-CoV-2 (PASC) have persistent symptoms impacting physical and cognitive function, decreased health and health-related life quality. Monoclonal antibody (mAb) treatment was available to acutely infected patients which might improve these outcomes.

**Purpose:** To compare patient perception of PASC symptoms for those receiving bamlanivimab or casirivimab and imdevimab (mAbs) to those not receiving this treatment (non-mAbs). To compare changes between these groups in symptoms, function and quality of life over a 6-month follow-up.

**Patients and Methods:** Consented adults >28 days post-infection with positive SARS-CoV-2 qPCR or antigen test and SARS-CoV-2 infection between March of 2020 and July of 2022 were enrolled. This prospective, repeated measure observational study reports baseline through 6-month follow-up. Extensive sociodemographic data, detailed medical history, COVID-19 symptom history, and standardized measures of well-being, depression, anxiety, stigma, cognition, symptom assessment, distress, and health status were collected.

**Results:** 323 participants [101 mAb, 221 non-mAb, 52.7±15.5 years, 47.7% male, body mass index (BMI) 31.4±8.4] were analyzed. Fewer symptoms at baseline were reported in mAb versus non-mAb participants (1.06±1.31 vs 1.78±2.15, respectively p=0.0177) 6 months: (0.911±1.276 mAb vs.1.75±2.22 non-mAb, p=0.0427). Both groups showed significant within-group decreases in symptom number (52 to 21 mAb, 126 to 63 non-mAb) and symptom burden (p=0.0088 mAb, p<0.00001 non-mAb). mAb patients had significantly shorter infection-to-baseline interval (days) (120.4±55.3 mAb vs 194.0±89.3 non-mAb, p<0.00001); less frequent history of myocardial infarction (0.0 vs 3.9%, p=0.0464); headache (2.0% vs.11.8%, p=0.0046), rash (3.1% vs 9.9%, p=0.0377), and miscellaneous muscle complaints (2.0% vs 12.3%, p=0.0035), plus significantly better 6-month mood. (2.2% vs 13.2%, p=0.0390).

**Conclusion:** mAb treated participants had reduced symptom burden and consistently reported fewer symptoms than non-mAb at all time points despite less time since acute illness. Both groups reported a statistically significant decrease in symptoms by 6-month visit with no statistically significant differences between them at follow-up.

**Keywords:** monoclonal antibodies, patient-reported outcomes, symptom burden, recovery, COVID-19

## Introduction

Many with post-acute SARS-CoV-2 (PASC) have persistent symptoms impacting physical and cognitive function, decreased health and health-related life quality, and is of global concern.[1–4] Monoclonal antibody (mAb) treatment was available in the early phase of the pandemic starting in 2020 to treat acutely infected patients to improve survival as well as possible PASC sequelae.[5]

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PASC is common (1 in 5, 20%), often chronic, multi-system and difficult to treat.[1–3] The study of PASC is complicated by varying definitions of the syndrome itself.[6] The United States Center for Disease Control (CDC) defines post-SARS-CoV-2 conditions as "a wide range of new, returning, or ongoing health problems people can experience four or more weeks after first being infected with the virus that causes SARS-CoV-2".[7] Severe infection or overt symptomatology are not necessary for the development of post-SARS-CoV-2 symptom persistence. Clinically significant symptoms can persist for weeks to months.[8–13] The World Health Organization (WHO) has also attempted to define "long COVID" though their definition has come under critique and has not been universally adopted.[14,15]

Research in this area becomes difficult as there may be limitations to generalizability because of definitional ambiguity, lack of precision about which symptoms are attributable to SARS-CoV-2 and their onset; and methods for collecting data. These factors when combined may lead to under or over representation of affected populations.[15–18] Even conservative estimates suggest millions of patients may require additional medical support to fully return to their pre-COVID functioning, well-being, quality of life, and valued life activities.[19]

A significant clinical problem is that published data have not included much behavioral data or patient perceptions of the impact of symptoms in large clinical databases. We believe that these types of data, when combined with natural history, clinical profile, standardized, valid patient self-reports, biosignatures, and lingering symptomatology, could help identify risk factors and inform intervention strategies.

Efforts continue to understand PASC prevention, recovery trajectory and factors leading to successful resolution of symptoms.[5] One potentially powerful influence on the natural history of SARS-CoV-2 is its treatment. We attempted to assess the use of monoclonal antibody (mAb) treatment efficacy and its effects on SARS-CoV-2 acute infection illness trajectory, resolution and possible impact of PASC. mAb have been well described for reducing severity of early variants (eg, delta, omicron BM but not omicron BQ).[20] What remains to be answered is how frequently do patients who received mAb experience PASC; and which symptoms persist. Further, does symptom severity and resolution appear similar to patients who did not receive mAb treatment.

This prospective, natural history study comprehensively assessed the sequelae and recovery of patients who visited a health system facility for treatment of acute SARS-CoV-2 and received mAbs as compared with those who received standard of care for acute SARS-CoV-2. This research study set out to determine whether patients treated with monoclonal antibody for acute SARS-CoV-2 infection have less symptom burden, intensity/severity and duration of newly acquired findings post-infection. Hospitalization, clinical status, laboratory findings, symptoms, patient functioning, patient reported outcomes measures (PROs), health behavior change, and health-related quality of life (HRQL) data were collected. The aim of the study was to compare patient perception of PASC symptoms for those receiving bamlanivimab or casirivimab and imdevimab (mAbs) to those not receiving this treatment (no-mAbs); and to compare changes between these groups in symptoms, function and quality of life over a 6-month follow-up period.

# Materials and Methods

## Design

This was a prospective study designed to collect in-depth data regarding cognitive, clinical, and patient-reported outcomes of patients who tested positive for SARS-CoV-2 between March 2020 and July 2022.

## Participants

Patients were contacted for study participation based on the search of our electronic medical record system for those who had tested positive for SARS-CoV-2 (diagnosed with a positive qPCR test or an antigen test) in one of our outpatient or inpatient facilities within our healthcare system. Further characterization of health system COVID population and treatment response can be found in our previous publications.[21–25] Eligible enrollees were required to have been at least 28 days post-SARS-CoV-2 diagnosis (no limit to participation was placed on time since time of acute SARS-CoV-2 or treatment), be at least 18 years of age and willing and able to give an informed consent. All patients regardless of current symptomology were invited to participate. Translation services were also utilized to ensure the inclusivity of our SARS-CoV-2 study participation and follow-up. Written consent was obtained for in-person patients and verbal consent

was obtained for virtual patients prior to participation. Both methods of consent and the study protocol received IRB approval through Inova Health System. Ethical review and approval for study conduct was also obtained from Western IRB prior to study initiation per national and international standards, including the Declaration of Helsinki. This study adhered to guidelines for reporting observational studies using routinely collected health data.

Patients who were treated for SARS-CoV-2 were called and invited to participate in the study in-person at our clinic or remotely (by phone or through online video conferencing). Baseline was first study contact and assessment of outcomes, not predicated on timing of acute illness or treatment. All participants were asked to verbally answer specifically curated questions about their social and medical history, details of their SARS-CoV-2 illness (eg duration and severity of illness, the use of healthcare during the illness, etc) and current exercise habits.

To assess PASC symptom burden, participants were verbally asked if they had any new symptoms that were not present prior to SARS-CoV-2 infection and were present around the time of the initial visit. Participants were not provided with a list of common symptoms from which to choose. Due to the variability in responses, symptoms were reviewed by investigators and categories were created based on the most commonly reported symptoms (See Supplemental Table 1). Symptoms were then reviewed by our study physician and placed into the appropriate categories.

## Main Measures

Our assessments included: 1) objective physical assessment measures, 2) standardized patient reported outcome (PRO) questionnaires, and 3) cognitive assessments. Because not all patients came on site due to ongoing concerns about contagion, we were not able to capture objective measures on everyone. Nonetheless, the virtual environment did permit interviews and completion of PROs and cognitive assessments.

### Physical & Functional Assessments

Our definition of function follows the International Classification of Functioning, Disability and Health (ICF) (ie "a dynamic interaction between her or his health conditions, environmental factors, and personal factors."[25] For the in-person arm of the study, physical assessments were performed at the outpatient clinic including a physical examination, vital signs, a two-minute walking distance (TMWD) test, and grip strength. See detailed descriptions of these measures in our prior study publication methodology and in assessment validation studies.[25,26–30]

### Patient-Reported Outcomes (PROs)

We used PRO instruments to assess various aspects of patients' well-being using standardized and validated instruments. Routinely, standardized measures of life satisfaction and fatigue (FACIT-F), depression (PHQ9), COVID cognition, symptom burden (ESAS), anxiety (GAD7), stigma (Stigma questionnaire), NCCN distress (Distress Thermometer), and health-related quality of life (EQ5D) measures were administered to the study participants electronically via a specifically designed web page, in-person, or over the phone.[31–41] Each of the eight PRO instruments is described in detail in our prior publication and in measure standardization and validation reporting[25,31–41]

### Cognitive Assessments

All subjects were asked to complete a battery of cognitive performance tests administered by a trained professional. Cognitive domains of processing speed and executive function (eg, working memory, inhibition, cognitive flexibility, and visual-spatial function/perceptual reasoning), were assessed with hand-selected subtests from the Delis Kaplan Executive Function System (DKEFS) and Wechsler Adult Intelligence Scale- Fourth Edition (WAIS-IV) cognitive batteries.[42,43] Tests were conducted online or in-person, depending on patient's preference and availability. Specifically, the CWIT, Arithmetic, and Matrix Reasoning tests could be conducted on-line, or in-person and the Coding and Symbol Search tests could only be conducted in-person. Individual tests and overall battery are described further in Supplement 1 of our prior publication.

## Statistical Analysis

SAS 9.4 (SAS Institute, Cary, NC) and Jamovi 3.2.1 were used for all analyses. Incomplete records were excluded from analysis. Parameters were compared between groups using chi-square or Kruskal–Wallis tests for categorical or continuous parameters, respectively. Two-sided alpha <0.05 was considered statistically significant. Cases lost to follow-up longitudinally were analyzed cross-sectionally for timepoints collected and excluded from time point comparisons. The study database was reviewed for variable completion and consistency with hard-copy case report forms confirmed prior to data analysis. Truly missing data collection variables were marked "unknown" for that instance of recording and excluded from analysis.

# Results

A total of 6865 patients were seen within the health system for SARS-CoV-2 within the study time frame of recruitment.[36] Of those capable of providing informed consent, reachable by the research team and willing to participate in our prospective follow-up study, there were 102 participants treated with mAb and 221 participants who did not receive mAb treatment enrolled in the study (Table 1). Participants who received mAb treatment were slightly older (55.7 ± 14.1 vs 51.3 ± 15.9, p=0.0184), were more likely to be married [56 (56.6%) vs.101 (52.6%), p=0.0203], and more likely to have hypertension [50 (49.0%) vs 77 (34.8%), p=0.0153] and hyperlipidemia [51 (50.0%) vs 68 (30.8%), p=0.0009]. Non-mAb participants were more likely to have arthritis [21 (20.6%) vs 33 (14.9%), p=0.0368] and chronic

**Table 1** Full Cohort Comparison of mAb versus Non-mAb Study Participants

| | mAb (102) Mean ±SD or N (%) | Non-mAb (221) Mean ±SD or N (%) | p-values |
|---|---|---|---|
| Age, years | 55.7 ± 14.1 | 51.3 ± 15.9 | 0.0184* |
| Male | 54 (52.9%) | 99 (44.8%) | 0.1963 |
| Non-Hispanic white | 50 (49.0%) | 102 (46.6%) | 0.6830 |
| Non-Hispanic black | 19 (18.6%) | 38 (17.4%) | 0.7806 |
| Hispanic | 18 (17.6%) | 59 (26.9%) | 0.0694 |
| Asian | 10 (9.8%) | 16 (7.3%) | 0.4450 |
| Other race | 1 (1.0%) | 0 (0.0%) | 0.2622 |
| Employed | 4 (3.9%) | 4 (1.8%) | 0.9707 |
| College degree | 65 (64.4%) | 127 (64.1%) | 0.5206 |
| Married | 56 (56.6%) | 101 (52.6%) | 0.0203* |
| Group living | 2 (2.0%) | 9 (4.7%) | 0.2552 |
| Body Mass Index | 32.7 ± 9.3 | 30.5 ± 7.8 | 0.1337 |
| Exercise ≥30 min ≥3/week | 54 (55.1%) | 100 (50.0%) | 0.4077 |
| Anxiety | 18 (17.6%) | 21 (9.5%) | 0.9573 |
| Arthritis | 21 (20.6%) | 33 (14.9%) | 0.0368* |
| Asthma | 8 (7.8%) | 14 (6.3%) | 0.2054 |
| Coronary artery disease | 20 (19.6%) | 32 (14.5%) | 0.6170 |
| Cancer | 3 (2.9%) | 8 (3.6%) | 0.2437 |

(*Continued*)

**Table 1** (Continued).

| | mAb (102) Mean ±SD or N (%) | Non-mAb (221) Mean ±SD or N (%) | p-values |
|---|---|---|---|
| Congestive heart failure | 2 (2.0%) | 19 (8.6%) | 0.7546 |
| Chronic kidney disease | 6 (5.9%) | 22 (10.0%) | 0.0245* |
| Chronic liver disease | 18 (17.6%) | 21 (9.5%) | 0.2266 |
| Chronic obstructive pulmonary disease | 7 (6.9%) | 8 (3.6%) | 0.1980 |
| Depression | 16 (15.7%) | 36 (16.3%) | 0.8909 |
| Diabetes | 23 (22.5%) | 51 (23.1%) | 0.9164 |
| Gastroesophageal reflux disease | 16 (15.7%) | 40 (18.1%) | 0.5944 |
| Hypertension | 50 (49.0%) | 77 (34.8%) | 0.0153* |
| Hyperlipidemia | 51 (50.0%) | 68 (30.8%) | 0.0009 ‡ |
| Non-alcoholic fatty liver disease | 6 (5.9%) | 15 (6.8%) | 0.7591 |
| Sleep apnea | 17 (16.7%) | 22 (10.0%) | 0.0853 |
| Stroke | 3 (2.9%) | 11 (5.0%) | 0.4035 |
| Thyroid disease | 15 (14.7%) | 27 (12.2%) | 0.5365 |
| Time since COVID diagnosis, days | 120.5 ± 55.1 | 195.6 ± 88.9 | 0.0000 ‡ |
| Received treatment for COVID | 85 (92.4%) | 94 (57.3%) | 0.0000 ‡ |
| Received antivirals | 4 (4.0%) | 25 (12.3%) | 0.0226* |
| Number of days sick with COVID | 16.8 ± 20.4 | 24.5 ± 31.2 | 0.0396* |
| Needed oxygen support (including at home) | 14 (13.9%) | 69 (33.7%) | 0.0002 ‡ |
| Was on a ventilator | 0 (0.0%) | 13 (6.3%) | 0.0097 † |
| Had no difficulties during COVID | 24 (23.8%) | 43 (21.0%) | 0.5794 |
| Less exercise/activity PASC | 37 (37.4%) | 90 (46.4%) | 0.1407 |
| Worse diet/eating habits PASC | 19 (19.4%) | 38 (19.5%) | 0.9838 |
| Worse weight PASC | 19 (19.6%) | 52 (27.5%) | 0.1419 |
| Worse sleep PASC | 35 (37.2%) | 72 (38.1%) | 0.8881 |

**Notes**: Significant difference level: *.05, †.01, ‡.001.
**Abbreviations**: N, number of subjects; SD, standard deviation; %, percent; mAb, monoclonal antibody treatment; COVID, SARS-CoV-2; PASC, post-acute SARS-CoV-2.

kidney disease [6 (5.9%) vs 22 (10.0%), p=0.0245] (Table 1). Participants who had received mAb had fewer sick days with SARS-CoV-2 and required less home oxygen.

## Comparison of Symptoms of Those Treated with mAb versus Non-mAb

Descriptions of symptom categories are in Supplemental Table 1. At baseline, participants treated with mAb have fewer symptoms, no cases of acute myocardial infarction, and significantly less headache, rash, and various muscle complaints (Table 2). By 1 month, mAb participants have completely resolved complaints of smell and other neurological symptoms- a significant difference from the non-mAb cohort (Table 3). At 3 months, the two cohorts do not appear

**Table 2** Patient Reported Outcomes (PROs) of Non-mAb and mAb Treated PASC Study Participants Over Time

| Non-mAb | Baseline (B) Mean ±SD | Month 6 (M6) Mean ±SD | B-M6 p-value |
|---|---|---|---|
| FACIT-F Physical Well-being (0–28, higher better) | 22.4 ± 5.4 | 22.7 ± 5.5 | 0.4182 |
| FACIT-F Emotional Well-being (0–24, higher better) | 18.5 ± 5.2 | 19.5 ± 4.3 | 0.0802 |
| FACIT-F Social Well-being (0–28, higher better) | 18.5 ± 6.3 | 19.6 ± 6.0 | 0.5892 |
| FACIT-F Functional Well-being (0–28, higher better) | 18.0 ± 6.3 | 19.0 ± 6.4 | 0.0124* |
| Fatigue Scale (0–52, higher better) | 36.4 ± 12.1 | 38.0 ± 1.7 | 0.0513 |
| FACIT-F Total (0–160, higher better) | 113.7 ± 28.1 | 118.8 ± 0.4 | 0.0142* |
| Patient Health Questionnaire-9 (27–0, higher worse) | 5.73 ± 5.91 | 5.08 ± 0.55 | 0.1635 |
| Post SARS-CoV-2 Cognitive Questions (1–5, higher better) | 3.79 ± 0.89 | 3.77 ± 0.87 | 0.9140 |
| EQ5D Index Score (0–1, higher better) | 0.784 ± 0.193 | 0.853 ± 0.137 | 0.0002 ‡ |
| EQ5D Health Score (0–100, higher better) | 74.8 ± 30.7 | 78.8 ± 16.3 | 0.0043 † |
| **mAb** | **Baseline (B) Mean ±SD** | **Month 6 (M6) Mean ±SD** | **B-M6 p-values** |
| FACIT-F Physical Well-being (0–28, higher better) | 23.8 ± 5.2 | 24.5 ± 3.6 | 0.8738 |
| FACIT-F Emotional Well-being (0–24, higher better) | 19.9 ± 4.2 | 20.4 ± 3.6 | 0.9160 |
| FACIT-F Social Well-being (0–28, higher better) | 19.8 ± 5.8 | 18.8 ± 6.7 | 0.9018 |
| FACIT-F Functional Well-being (0–28, higher better) | 19.4 ± 5.3 | 19.8 ± 4.3 | 0.8005 |
| Fatigue Scale (0–52, higher better) | 39.0 ± 11.2 | 40.3 ± 9.4 | 0.5449 |
| FACIT-F Total (0–160, higher better) | 121.6 ± 26.9 | 123.7 ± 18.0 | 0.8700 |
| Patient Health Questionnaire-9 (27–0, higher worse) | 4.95 ± 5.32 | 4.05 ± 4.55 | 0.9946 |
| Post SARS-CoV-2 Cognitive Questions (1–5, higher better) | 3.97 ± 0.88 | 3.79 ± 0.90 | 0.1882 |
| EQ5D Index Score (0–1, higher better) | 0.842 ± 0.157 | 0.838 ± 0.146 | 0.4962 |
| EQ5D Health Score (0–100, higher better) | 76.1 ± 19.9 | 71.9 ± 22.1 | 0.1030 |

**Notes**: Significant difference level: *.05, †.01, ‡.001.
**Abbreviations**: PASC, post-acute SARS-CoV-2; mAb, monoclonal antibody treatment; non-mAb, no mAb received; B-M6, baseline to 6-month comparison; SD, standard deviation; FACIT-F, Functional Assessment of Chronic Illness Therapy- Fatigue; EQ5D, EuroQOL-5D health status measure.

significantly different in symptom burden or category. By 6 months, mAb participants once more show significantly lower symptom burden, as well as decreased mood symptom reporting (Table 3). Both mAb and non-mAb cohorts have significant reduction in symptoms over 6 months (mAb p=0.0088 vs non-mAb p=0.00001). However, non-mAb participants still have lingering symptom reporting in all categories, while mAb participant symptom reporting has fully resolved in 8 categories- including full resolution of severe fatigue reporting- and 4 categories where symptoms were never initially reported. [See Table 3 for additional symptom burden detail.]

## PROs in mAb Treated versus Non-mAb Treated Participants Over Time

Comparing baseline values of participants who were mAb and non-mAb treated for statistically significant differences, patients receiving mAb had higher burden of symptoms on emotional well-being (ESAS, p=0.0334), less anxiety (GAD-7, p=0.0342), better overall health on EQ-5D (p=0.0121), and fewer PASC symptoms (Table 4). In general, while the

**Table 3** Baseline Comparison of Symptoms Over Time by mAb and Non-mAb[a]

| | | Baseline (B) | | | Month 6 (M6) | |
|---|---|---|---|---|---|---|
| | mAb Mean ±SD or N (%) | Non-mAb Mean ±SD or N (%) | p-values | mAb Mean ±SD or N (%) | Non-mAb Mean ±SD or N (%) | p-values |
| Number of Symptoms | 1.06 ± 1.31 | 1.78 ± 2.15 | 0.0177* | 0.911 ± 1.276 | 1.75 ± 2.22 | 0.0427* |
| B-M6 Symptom Decrease | | | | −0.333 ± 0.127 p=0.0088 † | −0.330 ± 0.069 p<0.0001 ‡ | 0.8293 |
| Any Symptoms | 52 (53.1%) | 126 (62.1%) | 0.1363 | 21 (46.7%) | 63 (59.4%) | 0.1486 |
| Acute Myocardial Infarction | 0 (0.0%) | 8 (3.9%) | 0.0464* | 0 (0.0%) | 4 (3.8%) | 0.1866 |
| Appetite | 1 (1.0%) | 6 (3.0%) | 0.2965 | 0 (0.0%) | 1 (0.9%) | 0.5133 |
| Bowel | 0 (0.0%) | 4 (2.0%) | 0.1618 | 0 (0.0%) | 2 (1.9%) | 0.3536 |
| Confusion | 1 (1.0%) | 3 (1.5%) | 0.7454 | 0 (0.0%) | 1 (0.9%) | 0.5133 |
| Cough | 6 (6.1%) | 6 (3.0%) | 0.1882 | 2 (4.4%) | 3 (2.8%) | 0.6121 |
| Difficulty Sleeping | 4 (4.1%) | 6 (3.0%) | 0.6095 | 1 (2.2%) | 3 (2.8%) | 0.8315 |
| Dizziness | 1 (1.0%) | 2 (1.0%) | 0.9770 | 1 (2.2%) | 2 (1.9%) | 0.8925 |
| Fatigue | 22 (22.4%) | 39 (19.2%) | 0.5127 | 9 (20.0%) | 23 (21.7%) | 0.8153 |
| Mild Fatigue | 8 (38.1%) | 16 (41.0%) | 0.8251 | 1 (11.1%) | 9 (40.9%) | 0.1072 |
| Moderate Fatigue | 10 (47.6%) | 17 (43.6%) | 0.7648 | 4 (44.4%) | 8 (36.4%) | 0.6750 |
| Severe Fatigue | 3 (14.3%) | 6 (15.4%) | 0.9095 | 0 (0.0%) | 4 (18.2%) | 0.1705 |
| Fever | 1 (1.0%) | 2 (1.0%) | 0.9770 | 1 (2.2%) | 1 (0.9%) | 0.5295 |
| Headache | 2 (2.0%) | 24 (11.8%) | 0.0046 † | 1 (2.2%) | 9 (8.5%) | 0.1566 |
| Heart Rate | 1 (1.0%) | 6 (3.0%) | 0.2965 | 0 (0.0%) | 1 (0.9%) | 0.5133 |
| Heartburn | 0 (0.0%) | 4 (2.0%) | 0.1618 | 0 (0.0%) | 2 (1.9%) | 0.3536 |
| Joint Pain | 3 (3.1%) | 8 (3.9%) | 0.7031 | 1 (2.2%) | 5 (4.7%) | 0.4729 |
| Smell | 7 (7.1%) | 24 (11.8%) | 0.2107 | 2 (4.4%) | 11 (10.4%) | 0.2345 |
| Memory | 11 (11.2%) | 38 (18.7%) | 0.0989 | 6 (13.3%) | 23 (21.7%) | 0.2327 |
| Muscle Weakness | 2 (2.0%) | 4 (2.0%) | 0.9674 | 1 (2.2%) | 2 (1.9%) | 0.8925 |
| Myalgia | 1 (1.0%) | 2 (1.0%) | 0.9770 | 0 (0.0%) | 2 (1.9%) | 0.3536 |
| Nasal | 2 (2.0%) | 2 (1.0%) | 0.4536 | 2 (4.4%) | 4 (3.8%) | 0.8469 |
| Nausea | 3 (3.1%) | 4 (2.0%) | 0.5563 | 0 (0.0%) | 6 (5.7%) | 0.1034 |
| Other Cardiac | 4 (4.1%) | 11 (5.4%) | 0.6174 | 0 (0.0%) | 5 (4.7%) | 0.1384 |
| Other Genito-urinary | 2 (2.0%) | 10 (4.9%) | 0.2306 | 2 (4.4%) | 11 (10.4%) | 0.2345 |
| Other Miscellany | 6 (6.1%) | 26 (12.8%) | 0.0779 | 2 (4.4%) | 8 (7.5%) | 0.4831 |
| Other Mood | 3 (3.1%) | 17 (8.4%) | 0.0829 | 1 (2.2%) | 14 (13.2%) | 0.0390* |
| Other Muscle | 2 (2.0%) | 25 (12.3%) | 0.0035 † | 3 (6.7%) | 12 (11.3%) | 0.3818 |

(*Continued*)

**Table 3** (Continued).

| | | Baseline (B) | | | Month 6 (M6) | |
|---|---|---|---|---|---|---|
| | mAb Mean ±SD or N (%) | Non-mAb Mean ±SD or N (%) | p-values | mAb Mean ±SD or N (%) | Non-mAb Mean ±SD or N (%) | p-values |
| Other Neurological | 6 (6.1%) | 25 (12.3%) | 0.0976 | 0 (0.0%) | 2 (1.9%) | 0.3536 |
| Pruritis | 1 (1.0%) | 3 (1.5%) | 0.7454 | 1 (2.2%) | 11 (10.4%) | 0.0901 |
| Rash | 3 (3.1%) | 20 (9.9%) | 0.0377* | 5 (11.1%) | 16 (15.1%) | 0.5176 |
| Shortness of Breath | 9 (9.2%) | 28 (13.8%) | 0.2538 | 0 (0.0%) | 1 (0.9%) | 0.5133 |
| Sore Throat | 0 (0.0%) | 4 (2.0%) | 0.1618 | 0.911 ± 1.276 | 1.75 ± 2.22 | 0.0427 |

**Notes**: [a]See Supplemental Table 1 for Symptom Category Descriptions; Significant difference level: * 0.05, † 0.01, ‡ 0.001.
**Abbreviations**: mAb, monoclonal antibody treatment; non-mAb, no mAb received; B-M6, change over time between baseline and 6 months, N, number of subjects; SD, standard deviation; %, percent.

**Table 4** Timepoints of Comparison of mAb and Non-mAb Cohorts by Patient-Reported Outcomes

| | | Baseline | | | Month 6 | |
|---|---|---|---|---|---|---|
| | mAb Mean ±SD | Non-mAb Mean ±SD | p-value | mAb Mean ±SD | Non-mAb Mean ±SD | p-value |
| 2 Minute Walk Distance | −5.85 ± 27.23 | 4.77 ± 25.16 | 0.3999 | −4.28 ± 16.87 | 3.20 ± 15.94 | 0.5952 |
| Grip Strength (kilogram) | −25.2 ± 15.2 | −14.0 ± 25.9 | 0.1382 | −22.1 ± 24.2 | −12.7 ± 21.8 | 0.5340 |
| FACIT-F Physical Well-being | 23.8 ± 5.2 | 22.4 ± 5.4 | 0.0679 | 24.5 ± 3.6 | 22.7 ± 5.5 | 0.2326 |
| FACIT-F Emotional Well-being | 19.9 ± 4.2 | 18.5 ± 5.2 | 0.1004 | 20.4 ± 3.6 | 19.5 ± 4.3 | 0.5129 |
| FACIT-F Social Well-being | 19.8 ± 5.8 | 18.5 ± 6.3 | 0.2891 | 18.8 ± 6.7 | 19.6 ± 6.0 | 0.6968 |
| FACIT-F Functional Well-being | 19.4 ± 5.3 | 18.0 ± 6.3 | 0.2206 | 19.8 ± 4.3 | 19.0 ± 6.4 | 0.8477 |
| FACIT-F Fatigue Scale | 39.0 ± 11.2 | 36.4 ± 12.1 | 0.3142 | 40.3 ± 9.4 | 38.0 ± 11.7 | 0.6581 |
| FACIT-F Total | 121.6 ± 26.9 | 113.7 ± 28.1 | 0.1008 | 123.7 ± 18.0 | 118.8 ± 28.4 | 0.8605 |
| Patient Health Questionnaire-9 | 4.95 ± 5.32 | 5.73 ± 5.91 | 0.6417 | 4.05 ± 4.55 | 5.08 ± 5.55 | 0.5735 |
| Post SARS-CoV-2 Cognitive Questions | 3.97 ± 0.88 | 3.79 ± 0.89 | 0.1838 | 3.79 ± 0.90 | 3.77 ± 0.87 | 0.9353 |
| Edmonton Symptom Assessment- Physical | 1.77 ± 1.65 | 2.06 ± 1.85 | 0.4797 | | | |
| Edmonton Symptom Assessment- Emotional | 1.02 ± 1.55 | 2.30 ± 2.79 | 0.0334* | | | |
| Edmonton Symptom Assessment- Total | 1.60 ± 1.60 | 2.26 ± 1.87 | 0.0868 | | | |
| Generalized Anxiety Disorder-7 | 1.55 ± 3.31 | 3.49 ± 4.26 | 0.0342* | | | |
| Stigma | 4.57 ± 3.98 | 4.98 ± 4.37 | 0.7081 | | | |
| Distress Thermometer | 1.82 ± 2.38 | 2.85 ± 2.93 | 0.1407 | | | |
| EQ5D Index Score | 0.842 ± 0.157 | 0.784 ± 0.193 | 0.0121 † | 0.838 ± 0.146 | 0.853 ± 0.137 | 0.6679 |
| EQ5D Health Score | 76.1 ± 19.9 | 74.8 ± 30.7 | 0.2172 | 71.9 ± 22.1 | 78.8 ± 16.3 | 0.1269 |

**Notes**: Significant difference level: * 05, †.01.
**Abbreviations**: mAb, monoclonal antibody treatment; non-mAb, no mAb received; SD, standard deviation; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; EQ5D, EuroQOL-5D health status measure.

majority of comparisons did not reach statistical significance, the mAb treated group had better raw scores for administered PROs. Overall, PRO score differences between mAb and non-mAb participants decrease over time and become more homogenous in nature over the 6-month follow-up period (Table 4). The mAb group does not change significantly from baseline to follow-up time points across 6 months of PROs (Table 2).

The non-mAb group, however, does show within-group changes between baseline and later timepoints (Table 2). Non-mAb participants show a decrease in PHQ9 depression reporting between baseline and 1 month (5.73 ± 5.91 vs 5.55 ± 5.76, p=0.0096), an increase in FACIT-F Emotional Well-being between baseline and 3 months (p=0.0032), FACIT-F Functional Well-being between baseline and 3 months (p=0.0120), and again between baseline and 6 months (p=0.0124), and overall FACIT-F Fatigue Score between baseline and 6 months (p=0.0142) (Table 2). Significant improvements in EQ-5D Index and Health Scores (p=0.0002 and p=0.0043, respectively) between baseline and 6 months also occur between baseline and 6 months (Table 2). EQ-5D index (p=0.0002) and health scores (p=0.0043) improved significantly only for non-mAb subjects at 6 months follow-up. Between baseline and 6 months in both cohorts, there was no improvement in 2MWT and minor, not statistically significant improvement in grip.

## Discussion

The SARS-CoV-2 pandemic has had a global impact, but the assessment of the impact of PASC is still evolving as is its treatment. This study attempted to contrast two treatments for SARS-CoV-2 during the first 18 months of the pandemic at our health facility; standard of care as compared with the use of monoclonal antibodies. This study indicates reduced symptom burden from use of mAb treatment. Symptoms improved over the period in which we studied the participants. Specifically, the patients that received mAb had better scores in all domains at baseline than those who did not receive mAb (non-mAb). This may be due to the non-mAb cohort having worse scores at baseline and hence their relatively greater improvement in scores, compared with the group receiving mAb. Numbers of participants reporting symptoms was also higher in the group not receiving mAbs.

Many studies have attempted to evaluate long COVID, but rates of PASC vary widely based on definition and method of data collection and vaccination status.[15,16] Free-response symptom reporting in the participants' own words was allowed in addition to checkboxes for major categories of symptoms already in-use in the AHA COVID-19 CVD registry study on-site and common SARS-CoV-2 symptoms per CDC guidance.[6,44] Our physician team and research coordinators met to discuss grouping of similar responses. In order to aid reproducibility and be fully transparent regarding any potential grouping bias, the resulting guidance including all free responses, are available in Supplemental Table 1. Anyone wishing to reproduce our grouping methodology can refer to these symptom groupings for reference. Many of the miscellany system symptom reporting could only be provided descriptively due to the small number of subjects reporting. We attempted to avoid bias by including all PASC symptoms reported to us within the grouping table. This observational study of the natural history of PASC took advantage of our ability to recruit participants who both had or had not received mAbs for early intervention treatment of COVID. This was not a randomized trial.

When we compared the outcomes of these two groups, we observed several notable differences (eg number of sick days, home oxygen, age, marital status, hypertension, hyperlipidemia, arthritis, and chronic kidney disease). These are interesting findings and suggest that early treatment of COVID-19, regardless of sex, age and hospitalization history may infer symptom reduction in a convenience sample of patients with PASC. Overall, our cohort does not carry as much pulmonary, cardiac, or kidney disease burden as reported by other studies. They did report significant symptomatology around general muscle concerns (weakness, aching), memory difficulties, changes in sense of smell, headache, and fatigue. The group that did not receive mAb had more headache, anosmia and a higher number of symptoms overall. The whole sample expressed substantial impact of these symptoms on quality of life on several indices. Participants who had received mAb treatment as part of their acute care reported less symptom burden, and life impact. Baseline results support other reports about the therapeutic benefit of mAb in reducing need for pulmonary support for infected people. Our group also reported that treatment with mAb was associated with reduced hospitalization.

The group who received mAb treatment as part of their acute COVID care had better baseline scores for physical function, cognitive performance, ESAS symptoms, anxiety and EQ-5D quality of life. This suggests that use of mAb treatment during acute care prior to high prevalence of solo product resistance may have contributed to improved PASC

physical and cognitive functioning and quality of life (QoL) and reduced symptom burden, including anxiety during the PASC stage. These differences were not sustained as significant differences between the groups over time. However, the group that received mAbs had higher scores among all the domains.

## Limitations

Participants were recruited from patients seen for SARS-CoV-2 at a large, regional health system, and agreed to participate, thus the sample may not accurately represent all patients with post-SARS-CoV-2 sequelae, which may be more imbalanced because this cohort was, on average >6 months since acute illness and may have self-selected for severity or persistence of symptoms. Only a fraction of patients seen by the health system were interested or otherwise eligible for inclusion. Patients who received mAb and agreed to participate in the study had a significantly shorter period between acute illness and participation yet had less symptom burden. A time post-acute infection analysis showed that those contacted further from their acute SARS-CoV-2 illness treated earlier in the pandemic and agreed to participate in the study were more likely to report long COVID symptoms. This study does not consider the wave or variant of SARS-CoV-2 infection, which has been shown in some research to be associated with likelihood of PASC.[15,24,45,46] Enrollment also ended prior to the prevalence of newer, high consequence strains and cannot speak to their relative rates of PASC.[47,48] This study also cannot speak to the phenomena of SARS-CoV-2 coinfections and their implications for PASC.[49]

While attrition remains a significant obstacle for all prospective studies, our study faced challenges due to varying COVID waves reducing participants' willingness to engage in follow up. When possible, we obtained data virtually, and were successful in this effort with respect to PROs, but not for objective clinical measures. Baseline symptom burden, as reported by patient recall not using a pre-specified checklist, was greater in people who did not receive mAb.

## Conclusion

Participants who received mAb treatment had reduced symptom burden and consistently reported fewer symptoms than non-mAb at all time points despite less time since acute illness. The use of mAbs is likely to contribute to improved physical and cognitive functioning and QoL and reduced symptom burden, including anxiety during the PASC stage. Both groups reported a statistically significant decrease in symptoms by 6-month visit. Encouragingly, the number of cases with symptom reporting and symptom severity continued to decrease over time indicating continued resolution.

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