# POST-ACUTE SEQUELAE OF SARS-COV-2 IN NON-HOSPITALIZED ACTIV-2 TRIAL PARTICIPANTS

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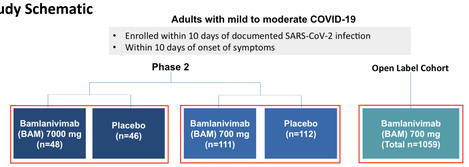
## BACKGROUND

- Many persons with COVID-19 experience clinical symptoms beyond acute infection, often termed "long COVID" or "Post-Acute Sequelae of SARS-CoV-2 infection (PASC)".
- Randomized COVID-19 trials provide opportunities to describe PASC-related symptom burden longitudinally and assess the impact of early use of antivirals on PASC prevalence.

## METHODS

- ACTIV-2 evaluates safety and efficacy of investigational agents for non-hospitalized adults with mild to moderate COVID-19 in a Phase 2/3 trial.

**Fig 1. Study Schematic**




- Participants completed an Acute Viral Illness 13-symptom daily diary from enrollment through Day 28. A long-term (LT) diary (14 additional symptoms) introduced after the study was underway was completed by a subset of individuals every 12 weeks (Fig 2).
- The primary PASC analysis outcome was whether or not a participant considered that they still had COVID symptoms, coded as "No Symptoms" versus "Symptoms Present".
- We report Week 24 findings for participants who received BAM 700mg in either Phase 2 or Open Label Cohort (Table 1).

**Fig 2. Schedule of Events**

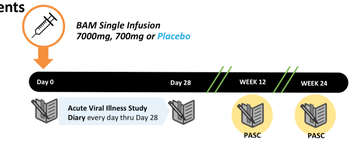



**Table 1. Baseline Characteristics**

| | 700mg BAM (n=543) |
|---|---|
| Age, median (Q1, Q3) yrs | 50 (40, 60) |
| Female sex, n (%) | 276 (51%) |
| Cis-gender, n (%) | 538 (99%) |
| Race, n (%)<br>Black or African American<br>White | <br>24 (4%)<br>462 (85%) |
| Hispanic/Latino ethnicity, n (%) | 195 (36%) |
| Reporting ≥1 high-risk co-morbidity, n (%) | 298 (55%) |
| SARS-CoV-2 Vaccination, n (%) | 2 (0.4%) |

The **frequency of PASC at 24 weeks** after largely open-label bamlanivimab treatment for COVID-19 **in the ACTIV-2 trial was moderately low (17%)**.

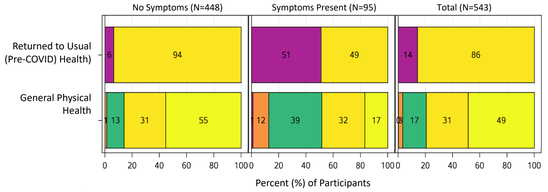
**Female sex, smoking** at the time of acute COVID-19 illness, and **persistence of acute viral illness symptoms at 3-4 weeks**, but not viral shedding, were **associated with increased risk of PASC** symptoms.

These findings highlight **potential directions for future investigation** to understand mechanisms and develop interventions for PASC.

## RESULTS

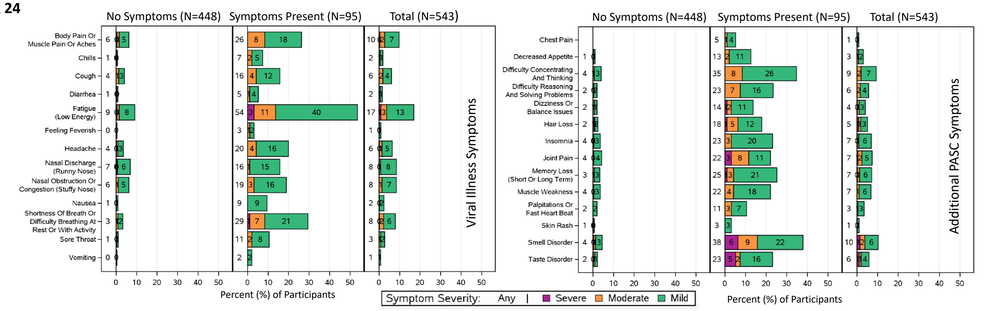
- At 24 weeks after bamlanivimab treatment, 17% reported the ongoing presence of COVID-19 symptoms and 14% that they had not returned to their pre-COVID-19 health (Fig 3).
- Reported symptoms were generally mild, but multiple (Fig 3, Fig 4, Table 2).
- Female sex and current smoking status were associated with increased risk of PASC symptoms. The risk was decreased among those of Hispanic/Latino ethnicity (Table 3).
- SARS CoV-2 Nasal RNA AUC from Day 0 to Day 28 was not associated with risk of PASC at Week 24 (Table 3).
- Presence of acute viral illness symptoms at 3-4 weeks was associated with an increased risk of PASC symptoms at Week 24 (Table 3).

**Fig 3. Self-reported Return To Usual (Pre-COVID) Health + Global Assessments at Week 24 by Status of Overall COVID-19 Symptoms Self-reported at Week 24**




- **95/543 (17%) reported the presence of COVID-19 symptoms at Week 24**

**Fig 4. Severity of Viral Illness Symptoms and Additional PASC Symptoms at Week 24 by Status of Overall COVID-19 Symptoms (Global Assessment Question) Self-reported at Week 24**




## CONCLUSIONS

- In this study of outpatients with mild to moderate COVID-19, at 24 weeks after open label bamlanivimab treatment, 17% reported the ongoing presence of COVID-19 symptoms and 14% that they had not returned to their pre-COVID-19 health. Reported symptoms were generally mild, but multiple.
- Mechanisms for associations between female sex, current smoking and Hispanic/Latino ethnicity with PASC symptoms should be explored.
- Viral burden over the first 28 days of follow-up did not predict PASC.
- Presence of acute viral illness symptoms at 3-4 weeks may serve as an indicator for additional intervention.

## ADDITIONAL INFORMATION

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More information about ACTIV-2 can be found at www.riseabovecovid.org
**Trial Registration**: ClinicalTrials.gov Identifier: NCT04518410

**Table 2. Number of 27 PASC Symptoms by Overall COVID-19 Symptoms Reported at Week 24**

| | | Overall COVID-19 | |
|---|---|---|---|
| | | No Symptoms (n=448) | Symptoms Present (n=95) |
| PASC Symptom Presence | None Reported | 338 (75%) | 3 (3%) |
| | Any Present | 110 (25%) | 92 (97%) |
| Number of PASC Symptoms | One | 31 (7%) | 17 (18%) |
| | Two | 27 (6%) | 17 (18%) |
| | Three | 22 (5%) | 10 (11%) |
| | Four or More | 30 (7%) | 48 (51%) |

Supports internal validity of "Overall COVID-19 Symptoms" Question

**Table 3. Association between Participant Characteristics, Biomarkers, and Viral Shedding with Overall COVID-19 Symptoms Reported at Week 24**

| Variable | | Univariable Model | | Multivariable or Adjusted Model | |
|---|---|---|---|---|---|
| | | Relative Risk | P-Value | Relative Risk | P-value |
| Age [years] | | 0.99985 | 0.9793 | 1.00217 | 0.7366 |
| Sex | Female | 1.72935 | 0.0052* | 1.81739 | 0.0032* |
| | Male | 1.00000 | | 1.00000 | |
| Ethnicity | Hispanic Or Latino | 0.53783 | 0.0061* | 0.56271 | 0.0161* |
| | Not Hispanic Or Latino | 1.00000 | | 1.00000 | |
| Smoking Status | Current | 1.91760 | 0.0170* | 2.21496 | 0.0092* |
| (Cigarette) | Former | 1.04002 | 0.8799 | 0.87754 | 0.6482 |
| | Never | 1.00000 | | 1.00000 | |
| SARS CoV-2 Nasal RNA AUC from Day 0 to Day 28 | | 0.99698 | 0.7112 | 0.99902 | 0.9113 |
| Symptom Presence from Day 22 to Day 28 (Any Present) | | 2.74183 | <0.001* | 2.31003 | 0.0007* |

*Statistically significant with p<0.05. AUC=Area under the curve