**SUPPLEMENTAL MATERIAL**

**Oral Famotidine vs. Placebo in Diverse Non-Hospitalized Patients with COVID-19: A Randomized, Double-Blinded Phase 2 Clinical Trial**

Brennan *et al.*

## Extended Methods

*Study design.* The data were gathered via FDA-approved Bluetooth-compatible devices: Jumper Pulse Oximeter, Jumper thermometer, MIR Spirobank II spirometer, and Taiza weight scale. Electronic devices and study medication were sent to the patient at their place of residence by overnight delivery after consent (day 0). Blood samples were processed and analyzed at a central laboratory. Research samples were processed, snap frozen, and stored at -80°C until use.

*Randomization and masking.* Unblinding of the investigators and determining plasma famotidine levels occurred only after the final report of the clinical endpoints had been reviewed and accepted by the DSMB.

*Treatment.* Capsules in sterile, sealed bottles labeled with the blinded code for the study arm were shipped to study participants together with the remote monitoring devices. Self-reported concordance was documented on study days 7 and 14.

*Statistical analysis*

Cumulative incidence of symptom resolution at day 28: The analysis did not consider any competing risk event, as no death event occurred.

*Plasma Interferon-α (IFN- α) level*



Brennan CM, *et al. Gut* 2022; 71:879–888. doi: 10.1136/gutjnl-2022-326952

Plasma IFN-α concentrations were determined using VeriKine-HS Human Interferon Alpha All Subtype ELISA kit (Cat. No. 41115-1, PBL Assay Science, New Jersy, USA) and read on a SpectraMax i3x microplate reader (Molecular Devices, California, USA). Samples were diluted if optical reading exceeded the upper linear range.

*Data access*

The transcriptional data will be made available at the point of publication of the peer-reviewed manuscript.



Brennan CM, *et al. Gut* 2022; 71:879–888. doi: 10.1136/gutjnl-2022-326952

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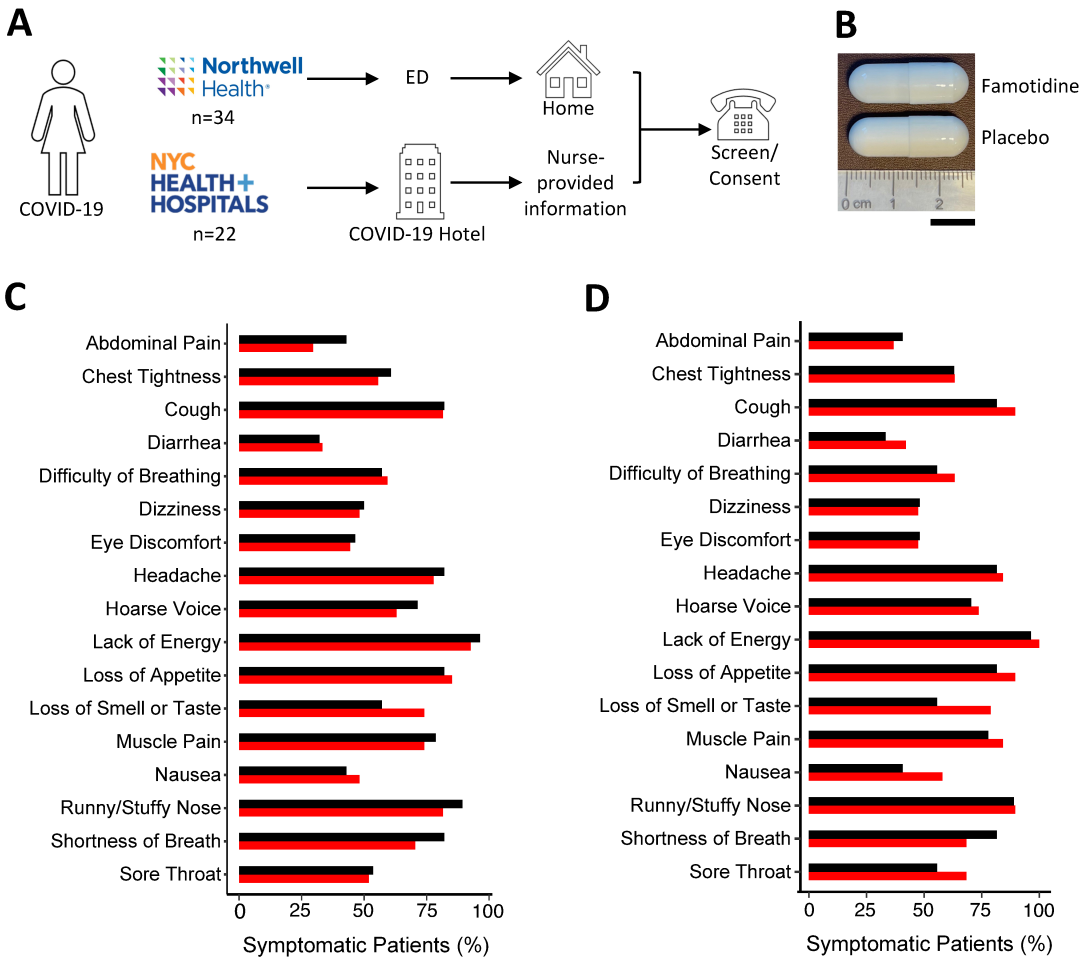


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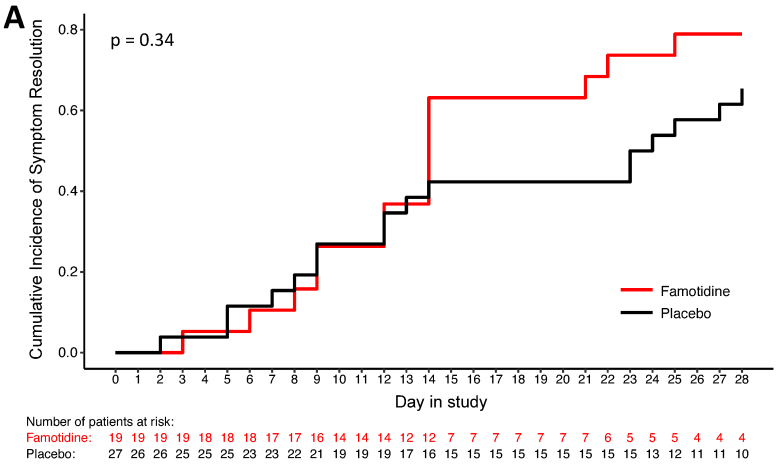
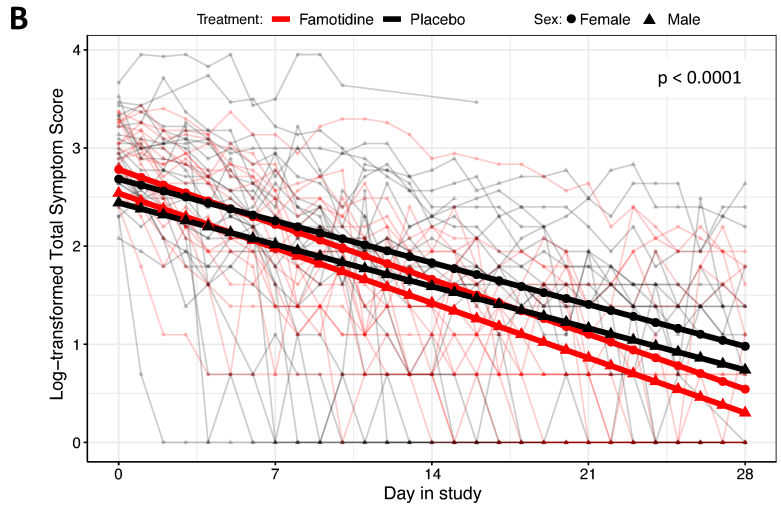
41 **Figure S1. Extended trial overview and baseline symptom scores.** (**A**) The candidate patient
42 identification schematic is shown. (**B**) A photograph of example capsules filled with famotidine or
43 placebo is displayed. Scale bar: 10mm. (**C-D**) The symptom frequencies at baseline for all 17 assessed
44 individual symptoms are shown for each study arm for the (**C**) ITT and (**D**) PP group. Black bars: placebo,
45 red bars: famotidine
46 ED = emergency department.


A
p = 0.34
Cumulative Incidence of Symptom Resolution
Famotidine
Placebo
Day in study
Number of patients at risk:
Famotidine: 19 19 19 19 18 18 18 17 17 16 14 14 14 12 12 7 7 7 7 7 7 7 6 5 5 5 4 4 4
Placebo: 27 26 26 25 25 25 23 23 22 21 19 19 19 17 16 15 15 15 15 15 15 15 15 15 13 12 11 11 10


B
Treatment: Famotidine Placebo
Sex: Female Male
p < 0.0001
Log−transformed Total Symptom Score
Day in study

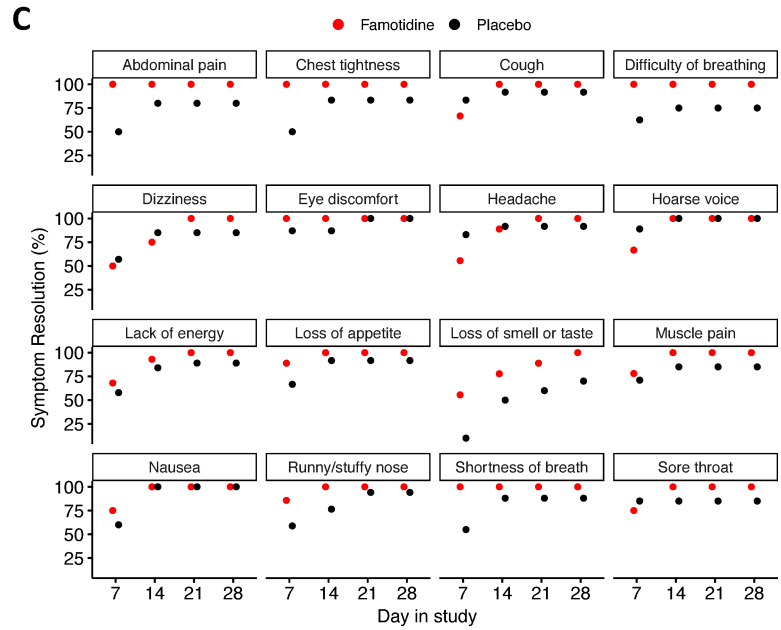

C
Famotidine Placebo
Abdominal pain
Chest tightness
Cough
Difficulty of breathing
Dizziness
Eye discomfort
Headache
Hoarse voice
Lack of energy
Loss of appetite
Loss of smell or taste
Muscle pain
Nausea
Runny/stuffy nose
Shortness of breath
Sore throat
Symptom Resolution (%)
Day in study

**Figure S2. Per-protocol symptom resolution analyses.** (**A**) The cumulative incidence of total symptom resolution for both study arms as defined in the primary trial endpoint is plotted. The famotidine and placebo arms were compared using stratified log-rank test. (**B**) The logarithmically transformed patient-level total symptom score (thin lines) and their estimated means based on linear mixed effect model are shown for each study arm. The p-value for the interaction term of group and day in study is displayed. (**C**) The estimated cumulative incidence of symptom resolution for each individual symptom at day 7, 14, 21, and 28 are displayed for each study arm. The results for diarrhea are not included because neither arm had symptomatic patients at the displayed timepoints. All timepoints with no remaining symptomatic patient are displayed as 100% symptom resolution.

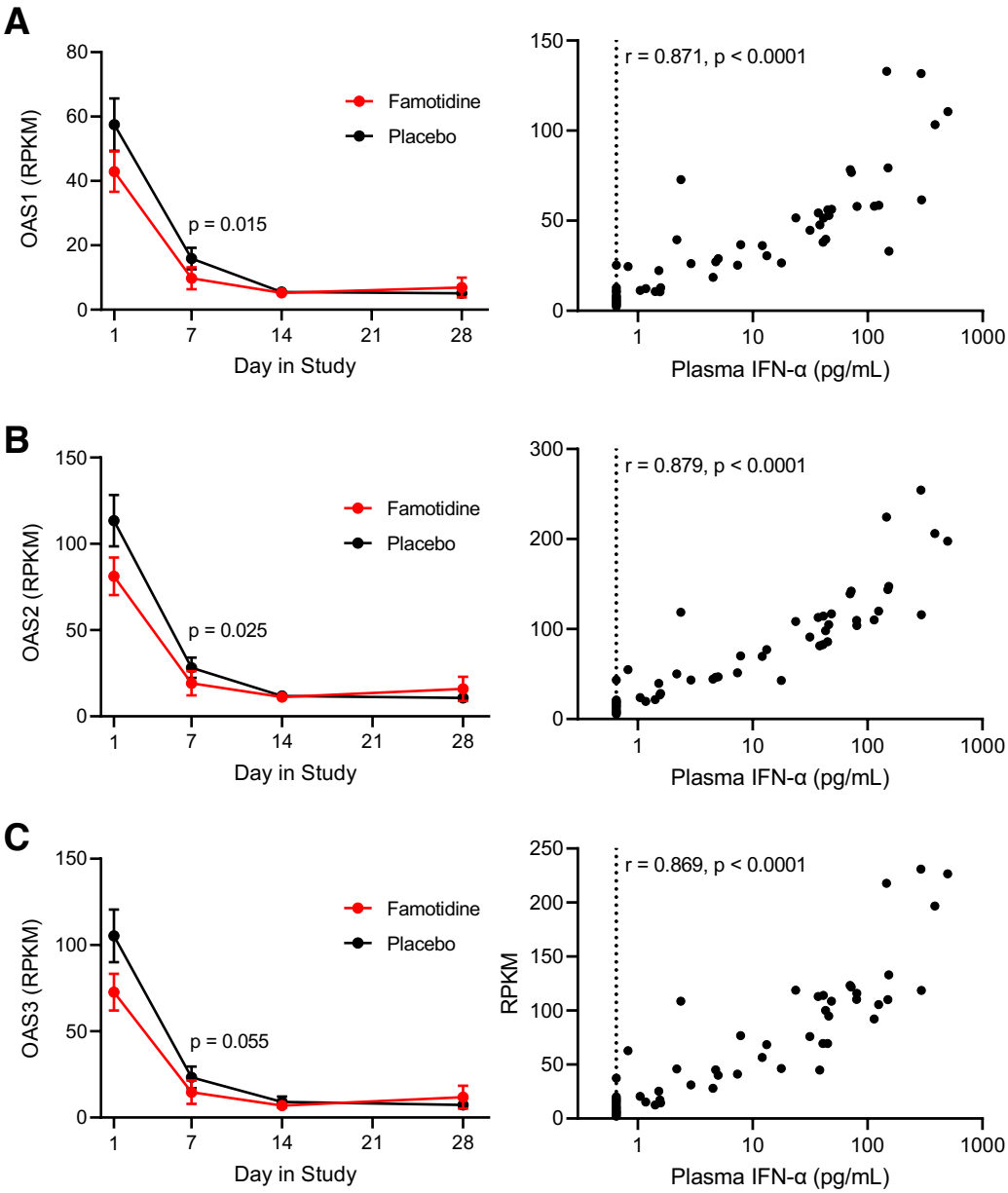



**Figure S3. Analysis of 2´-5´oligoadenylate synthetase (OAS) gene expression in PBMCs. (A-C)** The expression levels of OAS genes (*OAS1*, *OAS2* and *OAS3*) in PBMCs at day 1, 7, 14, 28 (left panel) and the correlation of OAS gene expression and plasma IFN-α levels (right panel) are shown. Dashed vertical lines indicate the lower limit of detection (LLD), and all IFN-α measuremnts falling below were treated as LLD. Gene expression levels between famotidine and placebo arms were compared by Wilcoxon rank sum test. P-values for day 7 are displayed. For all other comparisons at day 1, 14 and 28, p values were greater than 0.2. Statistical comparison of correlation was by Spearman rank analysis.

**Table S1A. Patient and baseline characteristics from the per-protocol analysis.**

| Variable | Level | Total (N=46) | Placebo (N=27) | Famotidine (N=19) | P-value* |
|---|---|---|---|---|---|
| **Patients' characteristics** | | | | | |
| Age (year) | | 35.0±19.0 | 31.0±13.0 | 39.0±18.0 | 0.113 |
| Gender | Female | 30 (65.2%) | 17 (63.0%) | 13 (68.4%) | 0.702 |
| | Male | 16 (34.8%) | 10 (37.0%) | 6 (31.6%) | |
| Race | Black or African American | 15 (32.6%) | 10 (37.0%) | 5 (26.3%) | 0.655 |
| | More than one race | 10 (21.7%) | 7 (25.9%) | 3 (15.8%) | |
| | Unknown/not reported | 2 (4.4%) | 1 (3.7%) | 1 (5.3%) | |
| | White | 19 (41.3%) | 9 (33.3%) | 10 (52.6%) | |
| Ethnicity | Hispanic or Latino | 11 (23.9%) | 5 (18.5%) | 6 (31.6%) | 0.455 |
| | Not Hispanic or Latino | 19 (41.3%) | 13 (48.2%) | 6 (31.6%) | |
| | Unknown/not reported | 16 (34.8%) | 9 (33.3%) | 7 (36.8%) | |
| **COVID-19 Symptom Score at Baseline**** | | | | | |
| Total Symptom Score | | 18.0±11.0 | 18.0±13.0 | 18.0±11.0 | 0.927 |
| **History of Present Illness** | | | | | |
| Symptomatic days prior to randomization | | 4.0±3.0 | 4.0±2.0 | 4.0±3.0 | 0.339 |
| **Vital Signs at Baseline**** | | | | | |
| BMI ($kg/m^2$) | | 26.75±7.33 | 24.94±8.28 | 27.48±6.79 | 0.158 |
| Temperature (°F) | | 98.40±0.80 | 98.30±0.80 | 98.60±0.80 | 0.269 |
| Heart Rate (bpm) | | 87.0±16.0 | 86.5±21.0 | 88.0±16.0 | 0.370 |
| SpO2(%) | | 99.0±2.0 | 99.0±3.0 | 99.0±2.0 | 0.812 |
| FEV1/FVC | | 0.89±0.21 | 0.88±0.18 | 0.89±0.29 | 0.465 |

*: For categorical variables, p-values were based on Chi-squared test with exact p-value from Monte Carlo simulation; for the continuous variable, the p-value was based on Wilcoxon rank sum test.
**: Reason of missing data: IRB013 in the placebo group withdrew early without baseline symptom scores and vitals completed.
Note: For the continuous variable, median+/-IQR was reported.

68 **Table S1B. Patient and baseline characteristics from the experimental medicine analysis.**

| Variable | Level | Total (N=35) | Placebo (N=20) | Famotidine (N=15) | P-value* |
|---|---|---|---|---|---|
| **Patients' characteristics** | | | | | |
| Age (year) | | 36.0±17.0 | 33.5±14.5 | 41.0±17.0 | 0.182 |
| Gender | Female | 24 (68.6%) | 15 (75.0%) | 9 (60.0%) | 0.344 |
| | Male | 11 (31.4%) | 5 (25.0%) | 6 (40.0%) | |
| Race | Black or African American | 9 (25.7%) | 6 (30.0%) | 3 (20.0%) | 0.369 |
| | More than one race | 9 (25.7%) | 7 (35.0%) | 2 (13.3%) | |
| | Unknown/not reported | 2 (5.7%) | 1 (5.0%) | 1 (6.7%) | |
| | White | 15 (42.9%) | 6 (30.0%) | 9 (60.0%) | |
| Ethnicity | Hispanic or Latino | 7 (20.0%) | 3 (15.0%) | 4 (26.7%) | 0.492 |
| | Not Hispanic or Latino | 14 (40.0%) | 10 (50.0%) | 4 (26.7%) | |
| | Unknown/not reported | 14 (40.0%) | 7 (35.0%) | 7 (46.7%) | |
| **COVID-19 Symptom Score at Baseline** | | | | | |
| Total Symptom Score | | 19.0±11.0 | 18.5±13.5 | 19.0±9.0 | 0.789 |
| **History of Present Illness** | | | | | |
| Symptomatic days prior to randomization | | 4.00±2.0 | 3.00±1.5 | 4.00±3.0 | 0.198 |
| **Vital Signs at Baseline** | | | | | |
| BMI ($kg/m^2$) | | 26.73±12.79 | 25.99±13.17 | 27.27±6.79 | 0.395 |
| Temperature (°F) | | 98.40±0.80 | 98.25±0.75 | 98.60±0.80 | 0.404 |
| Heart Rate (bpm) | | 87.0±15.0 | 85.0±23.5 | 88.0±11.0 | 0.582 |
| SpO2(%) | | 99.0±2.0 | 99.0±2.0 | 99.0±2.0 | 0.704 |
| FEV1/FVC | | 0.89±0.21 | 0.90±0.16 | 0.89±0.29 | 0.545 |

*: For categorical variables, p-values were based on Chi-squared test with exact p-value from Monte Carlo simulation; for the continuous variable, the p-value was based on Wilcoxon rank sum test.
Note: For the continuous variable, median+/-IQR was reported.

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**Table S2A. Estimated cumulative incidences (CIN) of individual symptom resolution and corresponding 95% confidence intervals for symptom resolution at day 7, 14, 21, 28 from the intention-to-treat analysis.**

| Treatment | Day 7 | Day 14 | Day 21 | Day 28 |
|---|---|---|---|---|
| **Lack of energy** | | | | |
| Famotidine | 72.7% (47.8%, 87.2%) | 90.9% (62.7%, 98.1%) | 95.5% (55.6%, 99.6%) | 95.5% (55.6%, 99.6%) |
| Placebo | 55.0% (30.4%, 74.1%) | 85.0% (56.9%, 95.4%) | 90.0% (59.6%, 97.9%) | 90.0% (59.6%, 97.9%) |
| **Shortness of breath** | | | | |
| Famotidine | NSP | NSP | NSP | NSP |
| Placebo | 60.0% (22.2%, 84.1%) | 90.0% (25.4%, 99.2%) | 90.0% (25.4%, 99.2%) | 90.0% (25.4%, 99.2%) |
| **Cough** | | | | |
| Famotidine | 75.0% (23.4%, 94.5%) | NSP | NSP | NSP |
| Placebo | 83.3% (40.8%, 96.4%) | 91.7% (32.9%, 99.3%) | 91.7% (32.9%, 99.3%) | 91.7% (32.9%, 99.3%) |
| **Headache** | | | | |
| Famotidine | 50.0% (19.3%, 74.7%) | 75.0% (37.3%, 91.9%) | 87.5% (23.5%, 98.8%) | 87.5% (23.5%, 98.8%) |
| Placebo | 83.3% (40.8%, 96.4%) | 91.7% (32.9%, 99.3%) | 91.7% (32.9%, 99.3%) | 91.7% (32.9%, 99.3%) |
| **Loss of smell or taste** | | | | |
| Famotidine | 50.0% (19.3%, 74.7%) | 66.7% (30.7%, 87.0%) | 88.9% (23.8%, 99.0%) | NSP |
| Placebo | 10.0% (0.5%, 37.4%) | 50.0% (16.3%, 76.7%) | 60.0% (22.2%, 84.1%) | 70.0% (28.2%, 90.4%) |
| **Loss of appetite** | | | | |
| Famotidine | 85.7% (46.8%, 96.9%) | NSP | NSP | NSP |
| Placebo | 69.2% (34.3%, 88.1%) | 92.3% (35.8%, 99.4%) | 92.3% (35.8%, 99.4%) | 92.3% (35.8%, 99.4%) |
| **Difficulty of breathing** | | | | |
| Famotidine | NSP | NSP | NSP | NSP |
| Placebo | 62.5% (19.0%, 87.5%) | 75.0% (23.6%, 94.4%) | 75.0% (23.6%, 94.4%) | 75.0% (23.6%, 94.4%) |
| **Diarrhea** | | | | |
| Famotidine | NSP | NSP | NSP | NSP |
| Placebo | NSP | NSP | NSP | NSP |
| **Sore throat** | | | | |
| Famotidine | 75.0% (1.9%, 97.9%) | NSP | NSP | NSP |
| Placebo | 85.7% (13.0%, 98.8%) | 85.7% (13.0%, 98.8%) | 85.7% (13.0%, 98.8%) | 85.7% (13.0%, 98.8%) |
| **Muscle pain** | | | | |
| Famotidine | 84.6% (44.1%, 96.7%) | NSP | NSP | NSP |

| Treatment | Day 7 | Day 14 | Day 21 | Day 28 |
|---|---|---|---|---|
| Placebo | 71.4% (38.0%, 89.0%) | 85.7% (48.2%, 96.8%) | 85.7% (48.2%, 96.8%) | 85.7% (48.2%, 96.8%) |
| **Hoarse voice** | | | | |
| Famotidine | 71.4% (18.3%, 93.6%) | NSP | NSP | NSP |
| Placebo | 89.0% (29.2%, 98.9%) | NSP | NSP | NSP |
| **Runny/stuffy nose** | | | | |
| Famotidine | 88.2% (56.3%, 97.3%) | NSP | NSP | NSP |
| Placebo | 58.8% (31.2%, 78.5%) | 76.5% (46.1%, 91.1%) | 94.1% (47.1%, 99.5%) | 94.1% (47.1%, 99.5%) |
| **Chest tightness** | | | | |
| Famotidine | NSP | NSP | NSP | NSP |
| Placebo | 50.0% (7.7%, 82.9%) | 83.3% (8.6%, 98.7%) | 83.3% (8.6%, 98.7%) | 83.3% (8.6%, 98.7%) |
| **Abdominal pain** | | | | |
| Famotidine | NSP | NSP | NSP | NSP |
| Placebo | 80.0% (4.7%, 98.4%) | 80.0% (4.7%, 98.4%) | 80.0% (4.7%, 98.4%) | 80.0% (4.7%, 98.4%) |
| **Nausea** | | | | |
| Famotidine | 80.0% (5.3%, 98.3%) | NSP | NSP | NSP |
| Placebo | 60.0% (6.7%, 90.8%) | NSP | NSP | NSP |
| **Dizziness** | | | | |
| Famotidine | 66.7% (12.2%, 92.5%) | 83.3% (8.6%, 98.7%) | NSP | NSP |
| Placebo | 57.1% (13.2%, 85.7%) | 85.7% (12.9%, 98.9%) | 85.7% (12.9%, 98.9%) | 85.7% (12.9%, 98.9%) |
| **Eye discomfort** | | | | |
| Famotidine | NSP | NSP | NSP | NSP |
| Placebo | 87.5% (24.6%, 98.7%) | 87.5% (24.6%, 98.7%) | NSP | NSP |

NSP: No symptomatic patient, corresponding to 100% cumulative symptom resolution.

**Table S2B. Estimated cumulative incidences (CIN) of individual symptom resolution and corresponding 95% confidence intervals for symptom resolution at day 7, 14, 21, 28 from the per-protocol analysis.**

| Treatment | Day 7 | Day 14 | Day 21 | Day 28 |
|---|---|---|---|---|
| **Lack of energy** | | | | |
| Famotidine | 68.8% (38.7%, 86.2%) | 93.8% (44.1%, 99.5%) | NSP | NSP |
| Placebo | 57.9% (32.1%, 76.9%) | 84.2% (55.0%, 95.2%) | 89.5% (57.9%, 97.8%) | 89.5% (57.9%, 97.8%) |
| **Shortness of breath** | | | | |
| Famotidine | NSP | NSP | NSP | NSP |
| Placebo | 55.6% (17.5%, 82.0%) | 88.9% (21.5%, 99.1%) | 88.9% (21.5%, 99.1%) | 88.9% (21.5%, 99.1%) |
| **Cough** | | | | |
| Famotidine | 66.7% (12.3%, 92.5%) | NSP | NSP | NSP |
| Placebo | 83.3% (40.8%, 96.4%) | 91.7% (32.9%, 99.3%) | 91.7% (32.9%, 99.3%) | 91.7% (32.9%, 99.3%) |
| **Headache** | | | | |
| Famotidine | 55.6% (17.7%, 81.9%) | 88.9% (32.9%, 98.8%) | NSP | NSP |
| Placebo | 83.3% (40.8%, 96.4%) | 91.7% (32.9%, 99.3%) | 91.7% (32.9%, 99.3%) | 91.7% (32.9%, 99.3%) |
| **Loss of smell or taste** | | | | |
| Famotidine | 55.6% (17.8%, 81.9%) | 77.8% (28.3%, 95.1%) | 88.9% (21.5%, 99.1%) | NSP |
| Placebo | 10.0% (0.5%, 37.4%) | 50.0% (16.3%, 76.7%) | 60.0% (22.2%, 84.1%) | 70.0% (28.2%, 90.4%) |
| **Loss of appetite** | | | | |
| Famotidine | 88.9% (21.5%, 99.1%) | NSP | NSP | NSP |
| Placebo | 66.7% (30.7%, 87.0%) | 91.7% (32.6%, 99.3%) | 91.7% (32.6%, 99.3%) | 91.7% (32.6%, 99.3%) |
| **Difficulty of breathing** | | | | |
| Famotidine | NSP | NSP | NSP | NSP |
| Placebo | 62.5% (19.0%, 87.5%) | 75.0% (23.6%, 94.4%) | 75.0% (23.6%, 94.4%) | 75.0% (23.6%, 94.4%) |
| **Diarrhea** | | | | |
| Famotidine | NSP | NSP | NSP | NSP |
| Placebo | NSP | NSP | NSP | NSP |
| **Sore throat** | | | | |
| Famotidine | 75.0% (1.9%, 97.9%) | NSP | NSP | NSP |
| Placebo | 85.7% (13.0%, 98.8%) | 85.7% (13.0%, 98.8%) | 85.7% (13.0%, 98.8%) | 85.7% (13.0%, 98.8%) |
| **Muscle pain** | | | | |
| Famotidine | 77.8% (30.2%, 94.9%) | NSP | NSP | NSP |
| Placebo | 71.4% (38.0%, 89.0%) | 85.7% (48.2%, 96.8%) | 85.7% (48.2%, 96.8%) | 85.7% (48.2%, 96.8%) |

| Treatment | Day 7 | Day 14 | Day 21 | Day 28 |
|---|---|---|---|---|
| **Hoarse voice** | | | | |
| Famotidine | 66.7% (13.7%, 92.1%) | NSP | NSP | NSP |
| Placebo | 88.9% (29.2%, 98.9%) | NSP | NSP | NSP |
| **Runny/stuffy nose** | | | | |
| Famotidine | 85.7% (48.1%, 96.9%) | NSP | NSP | NSP |
| Placebo | 58.8% (31.2%, 78.5%) | 76.5% (46.1%, 91.1%) | 94.1% (47.1%, 99.5%) | 94.1% (47.1%, 99.5%) |
| **Chest tightness** | | | | |
| Famotidine | NSP | NSP | NSP | NSP |
| Placebo | 50.0% (7.7%, 82.9%) | 83.3% (8.6%, 98.7%) | 83.3% (8.6%, 98.7%) | 83.3% (8.6%, 98.7%) |
| **Abdominal pain** | | | | |
| Famotidine | NSP | NSP | NSP | NSP |
| Placebo | 80.0% (4.7%, 98.4%) | 80.0% (4.7%, 98.4%) | 80.0% (4.7%, 98.4%) | 80.0% (4.7%, 98.4%) |
| **Nausea** | | | | |
| Famotidine | 75.0% (1.9%, 97.9%) | NSP | NSP | NSP |
| Placebo | 60.0% (6.7%, 90.8%) | NSP | NSP | NSP |
| **Dizziness** | | | | |
| Famotidine | 50.0% (2.3%, 88.1%) | 75.0% (1.7%, 98.0%) | NSP | NSP |
| Placebo | 57.1% (13.2%, 85.7%) | 85.7% (12.9%, 98.9%) | 85.7% (12.9%, 98.9%) | 85.7% (12.9%, 98.9%) |
| **Eye discomfort** | | | | |
| Famotidine | NSP | NSP | NSP | NSP |
| Placebo | 87.5% (24.6%, 98.7%) | 87.5% (24.6%, 98.7%) | NSP | NSP |

78 NSP: No symptomatic patient, corresponding to 100% cumulative symptom resolution.

79

**Table S3A Estimated mean and relative change in CRP levels from the intention-to-treat analysis.**

| Treatment | Visit | Estimated mean (95% CI) | Time | Relative change (95% CI) | P-value* |
|---|---|---|---|---|---|
| Famotidine | Day 1 | 0.919 (0.540, 1.565) | | | |
| | Day 7 | 0.954 (0.510, 1.784) | Day 7 vs Day 1 | 0.038 (-0.494, 1.131) | 0.917 |
| | Day 14 | 0.563 (0.308, 1.030) | Day 14 vs Day 1 | -0.388 (-0.698, 0.242) | 0.169 |
| | Day 28 | 0.621 (0.329, 1.17) | Day 28 vs Day 1 | -0.325 (-0.675, 0.402) | 0.284 |
| Placebo | Day 1 | 0.517 (0.302, 0.884) | | | |
| | Day 7 | 0.958 (0.474, 1.933) | Day 7 vs Day 1 | 0.853 (-0.164, 3.106) | 0.125 |
| | Day 14 | 0.261 (0.108, 0.632) | Day 14 vs Day 1 | -0.495 (-0.802, 0.289) | 0.149 |
| | Day 28 | 0.642 (0.297, 1.384) | Day 28 vs Day 1 | 0.242 (-0.462, 1.868) | 0.604 |

*: P-values were based on T-test from a linear mixed model.

**Table S3B Estimated mean and relative change in CRP levels from the per-protocol analysis.**

| Treatment | Visit | Estimated mean (95% CI) | Time | Relative change (95% CI) | P-value* |
|---|---|---|---|---|---|
| Famotidine | Day 1 | 1.290 (0.672, 2.476) | | | |
| | Day 7 | 1.246 (0.577, 2.692) | Day 7 vs Day 1 | -0.035 (-0.601, 1.336) | 0.936 |
| | Day 14 | 0.633 (0.324, 1.238) | Day 14 vs Day 1 | -0.509 (-0.782, 0.106) | 0.084 |
| | Day 28 | 0.691 (0.344, 1.389) | Day 28 vs Day 1 | -0.464 (-0.766, 0.226) | 0.135 |
| Placebo | Day 1 | 0.508 (0.287, 0.902) | | | |
| | Day 7 | 0.982 (0.473, 2.036) | Day 7 vs Day 1 | 0.932 (-0.165, 3.469) | 0.120 |
| | Day 14 | 0.272 (0.108, 0.684) | Day 14 vs Day 1 | -0.465 (-0.801, 0.437) | 0.207 |
| | Day 28 | 0.667 (0.299, 1.490) | Day 28 vs Day 1 | 0.313 (-0.459, 2.185) | 0.537 |

*: P-values were based on T-test from a linear mixed model.

**Table S4. Estimated mean and relative change in ferritin levels from the per-protocol analysis.**

| Treatment | Visit | Estimated mean (95% CI) | Time | Relative change (95% CI) | P-value* |
|---|---|---|---|---|---|
| Famotidine | Day 1 | 143.8 (95.2, 217.0) | | | |
| | Day 7 | 168.3 (111.3, 254.6) | Day 7 vs Day 1 | 0.17 (0.01, 0.36) | 0.039 |
| | Day 14 | 142.2 (93.8, 215.6) | Day 14 vs Day 1 | -0.01 (-0.15, 0.16) | 0.892 |
| | Day 28 | 103.1 (68.2, 155.8) | Day 28 vs Day 1 | -0.28 (-0.38, -0.17) | <.0001 |
| Placebo | Day 1 | 138.9 (98.0, 196.9) | | | |
| | Day 7 | 168.0 (118.3, 238.6) | Day 7 vs Day 1 | 0.21 (0.06, 0.39) | 0.007 |
| | Day 14 | 127.0 (89.1, 180.9) | Day 14 vs Day 1 | -0.09 (-0.21, 0.05) | 0.215 |
| | Day 28 | 91.6 (64.1, 130.8) | Day 28 vs Day 1 | -0.34 (-0.43, -0.24) | <.0001 |

*: P-values were based on T-test from a linear mixed model.

88 **Table S5. List of type-I interferon-related genes used in ssGSEA analysis.**

| Gene Name | Entrez Gene ID | Description |
|---|---|---|
| ABCE1 | 6059 | ATP binding cassette subfamily E member 1 [Source:HGNC Symbol;Acc:HGNC:69] |
| ADAR | 103 | adenosine deaminase RNA specific [Source:HGNC Symbol;Acc:HGNC:225] |
| BST2 | 684 | bone marrow stromal cell antigen 2 [Source:HGNC Symbol;Acc:HGNC:1119] |
| GBP2 | 2634 | guanylate binding protein 2 [Source:HGNC Symbol;Acc:HGNC:4183] |
| HLA-A | 3105 | major histocompatibility complex, class I, A [Source:HGNC Symbol;Acc:HGNC:4931] |
| HLA-B | 3106 | major histocompatibility complex, class I, B [Source:HGNC Symbol;Acc:HGNC:4932] |
| HLA-C | 3107 | major histocompatibility complex, class I, C [Source:HGNC Symbol;Acc:HGNC:4933] |
| IFI35 | 3430 | interferon induced protein 35 [Source:HGNC Symbol;Acc:HGNC:5399] |
| IFI6 | 2537 | interferon alpha inducible protein 6 [Source:HGNC Symbol;Acc:HGNC:4054] |
| IFIT1 | 3434 | interferon induced protein with tetratricopeptide repeats 1 [Source:HGNC Symbol;Acc:HGNC:5407] |
| IFIT2 | 3433 | interferon induced protein with tetratricopeptide repeats 2 [Source:HGNC Symbol;Acc:HGNC:5409] |
| IFIT3 | 3437 | interferon induced protein with tetratricopeptide repeats 3 [Source:HGNC Symbol;Acc:HGNC:5411] |
| IFITM2 | 10581 | interferon induced transmembrane protein 2 [Source:HGNC Symbol;Acc:HGNC:5413] |
| IRF2 | 3660 | interferon regulatory factor 2 [Source:HGNC Symbol;Acc:HGNC:6117] |
| IRF3 | 3661 | interferon regulatory factor 3 [Source:HGNC Symbol;Acc:HGNC:6118] |
| IRF6 | 3664 | interferon regulatory factor 6 [Source:HGNC Symbol;Acc:HGNC:6121] |
| IRF9 | 10379 | interferon regulatory factor 9 [Source:HGNC Symbol;Acc:HGNC:6131] |
| ISG15 | 9636 | ISG15 ubiquitin like modifier [Source:HGNC Symbol;Acc:HGNC:4053] |
| ISG20 | 3669 | interferon stimulated exonuclease gene 20 [Source:HGNC Symbol;Acc:HGNC:6130] |
| MX1 | 4599 | MX dynamin like GTPase 1 [Source:HGNC Symbol;Acc:HGNC:7532] |
| MX2 | 4600 | MX dynamin like GTPase 2 [Source:HGNC Symbol;Acc:HGNC:7533] |
| OAS1 | 4938 | 2'-5'-oligoadenylate synthetase 1 [Source:HGNC Symbol;Acc:HGNC:8086] |
| OAS2 | 4939 | 2'-5'-oligoadenylate synthetase 2 [Source:HGNC Symbol;Acc:HGNC:8087] |
| OAS3 | 4940 | 2'-5'-oligoadenylate synthetase 3 [Source:HGNC Symbol;Acc:HGNC:8088] |
| OASL | 8638 | 2'-5'-oligoadenylate synthetase like [Source:HGNC Symbol;Acc:HGNC:8090] |
| PSMB8 | 5696 | proteasome 20S subunit beta 8 [Source:HGNC Symbol;Acc:HGNC:9545] |
| RNASEL | 6041 | ribonuclease L [Source:HGNC Symbol;Acc:HGNC:10050] |

| | | |
|---|---|---|
| RSAD2 | 91543 | radical S-adenosyl methionine domain containing 2 [Source:HGNC Symbol;Acc:HGNC:30908] |
| SAMHD1 | 25939 | SAM and HD domain containing deoxynucleoside triphosphate triphosphohydrolase 1 [Source:HGNC Symbol;Acc:HGNC:15925] |

89