Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Comparison of Demographic and Clinical Characteristics – As-Treated Population

Characteristic	Ivermectin (N=275)	Placebo (N=198)	Differences (95% CI)[a]
Age, median (IQR) – yrs	38 (29 to 49)	37 (28.7 to 49.2)	1.0 (-2.5 to 3.0)
Age Groups – No. (%)			
<40 yr	159 (57.8)	112 (56.6)	1.2 (-7.8 to 10.3)
40-64 yr	104 (37.8)	70 (35.3)	2.5 (-6.3 to 11.2)
≥ 65 yr	12 (4.4)	16 (8.1)	-3.7 (-8.2 to 0.8)
Sex – No. (%)			
Male	112 (40.7)	89 (44.9)	-4.2 (-13.3 to 4.8)
Female	163 (59.3)	109 (55.1)	4.2 (-4.8 to 13.3)
Race or ethnic group[b] – No. (%)			
Mixed Race	243 (88.4)	179 (90.4)	-2.0 (-7.6 to 3.5)
Black or African American	24 (8.7)	16 (8.1)	0.6 (-4.4 to 5.7)
Colombian Native	8 (2.9)	3 (1.5)	1.4 (-1.2 to 4.0)
History of BCG vaccination – No./n (%)	244/264 (92.4)	184/195 (94.5)	-1.9 (-6.5 to 2.6)
Health Insurance – No. (%)			
Private/semiprivate	239 (86.9)	174 (87.9)	-1.0 (-7.0 to 5.1)
Government subsidized	33 (12.0)	23 (11.6)	0.4 (-5.5 to 6-3)
Uninsured	3 (1.1)	1 (0.5)	0.6 (-1.0 to 2.2)
No. of persons in same household, median (IQR)	3 (3 to 4)	3 (3 to 4)	0 (-1 to 1)
Current smoker – No./n (%)	6/275 (2.2)	8 /197 (4.1)	-1.9 (-5.1 to 1.4)
BMI (kg/m^2) – median (IQR)	26.3 (23.0 to 28.9)	26.4 (22.7 to 29.0)	-0.1 (-1.3 to 0.8)
Coexisting conditions[c] – No. (%)			
Obesity (BMI ≥ 30 kg/m^2) – No./n (%)	55 (20.0)	38 (19.4)	0.6 (-6.7 to 7.9)

Hypertension	34 (12.4)	25 (12.6)	-0.2 (-6.3 to 5.8)
Diabetes	14 (5.1)	12 (6.1)	-1.0 (-5.2 to 3.2)
Thyroid disease	12 (4.3)	8 (4.0)	-0.3 (-3.3 to 4.0)
Respiratory disease	10 (3.6)	6 (3.0)	-0.6 (-2.6 to 3.9)
Cardiovascular disease	7 (2.5)	3 (1.5)	1.0 (-1.5 to 3.5)
Any coexisting conditions – No. (%)	61 (22.2)	38 (19.2)	3.0 (-4.4 to 10.3)
Median time (IQR) from symptom onset to randomization – days	5 (4-6)	5 (4-6)	0 (0 to 0)
Characteristic	Ivermectin (N=275)	Placebo (N=198)	Differences (95% CI)[a]
NEWS2[d] score at randomization – median (IQR)	3 (1-4)	3 (2-4)	0 (0 to 0)
Score on ordinal scale at randomization – No. (%)			
1: Not hospitalized and no limitation of activities	164 (59.6)	109 (55.0)	4.6 (-4.4 to 13.6)
2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	109 (39.6)	87 (43.9)	-4.3 (-13.3 to 4.7)
3. Hospitalized, not requiring supplemental oxygen	1 (0.4)	1 (0.5)	-
4. Hospitalized, requiring supplemental oxygen[e]	1 (0.4)	1 (0.5)	-
Medications initiated between symptom onset and enrollment – No. (%)			
NSAIDs	79 (28.7)	61 (30.8)	-2.1 (-10.4 to 6.3)
Other[f]	58 (21.1)	38 (19.2)	1.9 (-5.4 to 9.2)
Other antipyretics	37 (13.4)	23 (11.6)	1.8 (-4.2 to 7.8)
Macrolides	33 (12.0)	22 (11.1)	0.9 (-4.9 to 6.7)
Non-macrolide antibiotics	22 (8.0)	11 (5.6)	2.4 (-2.1 to 7.0)
Glucocorticoids	7 (2.6)	12 (6.1)	-3.5 (-7.3 to 0.3)

Other immunomodulating agents[g]	4 (1.4)	2 (1.0)	0.4 (-1.5 to 2.4)
Anticoagulants	1 (0.4)	7 (3.5)	-3.2 (-5.8 to 0.5)

IQR denotates interquartile range and NSAIDs nonsteroidal anti-inflammatory drugs
n = number with available information
[a] 95% confidence interval for difference in medians estimated by bootstrap sampling and for difference in proportions estimated using the standard normal distribution.
[b] Race/ethnic group was collected by study personnel based on fixed categories as selected by the study participants “Mixed race” refers to an individual of mixed European/Colombian native heritage.
[c] Coexisting conditions were determined by self-report.
[d] NEWS-2 is the National Early Warning Score. It includes six physiological measures; total scores range from 0 to 20, with higher scores indicating greater clinical risk. Score of 3 indicates low clinical risk.
[e] Not high-flow nasal oxygen nor mechanical ventilation
[f] Acyclovir, antidiarrheals, antiemetics, antihistamines, antiparasitics, antispasmodics, antitussives, natural or homeopathic medications, proton pump inhibitors, salbutamol.
[g] Oral interferon and colchicine

eTable 2. Clinical Manifestations of Patients at Baseline – Primary Analysis Population

Characteristic n (%)	All Participants (N=398)	Ivermectin (N=200)	Placebo (N=198)
Myalgia	310 (77.9)	156 (78.0)	154 (77.8)
Headache	305 (76.6)	156 (78.0)	149 (75.2)
Fever	172 (43.2)	82 (41.0)	90 (45.5)
Anosmia/hyposmia	223 (56.0)	113 (56.5)	110 (55.6)
Dysgeusia/hypogeusia	199 (50.0)	92 (46.0)	107 (54.0)
Dry cough	181 (45.5)	83 (41.5)	98 (49.5)
Rhinitis	160 (40.2)	83 (41.5)	77 (38.9)
Sore throat	144 (36.2)	80 (40.0)	64 (32.3)
Diarrhea	98 (24.6)	53 (26.5)	45 (22.7)
Dyspnea	52 (13.1)	22 (11.0)	30 (15.1)
Wet cough	30 (7.5)	14 (7.0)	16 (8.1)
Abdominal pain	19 (7.3)	15 (7.5)	14 (7.1)
Vomiting	17 (4.3)	5 (2.5)	12 (6.1)
Skin rash	14 (3.5)	8 (4.0)	6 (3.0)

eTable 3. Comparison of Demographic and Clinical Characteristics between the 75 Patients Receiving Ivermectin who were Excluded from Primary Analysis due to Error During Product Labeling and the Rest of the Cohort

Characteristic	Patients receiving ivermectin during the product-labeling error period (N=75)	Rest of the cohort (N=398)	Differences (95% CI)[a]
Age, median (IQR) – yr	39.0 (28.0 to 51.0)	37.0 (29.0 to 48.0)	2.0 (-0.5 to 9.0)
Sex – No. (%)			
Male	34 (45.3)	167 (41.9)	3.4 (-8.9 to 15.6)
Female	41 (54.7)	231 (58.1)	-3.4 (-15.6 to 8.9)
Race or ethnic group[b] – No. (%)			
Mixed Race	65 (86.7)	357 (89.7)	-3.0 (-11.3 to 5.2)
Black or African American	8 (10.7)	32 (8.0)	2.6 (-4.8 to 10.1)
Native Colombian	2 (2.7)	9 (2.3)	0.4 (-3.5 to 4.3)
History of BCG vaccination – No./n (%)	61/65 (93.8)	367 /394 (93.1)	0.7 (-5.6 to 7.0)
Health Insurance – No. (%)			
Private/semiprivate	62 (82.7)	351 (88.2)	-5.5 (-14.6 to 3.6)
Government subsidized	13 (17.3)	42 (10.8)	6.5 (-2.6 to 15.6)
Uninsured	0 (0.0)	4 (1.0)	-
Number of persons in the same household, Median (IQR)	3 (2-4)	4 (3-4)	-1 (-1 to 0)
Current smoker – No. (%)	3 (4.0)	11 (2.8)	1.2 (-3.5 to 5.9)
Coexisting conditions[c] – No. (%)			
Obesity	18 (24.0)	75 (18.9)	5.1 (-5.3 to 15.5)
Hypertension	6 (8.0)	53 (13.3)	-5.3 (-12.3 to 1.7)
Thyroid disease	5 (6.7)	15 (3.8)	2.9 (-3.0. to 8.8)
Respiratory disease	4 (5.3)	12 (3.0)	2.3 (-3.0 to 7.7)

Diabetes	4 (5.3)	22 (5.5)	-0.2 (-5.7 to 5.4)
Cardiovascular disease	3 (4.0)	7 (1.8)	2.2 (-2.4 to 6.9)
Cerebrovascular disease	0	0	-
Median time (IQR) from symptom onset to randomization – days	6 (5-7)	5 (4-6)	1 (0 to 1)
NEWS2 [d] score at randomization – median (IQR)	2 (1-3)	3 (2-4)	-1 (-1 to 0)
Score on ordinal scale at randomization – No. (%)			
1: Not hospitalized and no limitation of activities	41 (54.7)	232 (58.3)	-3.6 (-15.9 to 8.6)
2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	34 (45.3)	162 (40.7)	4.6 (-7.6 to 16.9)
Characteristic	**Patients receiving ivermectin during the product-labeling error period (N=75)**	**Rest of the cohort (N=398)**	**Differences (95% CI)[c]**
3. Hospitalized, not requiring supplemental oxygen	0	2 (0.5)	-
4. Hospitalized, requiring supplemental oxygen[e]	0	2 (0.5)	-
Clinical Manifestations at Baseline – No. (%)			
Myalgias	55 (73.3)	310 (77.9)	-4.6 (-15.4 to 6.2)
Headache	55 (73.3)	305 (76.6)	-3.3 (-14.1 to 7.5)
Anosmia/hyposmia	50 (66.7)	223 (56.0)	10.6 (-1.1 to 22.4)
Dysgeusia/hypogeusia	44 (58.7)	199 (50.0)	8.7 (-3.5 to 20.1)
Dry cough	42 (56.0)	181 (45.5)	10.5 (-1.7 to 22.8)
Fever	37 (49.3)	172 (43.2)	6.1 (-6.2 to 18.4)

Sore throat	29 (38.7)	144 (36.2)	2.5 (-9.5 to 14.5)
Diarrhea	28 (37.3)	98 (24.6)	12.7 (1.0 to 24.4)
Rhinitis	27 (36.0)	160 (40.2)	-4.2 (-16.1 to 7.7)
Dyspnea	12 (16.0)	52 (13.1)	2.9 (-6.0 to 11.9)
Abdominal pain	8 (10.7)	29 (7.3)	3.4 (-4.0 to 10.8)
Wet cough	5 (6.7)	30 (7.5)	-0.8 (-7.1 to 5.3)
Vomiting	4 (5.3)	17 (4.3)	1.1 (-4.4 to 6.5)
Skin rash	0 (0.0)	14 (3.5)	-3.5 (-5.3 to 1.7)
Medications initiated between symptom onset and enrollment – No. (%)			
NSAIDs	22 (29.3)	118 (29.6)	-3.1 (-11.5 to 10.9)
Other[f]	17 (22.7)	79 (19.8)	2.8 (-7.4 to 13.1)
Other antipyretics	11 (14.7)	49 (12.3)	2.3 (-6.3 to 10.9)
Non-macrolide antibiotics	9 (12.0)	24 (6.0)	6.0 (-1.7 to 13.7)
Macrolides	6 (8.0)	49 (12.3)	-4.3 (-11.2 to 2.6)
Glucocorticoids	1 (1.3)	18 (4.5)	-3.2 (-6.5 to 0.1)
Other immunomodulating agents[g]	0 (0.0)	6 (1.5)	-1.5 (-2.7 to 0.3)
Anticoagulants	0 (0.0)	8 (2.0)	-2.0 (-3.3 to -0.6)

IQR denotates interquartile range and NSAIDs nonsteroidal anti-inflammatory drugs
n = number with available information
[a] 95% confidence interval for difference in medians estimated by bootstrap sampling and for difference in proportions estimated using the standard normal distribution.
[b] Race/ethnic group was collected by study personnel based on fixed categories as selected by the study participants. “Mixed race” refers to an individual of mixed European/Colombian native heritage.
[c] Coexisting conditions were determined by self-report.

[d] NEWS-2 is the National Early Warning Score. It includes six physiological measures; total scores range from 0 to 20, with higher scores indicating greater clinical risk. Score of 3 indicates low clinical risk.
[e] Not high-flow nasal oxygen nor mechanical ventilation
[f] Acyclovir, antidiarrheals, antiemetics, antihistamines, antiparasitics, antispasmodics, antitussives, natural or homeopathic medications, proton pump inhibitors, salbutamol.
[g] Oral interferon and colchicine

eTable 4. Outcomes – As-Treated Population

Characteristic	Ivermectin (N=275)	Placebo (N=198)	Absolute Differences (95% CI)	Effect Estimates (95% CI)
Primary Outcome: Resolution of symptoms[a]				
Time to resolution of symptoms – median no. of days (IQR)	10 (9-13)	12 (9-13)	-2 (-3 to 3)[b]	1.09 (0.90 to 1.32)[c] [p=0.38]
Symptoms resolved at 21 days. No. (%)	232 (84.4)	156 (78.8)	5.57 (-1.56 to 12.71)[d]	1.45 (0.81 to 2.32)[e]
Secondary Outcomes				
Deterioration of 2 or more points in an ordinal 8 points scale,[f] No. (%)	5 (1.8)	7 (3.5)	-1.72 (-4.73 to 1.30)[d]	0.50 (0.16 to 1.62)[e]
Fever since randomization,[g] No. (%)	21 (7.6)	21 (10.6)	-2.97 (-8.28 to 2.34)[d]	0.70 (0.37 to 1.32)[e]
Median duration of febrile episode, days (IQR)	1 (1 to 2.5)	2 (1-3)	-1 (-2.0 to 0)[b]	
Escalation of care since randomization,[h] No. (%)	6 (2.2)	10 (5.0)	-2.87 (-6.37 to 0.64)[d]	0.42 (0.15 to 1.17)[e]
Median duration[i], days (IQR)	6.5 (4.5-21.0)	6 (3.7-10.7)	0.5 (-5.0 to 15.5)[b]	
Escalation of care occurring 12 or more hours since randomization,[h] No. (%)	6 (2.2)	6 (3.0)	-0.8 (-3.79 to 2.09)[d]	0.71 (0.23 to 2.25)[e]
Median duration[i], days (IQR)	6.5 (4.5-21)	8 (4.2-13.2)	-1.5 (-7.5 to 15.5)[b]	
Emergency department visits or telemedicine consultations, No. of patients (%)	22 (8.0)	13 (6.6)	1.43 (-3.27 to 6.14)[d]	1.24 (0.58 to 2.61)[e]
Deaths, No. (%)	0	1 (0.5)		

[a] Resolution of Symptoms was defined as the first day free of symptoms.
[b] Absolute Difference is the median difference with 95% confidence intervals estimated by bootstrap sampling.
[c] Hazard ratio for resolution of symptoms was estimated by the Cox proportional-hazard model. The P value for this ratio was calculated with the log-rank test.
[d] Absolute Difference is the difference in proportions.
[e] Effect estimate is odds ratio (2-sided 95% CI) from a logistic model.
[f] Ordinal scale: 0 = no clinical evidence of infection; 1 = not hospitalized and no limitation of activities; 2 = not hospitalized, with limitation of activities, home oxygen requirement, or both; 3 = hospitalized, not requiring supplemental oxygen; 4 = hospitalized, requiring supplemental oxygen; 5 = hospitalized, requiring nasal high-flow oxygen, non-invasive mechanical ventilation, or both; 6 = hospitalized, requiring ECMO, invasive mechanical ventilation, or both; 7 = death.
[g] Fever defined as an axillary temperature ≥ 38 °C. Patients took their own temperatures while at home.
[h] Escalation of care defined as new-onset hospitalization in the general ward or intensive care unit, or new-onset supplementary oxygen requirement for more than 24 hours
[i] Number of days that patients required hospitalization or supplementary oxygen. If both were required, the longer duration was recorded.

eTable 5. Ordinal Scale Measure by Treatment Group and Study Visit – Primary Analysis Population

		All (N=398)			Ivermectin (N=200)			Placebo (N=198)		
Study Visit	**Ordinal Scale Measure**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Day 2	0: No Symptoms	10	2.5	1.3–4.6	6	3.0	1.3–6.5	4	2.0	0.8–5.3
	1: Not hospitalized and no limitation of activities	221	55.5	50.6–60.4	112	56.0	49.0–62.7	109	55.0	48.0–61.9
	2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	157	39.4	34.7–44.3	79	39.5	32.9–46.5	78	39.4	32.8–46.4
	3. Hospitalized, not requiring supplemental oxygen	3	0.7	0.2–2.3	1	0.5	0.1–3.5	2	1.0	0.2–4.0
	4. Hospitalized, requiring supplemental oxygen	6	1.5	0.7–3.3	1	0.5	0.1–3.5	5	2.5	1.0–5.9
	5. Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	1	0.2	0.0–1.8	1	0.5	0.1–3.5	0	0	NA
	6. Hospitalized, requiring ECMO, invasive mechanical ventilation, or both	0	0	NA	0	0	NA	0	0	NA
	7. Death	0	0	NA	0	0	NA	0	0	NA
	Odds Ratio [95%CI]	**1.13 [0.77–1.67]**								
Day 5	0: No Symptoms	83	20.8	17.1–25.1	43	21.5	16.3–27.7	40	20.2	15.2–26.4
	1: Not hospitalized and no limitation of activities	198	49.7	44.8–54.7	102	51.0	44.1–57.9	96	48.5	41.6–55.4
	2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	108	27.1	23.0–31.7	52	26.0	20.4–32.5	56	28.3	22.4–35.0
	3. Hospitalized, not requiring supplemental oxygen	1	0.2	0.0–1.8	0	0	NA	1	0.5	0.1–3.5

	4. Hospitalized, requiring supplemental oxygen	4	1.0	0.4–2.6	1	0.5	0.1–3.5	3	1.5	0.5–4.6
		All (N=398)			**Ivermectin (N=200)**			**Placebo (N=198)**		
	Ordinal Scale Measure	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
	5. Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	2	0.5	0.1–2.0	1	0.5	0.1–-3.5	1	0.5	0.1–3.5
	6. Hospitalized, requiring ECMO, invasive mechanical ventilation, or both	2	0.5	0.1–2.0	1	0.5	0.1–3.5	1	0.5	0.1–3.5
	7. Death	0	0	NA	0	0	NA	0	0	NA
	Odds Ratio [95%CI]	**1.16 [0.80–1.68]**								
Day 8	0: No Symptoms	147	36.9	32.3–41.8	74	37.0	30.6–43.9	73	36.9	30.4–43.8
	1: Not hospitalized and no limitation of activities	191	48.0	43.1–52.9	96	48.0	41.1–54.9	95	48.0	41.1–54.9
	2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	52	13.1	10.1–16.8	26	13.0	9.0–18.4	26	13.1	9.1–18.6
	3. Hospitalized, not requiring supplemental oxygen	0	0	NA	0	0	NA	0	0	NA
	4. Hospitalized, requiring supplemental oxygen	4	1.0	0.4–2.6	2	1.0	0.2–3.9	2	1.0	0.2–4.0
	5. Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	2	0.5	0.1–2.0	1	0.5	0.1–3.5	1	0.5	0.1–3.5
	6. Hospitalized, requiring ECMO, invasive mechanical ventilation, or both	2	0.5	0.1–2.0	1	0.5	0.1–3.5	1	0.5	0.1–3.5
	7. Death	0	0	NA	0	0	NA	0	0	NA
	Odds Ratio [95%CI]	**1.01 [0.69–1.46]**								

Day 11	0: No Symptoms	197	49.5	44.6–54.4	102	51.0	44.1–57.9	95	48.0	41.1–54.9
	1: Not hospitalized and no limitation of activities	168	42.2	37.4–47.1	82	41.0	34.4–48.0	86	43.4	36.7–50.4
		All (N=398)			**Ivermectin (N=200)**			**Placebo (N=198)**		
	Ordinal Scale Measure	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95%CI**
	2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	26	6.5	4.5–9.4	11	5.5	3.1–9.7	15	7.6	4.6–12.2
	3. Hospitalized, not requiring supplemental oxygen	2	0.5	0.1–2.0	2	1.0	0.2–3.9	0	0	NA
	4. Hospitalized, requiring supplemental oxygen	3	0.7	0.2–2.3	2	1.0	0.2–3.9	1	0.5	0.1–3.5
	5. Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	1	0.2	0.0–1.8	0	0	NA	1	0.5	0.1–3.5
	6. Hospitalized, requiring ECMO, invasive mechanical ventilation, or both	1	0.2	0.0–1.8	1	0.5		0	0	NA
	7. Death	0	0	NA	0	0	NA	0	0	NA
	Odds Ratio [95%CI]	**1.11 [0.76–1.63]**								
Day 15	0: No Symptoms	246	61.8	56.9–66.5	126	63.0	56.1–69.4	120	60.6	53.6–67.2
	1: Not hospitalized and no limitation of activities	139	34.9	30.4–39.8	67	33.5	27.3–40.3	72	36.4	29.9–43.3
	2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	9	2.3	1.2–4.3	5	2.5	1.0–5.9	4	2.0	0.8–5.3
	3. Hospitalized, not requiring supplemental oxygen	1	0.2	0.0–1.8	1	0.5	0.1–3.5	0	0.0	NA
	4. Hospitalized, requiring supplemental oxygen	1	0.2	0.0–1.8	0	0	NA	1	0.50	0.1–3.5

	5. Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	0	0	NA	0	0	NA	0	0	NA
	6. Hospitalized, requiring ECMO, invasive mechanical ventilation, or both	1	0.2	0.0–1.8	1	0.5	0.1–3.5	0	0	NA
	7. Death	1	0.2	0.0–1.8	0	0	NA	1	0.5	0.1–3.5
	Odds Ratio [95%CI]	**1.09 [0.73–1.63]**								
		All (N=398)			**Ivermectin (N=200)**			**Placebo (N=198)**		
	Ordinal Scale Measure	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Day 21	0: No Symptoms	320	80.4	76.2–84.0	164	82.0	76.0–86.7	156	78.8	72.5–83.9
	1: Not hospitalized and no limitation of activities	69	17.3	13.9–21.4	32	16.0	11.5–21.8	37	18.7	13.8–24.7
	2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	6	1.5	0.7–3.3	2	1.0	0.2–3.9	4	2.0	0.8-5.3
	3. Hospitalized, not requiring supplemental oxygen	0	0	NA	0	0	NA	0	0	NA
	4. Hospitalized, requiring supplemental oxygen	0	0	NA	0	0	NA	0	0	NA
	5. Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	0	0	NA	0	0	NA	0	0	NA
	6. Hospitalized, requiring ECMO, invasive mechanical ventilation, or both	2	0.5	0.1–2.0	2	1.0	0.2–3.9	0	0	NA
	7. Death	1	0.2	0.0–1.8	0	0	NA	1	0.5	0.1–3.5
	Odds Ratio [95%CI]	**1.23 [0.75–2.01]**								

N = Number of Participants in the Primary Analysis Population.
n = Number of participants with the respective score

eTable 6. Ordinal Scale Measure by Treatment Group and Study Visit – As-Treated Population

		All (N=473)			Ivermectin (N=275)			Placebo (N=198)		
Study Visit	**Ordinal Scale Measure**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Day 2	0: No Symptoms	10	2.1	1.1–3.9	6	2.2	0.9–4.8	4	2.0	0.8–5.3
	1: Not hospitalized and no limitation of activities	268	56.7	52.1–61.1	159	57.8	51.9–63.5	109	55.0	48.0–61.9
	2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	185	39.1	34.8–43.6	107	38.9	33.3–44.8	78	39.4	32.8–46.4
	3. Hospitalized, not requiring supplemental oxygen	3	0.6	0.2–1.9	1	0.4	0.0–2.6	2	1.0	0.2–4.0
	4. Hospitalized, requiring supplemental oxygen	6	1.3	0.6–2.8	1	0.4	0.0–2.6	5	2.5	1.0–5.9
	5. Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	1	0	0.0–1.5	1	0.4	0.0–2.6	0	0	NA
	6. Hospitalized, requiring ECMO, invasive mechanical ventilation, or both	0	0	NA	0	0	NA	0	0	NA
	7. Death	0	0	NA	0	0	NA	0	0	NA
	Odds Ratio [95%CI]	**1.17 [0.81–1.68]**								
Day 5	0: No Symptoms	93	19.7	16.3–23.5	53	19.3	15.0–24.4	40	20.2	15.2–26.4
	1: Not hospitalized and no limitation of activities	245	51.8	47.3–56.3	149	54.2	48.2–60.0	96	48.5	41.6–55.4
	2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	125	26.4	22.6–30.6	69	25.1	20.3–30.6	56	28.3	22.4–35.0
	3. Hospitalized, not requiring supplemental oxygen	1	0.2	0.0–1.5	0	0	NA	1	0.5	0.1–3.5
		All			**Ivermectin**			**Placebo**		

		(N=473)			(N=275)			(N=198)		
	Ordinal Scale Measure	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
	4. Hospitalized, requiring supplemental oxygen	5	1.1	0.4–2.5	2	0.7	0.2–2.9	3	1.5	0.5–4.6
	5. Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	2	0.4	0.1–1.7	1	0.4	0.0–2.6	1	0.5	0.1–3.5
	6. Hospitalized, requiring ECMO, invasive mechanical ventilation, or both	2	0.4	0.1–1.7	1	0.4	0.0–2.6	1	0.5	0.1–3.5
	7. Death	0	0	NA	0	0	NA	0	0	NA
	Odds Ratio [95%CI]	**1.13 [0.80–1.61]**								
Day 8	0: No Symptoms	175	37.0	32.7–41.5	102	37.1	31.6–43.0	73	36.9	30.4–43.8
	1: Not hospitalized and no limitation of activities	231	48.8	44.3–53.3	136	49.4	43.6–55.4	95	48.0	41.1–54.9
	2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	57	12.0	9.4–15.3	31	11.3	8.0–15.6	26	13.1	9.1–18.6
	3. Hospitalized, not requiring supplemental oxygen	2	0.4	0.1–1.7	2	0.7	0.2–2.9	0	0	NA
	4. Hospitalized, requiring supplemental oxygen	4	0.8	0.3–2.2	2	0.8	0.2–2.9	2	1.0	0.2–4.0
	5. Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	2	0.4	0.1–1.7	1	0.4	0.0–2.6	1	0.5	0.1–3.5
	6. Hospitalized, requiring ECMO, invasive mechanical ventilation, or both	2	0.4	0.1–1.7	1	0.4	0.0–2.6	1	0.5	0.1–3.5
	7. Death	0	0	NA	0	0	NA	0	0	NA
	Odds Ratio [95%CI]	**1.04 [0.74–1.48]**								
Day 11	0: No Symptoms	231	48.8	44.3–53.3	136	49.4	41.1–54.9	95	48.0	41.1–54.9
		All (N=473)			**Ivermectin (N=275)**			**Placebo (N=198)**		
	Ordinal Scale Measure	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**

	1: Not hospitalized and no limitation of activities	206	43.5	39.1–48.1	120	43.6	37.9–49.6	86	43.4	36.7–50.4
	2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	29	6.1	4.3–8.7	14	5.1	3.0–8.4	15	7.6	4.6–12.2
	3. Hospitalized, not requiring supplemental oxygen	2	0.4	0.1–1.7	2	0.7	0.2–2.9	0	0	NA
	4. Hospitalized, requiring supplemental oxygen	3	0.6	0.2–1.9	2	0.7	0.2–2.9	1	0.5	0.1–3.5
	5. Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	1	0.2	0.0–1.5	0	0	NA	1	0.5	0.1–3.5
	6. Hospitalized, requiring ECMO, invasive mechanical ventilation, or both	1	0.2	0.0–1.5	1	0.4	0.0–2.6	0	0	NA
	7. Death	0	0	NA	0	0	NA	0	0	NA
	Odds Ratio [95%CI]	**1.08 [0.76–1.54]**								
Day 15	0: No Symptoms	286	60.5	56.0–64.8	166	60.4	54.4–66.0	120	60.6	53.6–67.2
	1: Not hospitalized and no limitation of activities	174	36.8	32.5–41.2	102	37.1	31.6–43.0	72	36.4	29.9–43.3
	2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	9	1.9	1.0–3.6	5	1.8	0.8–4.3	4	2.0	0.8–5.3
	3. Hospitalized, not requiring supplemental oxygen	1	0.2	0.0–1.5	1	0.4	0.0–2.6	0	0.0	NA
	4. Hospitalized, requiring supplemental oxygen	1	0.2	0.0–1.5	0	0.0	NA	1	0.50	0.1–3.5
	5. Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	0	0	NA	0	0	NA	0	0	NA
		All (N=473)			**Ivermectin (N=275)**			**Placebo (N=198)**		
	Ordinal Scale Measure	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
	6. Hospitalized, requiring ECMO, invasive mechanical ventilation, or both	1	0.2	0.0–1.5	1	0.4	0.0–2.6	0	0	NA

	7. Death	1	0.2	0.0–1.5	0	0	NA	1	0.5	0.1–3.5
	Odds Ratio [95%CI]	**1.00 [0.69–1.45]**								
Day 21	0: No Symptoms	388	82.0	78.3–85.2	232	84.4	79.6–88.2	156	78.8	72.5–83.9
	1: Not hospitalized and no limitation of activities	76	16.1	13.0–-19.7	39	14.2	10.5–18.8	37	18.7	13.8–24.7
	2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	6	1.3	0.6-2.8	2	0.7	0.2–2.9	4	2.0	0.8–5.3
	3. Hospitalized, not requiring supplemental oxygen	0	0	NA	0	0	NA	0	0	NA
	4. Hospitalized, requiring supplemental oxygen	0	0	NA	0	0	NA	0	0	NA
	5. Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	0	0	NA	0	0	NA	0	0	NA
	6. Hospitalized, requiring ECMO, invasive mechanical ventilation, or both	2	0.4	0.1–1.7	2	0.7	0.2–2.9	0	0	NA
	7. Death	1	0.2	0.0–-1.5	0	0	NA	1	0.5	0.1–3.5
	Odds Ratio [95%CI]	**1.46 [0.91–2.34]**								

N = Number of Participants in the As-Treated Population.
n = Number of participants with the respective score.

eTable 7. Summary of Adverse Events – As-Treated Population

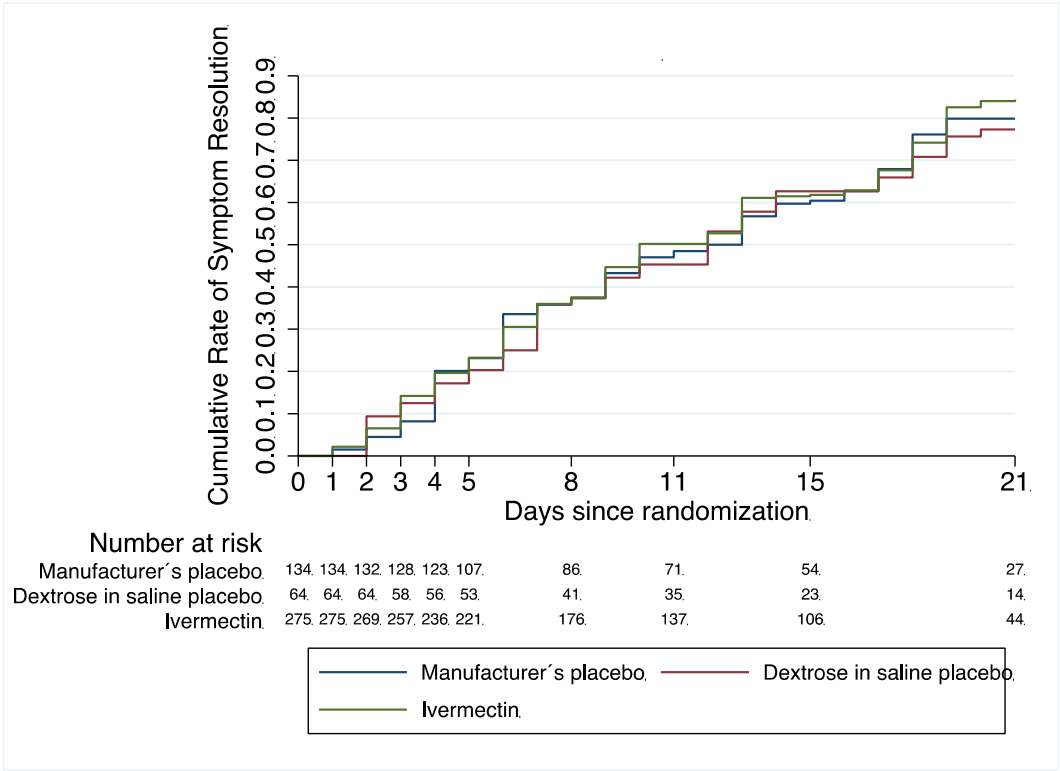
Event	Ivermectin (N=275)	Placebo (N=198)
	Any Grade[a]	Any Grade[a]
Solicited Adverse Events[b]		
Headache, No. (%)	140 (50.9)	111 (56.1)
Median duration, Days (IQR)	2 (1-5)	2 (1-5)
Dizziness, No. (%)	98 (35.6)	68 (34.3)
Median duration, Days (IQR)	2 (1-4)	2 (1-3.7)
Diarrhea, No. (%)	83 (30.2)	65 (32.8)
Median duration, Days (IQR)	2 (1-4)	2 (1-3)
Nausea, No. (%)	66 (24.0)	47 (23.7)
Median duration, Days (IQR)	1 (1-3)	2 (1-4)
Abdominal pain, No. (%)	55 (20.0)	49 (24.7)
Median duration, Days (IQR)	2 (1-4)	2 (1-3)
Disturbances of vision, No. (%)	44 (16.0)	28 (14.1)
Median duration, Days (IQR)	2 (1-3)	2 (1-4.7)
Photophobia, No. (%)	9 (3.3)	4 (2.0)
Blurry Vision, No. (%)	31 (11.3)	23 (11.6)
Reduction in visual acuity, No. (%)	5 (1.8)	2 (1.0)
Skin rash, No. (%)	17 (6.2)	19 (9.6)
Median duration, Days (IQR)	4 (3-7)	4 (1-8)
Tremor, No. (%)	17 (6.2)	6 (3.0)
Median duration, Days (IQR)	1 (1-7)	3.5 (1-6.5)
Skin Discoloration, No. (%)	13 (6.5)	4 (2.0)
Median duration, Days (IQR)	3 (1.7-5.2)	4 (2.5-13)
Swelling, No. (%)	7 (2.5)	3 (1.5)
Median duration, Days (IQR)	2 (1-4)	1 (1-1)
Vomiting, No. (%)	6 (2.2)	6 (3.0)
Median duration, Days (IQR)	1 (1-3)	1 (1-1.5)
Number of patients with one or more solicited adverse Events, No. (%)	211 (76.7)	161 (81.3)
Adverse Events Leading to Treatment Discontinuation, No. (%)	20 (7.3)	5 (2.5)

eTable 7. Summary of Adverse Events – As-Treated Population (continued)

Event	Ivermectin (N=275)	Placebo (N=198)
	Any Grade[a]	Any Grade[a]
Serious Adverse Events[c], No. (%)		
Respiratory Failure	2 (0.7)	1 (0.5)
Acute Kidney Injury[d]	2 (0.7)	1 (0.5)
Multi-organ failure[e]	2 (0.7)	2 (1.0)
Gastrointestinal Hemorrhage	2 (0.7)	0 (0)
Sepsis[f]	1 (0.4)	1 (0.5)
Number of patients with one or more Serious Adverse Event, No. (%)	2 (0.7)	2 (1.0)

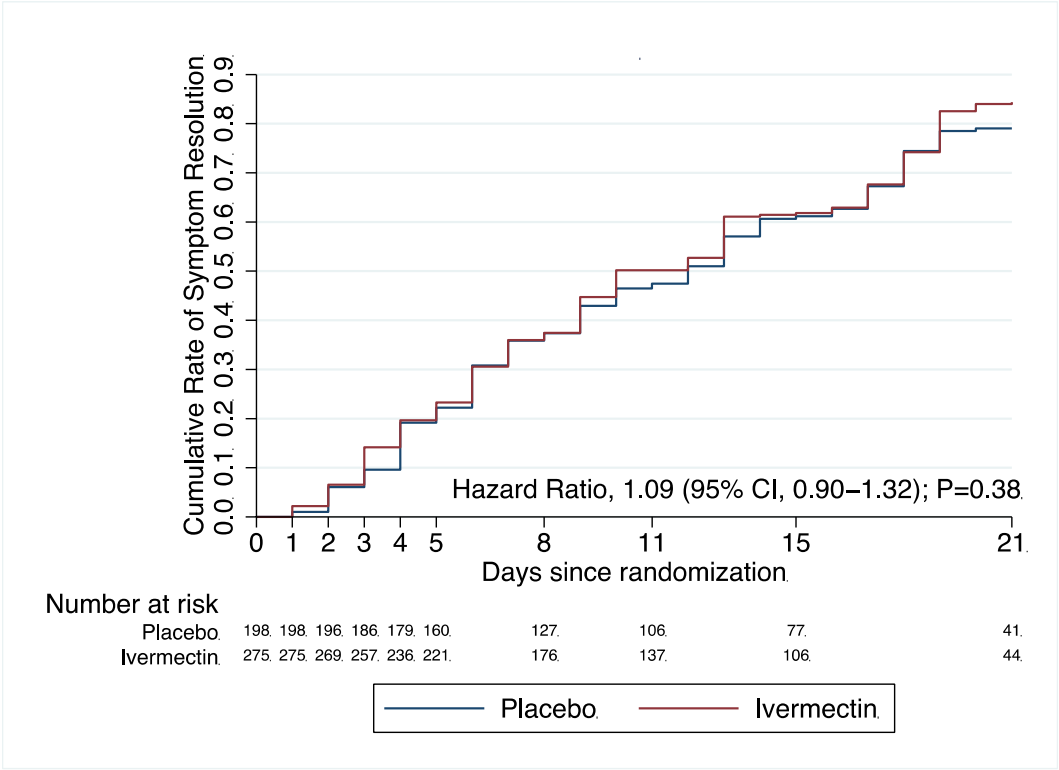
IQR denotates interquartile range.
[a] Grade refers to the severity of the adverse event determined according to the following: Grade 1 Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. Grade 2 Moderate; minimal, local or noninvasive intervention indicated; limiting age- appropriate instrumental activities of daily living (ADL). Grade 3 Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL. Grade 4 Life-threatening consequences; urgent intervention indicated. Grade 5 Death related to AE.
Grade 3 solicited adverse events: Headache, N=1 in the placebo group, duration of 6 days. Dizziness, N=1 in the ivermectin group, duration of 6 days; N=3 in the placebo group, median duration of 2 days (IQR, 1-8). Skin rash, N=2 in the ivermectin group, median duration of 8 days (IQR, 7-9). No grade 4 events occurred.
[b] Adverse Events were solicited by phone at each follow-up call.
[c] Serious adverse events were severe, medically significant or life-threatening conditions occurring in study patients documented from revision of patient´s electronic medical records. All were grade 3 or 4, except 1 patient in the placebo group who had grade 5 respiratory failure, acute kidney injury, multi-organ failure and sepsis.
[d] A disorder characterized by the acute loss of renal function
[e] A disorder characterized by progressive deterioration of the lungs, liver, kidney and clotting mechanisms.
[f] A disorder characterized by the presence of pathogenic microorganisms in the blood stream.

eFigure 1. Time to Resolution of Symptoms – As-Treated Population According to the Type of Placebo



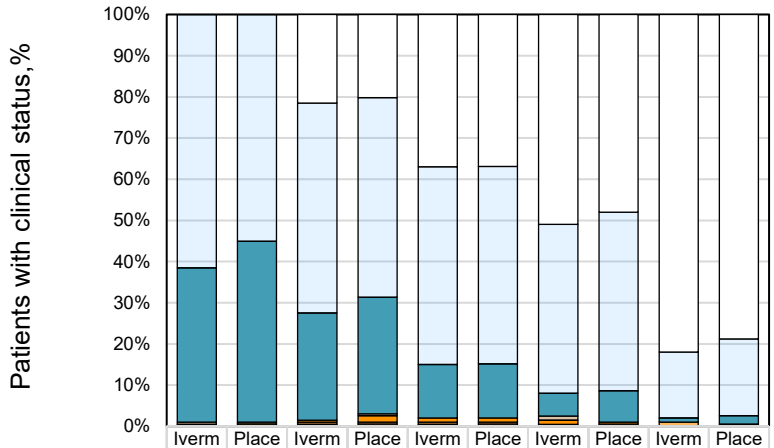
The cumulative rate of symptom resolution is the percentage of patients who experienced their first day free of symptoms. Hazard ratio of symptom resolution in the ivermectin vs. dextrose in saline placebo group: 1.14 (95% CI, 0.83-1.55); hazard ratio of symptom resolution in the ivermectin vs. manufacturer's placebo: 1.07 (95% CI 0.85-1.34).

eFigure 2. Time to Resolution of Symptoms – As-Treated Population



The cumulative rate of symptom resolution is the percentage of patients who experienced their first day free of symptoms.

eFigure 3. Clinical Status on an 8-Point Ordinal Scale on Study Days 5, 8, 11 and 21 by Treatment Group – Primary Analysis Population



	Day 0		Day 5		Day 8		Day 11		Day 21	
	Iverm ectin	Place bo	Iverm ectin	Place bo	Iverm ectin	Place bo	Iverm ectin	Place bo	Iverm ectin	Place bo
No Symptoms	0.0%	0.0%	21.5%	20.2%	37.0%	36.9%	51.0%	48.0%	82.0%	78.8%
Not hospitalized, no limitation in activity	61.5%	55.1%	51.0%	48.5%	48.0%	48.0%	41.0%	43.4%	16.0%	18.7%
Not hospitalized, limitation in activity, home oxygen requirement or both	37.5%	43.9%	26.0%	28.3%	13.0%	13.1%	5.5%	7.6%	1.0%	2.0%
Hospitalized without oxygen	0.5%	0.5%	0.0%	0.5%	0.0%	0.0%	1.0%	0.0%	0.0%	0.0%
Hospitalized with oxygen	0.5%	0.5%	0.5%	1.5%	1.0%	1.0%	1.0%	0.5%	0.0%	0.0%
Noninvasive ventilation or high-flow nasal cannula	0.0%	0.0%	0.5%	0.5%	0.5%	0.5%	0.0%	0.5%	0.0%	0.0%
Invasive mechanical ventilation or ECMO	0.0%	0.0%	0.5%	0.5%	0.5%	0.5%	0.5%	0.0%	1.0%	0.0%
Death	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.5%

Day 5: OR [95%CI]: 1.16 [0.80-1.68]
Day 8: OR [95%CI]: 1.01 [0.69-1.46]
Day 11: OR [95%CI]: 1.11 [0.76-1.63]
Day 21: OR [95%CI]: 1.23 [0.75-2.01]

Odds ratios greater than 1 indicate benefit with ivermectin. All percentage values and their 95% confidence intervals in each category are provided in eTable 5.