### S5 Table. Trial Characteristics: Treatment Groups, Participant Assessment, and Inclusion/Exclusion Criteria

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<th>Trial (blinding)</th>
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| ORCHID NCT04332991, Vanderbilt University, Massachusetts General, and PETAL Network (Blinded) [1] | 510 hospitalized participants | ≥18 years    | 2                | 5 days          | **HCQ**: Days 1-2 400 mg twice daily; Days 3-10 200 mg twice daily; **Placebo**: Matching placebo enterally twice daily matching the dosing regimen for HCQ | 12 months (Daily assessments Days 1-5, 8, 15, and 29, Months 3, 6, and 12) | • Age ≥18 years  
• Currently hospitalized or in an emergency department with anticipated hospitalization.  
• Symptoms of acute respiratory infection, defined as one or more of the following:  
  a. Cough  
  b. Fever (>37.5° C / 99.5° F)  
  c. Shortness of breath (operationalized as any of the following: subjective shortness of breath reported by patient or surrogate; tachypnea with respiratory rate ≥22/minute; hypoxemia, defined as SpO2 <92% on room air, new receipt of supplemental oxygen to maintain SpO2 ≥92%, or increased supplemental oxygen to maintain SpO2 ≥92% for a patient on chronic oxygen therapy).  
  d. Sore throat  
• Laboratory-confirmed SARS-CoV-2 infection within the past 10 days prior to randomization | • Prisoner  
• Pregnancy  
• Breast feeding  
• Unable to randomize within 10 days after onset of acute respiratory infection symptoms  
• Unable to randomize within 48 hours after hospital arrival  
• Seizure disorder  
• Porphyria cutanea tarda  
• QTc >500 ms on electrocardiogram within 72 hours prior to enrollment  
• Diagnosis of Long QT syndrome  
• Known allergy to hydroxychloroquine, chloroquine, or amodiaquine  
• Receipt in the 12 hours prior to enrollment, or planned administration during the 5-day study period that treating clinicians feel cannot be substituted for another medication, of any of the following:  
  ◦ amiodarone; cimetidine; dofetilide; phenobarbital; phenytoin; sotalol  
• Receipt of >1 dose of hydroxychloroquine or chloroquine in the 10 days prior to enrollment  
• Inability to receive enteral medications  
• Refusal or inability to be contacted on Day 15 for clinical outcome assessment if discharged prior to Day 15  
• Previous enrollment in this trial  
• The treating clinical team does not believe equipoise exists regarding the use of hydroxychloroquine for the treatment of this patient |
| WU352 NCT04341727, Washington University (Open-label) | 500 non-ventilated hospitalized participants expected; 30 participants | ≥18 years    | 4                | 5 days          | **HCQ**: Day 1 400 mg twice daily; Days 2-5 200 mg twice daily  
**HCQ + AZM**: HCQ: Day 1 400 mg twice daily; Days 2-6 weeks (Daily assessments Days 1-14, Weeks 3, 4, 5, and 6) | Hospitalization for management of SARS CoV-2 infection  
• Positive SARS CoV-2 test  
• Age ≥18 years  
• Provision of informed consent | • Contraindication or allergy to chloroquine, hydroxychloroquine or azithromycin  
• Current use hydroxychloroquine, chloroquine or azithromycin  
• Concurrent use of another investigational agent  
• Invasive mechanical ventilation |
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| NCT04335552, Duke University (Open-label) | 500 hospitalized participants | ≥12 years or older | 2 | 5 days | **Arm 1**: Supportive care alone  
**Arm 2**: Supportive care + HCQ (Day 1 800 mg once; Days 2-5 600 mg once daily)  
**Arm 3**: Supportive care + AZM (Day 1 500 mg once; Days 2-5 250 mg once daily)  
**Arm 4**: Supportive care + HCQ (Day 1 45 days (Daily assessment Days 1-14, 28, and 45)) | • Electrocardiogram (ECG) ≤48 hours prior to enrollment  
• Complete blood count, glucose-6 phosphate-dehydrogenase (G6PD), comprehensive metabolic panel and magnesium ≤48 hours prior to enrollment from standard of care  
• If participating in sexual activity that could lead to pregnancy, individuals of reproductive potential who can become pregnant must agree to use contraception throughout the study. At least one of the following must be used throughout the study:  
  ◦ Condom (male or female) with or without spermicide  
  ◦ Diaphragm or cervical cap with spermicide  
  ◦ Intrauterine device (IUD)  
  ◦ Hormone-based contraceptive | • Participants who have any severe and/or uncontrolled medical conditions such as: unstable angina pectoris; symptomatic congestive heart failure; myocardial infarction; cardiac arrhythmias or known prolonged QTc >470 males, >480 female on ECG; pulmonary insufficiency; epilepsy (interaction with chloroquine)  
• Prior retinal eye disease  
• Concurrent malignancy requiring chemotherapy  
• Known Chronic Kidney disease, eGFR<10 or dialysis  
• G-6-PD deficiency, if unknown requires G6PD testing prior to enrollment  
• Known Porphyria  
• Known myasthenia gravis  
• Currently pregnant or planning on getting pregnant while on study  
• Breast feeding  
• AST/ALT >five times the upper limit of normal ULN  
• Bilirubin >five times the UL  
• Magnesium <1.4 mEq/L  
• Calcium <8.4mg/dL >10.6mg/dL  
• Potassium <3.3 >5.5 mEq/L  
• Current concomitant use of contraindicated drugs including antiarrhythmics, antidepressant, anticonvulsants | • Participants who have any severe and/or uncontrolled medical conditions such as: unstable angina pectoris; symptomatic congestive heart failure; myocardial infarction; cardiac arrhythmias or known prolonged QTc >470 males, >480 female on ECG; pulmonary insufficiency; epilepsy (interaction with chloroquine)  
• Prior retinal eye disease  
• Concurrent malignancy requiring chemotherapy  
• Known Chronic Kidney disease, eGFR<10 or dialysis  
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<td>TEACH NCT04369742, New York University (Blinded) [2]</td>
<td>626 hospitalized adult and pediatric participants</td>
<td>&gt;0 2 5 days</td>
<td><strong>HCQ</strong>: Day 1 400 mg twice daily; Days 2-5 200 mg twice daily</td>
<td><strong>Placebo</strong>: Day 1 calcium citrate 400 mg twice daily; Days 2-5 200 mg twice daily</td>
<td>30 days (Baseline, End of treatment, Days 6, 14, and 30)</td>
<td>• Hospitalized with symptoms consistent with COVID-19 including but not limited to any of the following: fever (documented or subjective), cough, dyspnea, diarrhea, nausea, diffuse myalgias, and/or anosmia&lt;br&gt;• Informed consent signed by patient (if ≥18 years old) or parent (if &lt;18 years old). Additionally, assent will be obtained from children ages 7 and older who are capable of providing assent. Adults who are unable to provide informed consent may be consented by legally authorized representative (see 13.3.3).</td>
<td>• Presence of the primary endpoint (ICU admission, mechanical ventilation, ECMO, and/or vasopressor requirement) at time of randomization.&lt;br&gt;• Treatment with CQ or CQ within the 30 days prior to the start of the study drug treatment.&lt;br&gt;• Unable to take oral medications.&lt;br&gt;• History of allergic reaction or intolerance to CQ or CQ.&lt;br&gt;• Baseline corrected QTc interval (&gt;500 milliseconds, gender neutral) history of congenital QTc prolongation, and/or history of cardiac arrest.&lt;br&gt;• Concomitant therapy with flecainide, amiodarone, digoxin, procainamide, propafenone, thioridazine, or pimozide&lt;br&gt;• History of retinal disease including a documented history of diabetic retinopathy.</td>
<td>• Death anticipated within 48 hours of enrollment&lt;br&gt;• Inability to obtain informed consent from the patient or designated medical decision maker</td>
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<td>COVID MED NCT04328012, Bassett Medical Center (Blinded)</td>
<td>4,000 hospitalized participants</td>
<td>≥18 years</td>
<td>4</td>
<td>Up to 14 days</td>
<td>Arm 1: standard care and lopinavir/ritonavir: Dosing: 400 mg/100 mg twice daily for 5-14 days Arm 2: standard care and HCQ: Day 1 400 mg twice daily; Days 2-14 200 mg twice daily Arm 3: standard care and losartan •Losartan 25 mg once daily for 5-14 days •Placebo (Tic Tacs in blank capsules) once daily for 5-14 days to replicate/control for 'bid dosing' Arm 4: standard care and HCQ</td>
<td>60 days (Baseline, Day 1-7, Day 14, Day 30, Day 60)</td>
<td>• Positive SARS-CoV-2 RT-PCR testing (nasopharyngeal, oropharyngeal, sputum and/or bronchoalveolar lavage) The testing may: □ Occur up to ≤72h prior to informed consent of participation in the study □ Be undertaken either on-site or in an external laboratory certified by New York State to run testing for SARS-CoV-2</td>
<td>• Known history of G6PD deficiency. Pediatric Exclusion Criteria: □ Baseline QTc &gt;470 ms in males, &gt;480 ms in females (post puberty) or QTc &gt;460 ms in males, &gt;470 ms in females (pre puberty) □ History of congenital QT prolongation (LQTS) and/or history of cardiac arrest. □ Family history of LQTS □ Presence of Concomitant therapy QT prolongation: Medications will be checked against a list on <a href="http://www.CredibleMeds.com">www.CredibleMeds.com</a>, and those on concomitant medications with significant QT-prolonging potential will be excluded □ Basic metabolic panel (BMP) not performed within 72 hours of enrollment □ Presence of uncorrected hypokalemia (&lt;3.4 mmol/L), hypocalcemia (&lt;9.0 mg/dL, and/or hypomagnesemia (&lt;1.7 mg/dL) on most recent BMP (within 72 hours of enrollment).</td>
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<td>HAHPS NCT04329832, Intermountain Health Care (Open-label) [3,4]</td>
<td>300 hospitalized participants</td>
<td>≥18 years</td>
<td>2</td>
<td>5 days</td>
<td>HCQ: Day 1 400 mg twice daily; Days 2-5 200 mg twice daily AZM: Day 1 500 mg once; Days 2-5 250 mg once daily</td>
<td>6 months (Daily assessments Days 1-7 and 14, Month 6)</td>
<td>Adult (age ≥18 years) Confirmed OR suspected COVID-19 Confirmed: Positive assay for COVID-19 within the last 10 days Suspected: Pending assay for COVID-19 WITH high clinical suspicion Scheduled for admission or already admitted to an inpatient bed</td>
<td>• Recent malaria exposure (within 1 month) • History or current cardiac diseases (heart failure, ventricular arrhythmias, LBBB or RBBB, QTc prolongation) • History of retinopathy • Severe hypoglycemia • Auditory disorders • Known G6PD deficiency • Porphyria or psoriasis • Severe active alcohol use disorder • Seizure disorder • Co-administration of hepatotoxic agents • Co-administration with certain drugs due to CYP3A interactions if taken in &lt;24 hr</td>
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<td>NCT04344444, University Medical Center New Orleans (Open-label)</td>
<td>600 hospitalized participants</td>
<td>≥18 years</td>
<td>3</td>
<td>5 days</td>
<td>Control: Supportive Care Only HCQ: Day 1 400 mg twice daily; Days 2-5 200 mg twice daily HCQ + AZM: HCQ: Day 1 400 mg twice daily; Days 2-5 200 mg twice daily; AZM: Day 1 500 mg once; Days 2-5 250 mg daily</td>
<td>30 days (Daily assessments Days 1-14, and 30)</td>
<td>• Age greater than 18 years</td>
<td>• Unable to obtain informed consent • Prior enrollment in this study</td>
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<td>OAHU-COVID19, NCT04345692, Queen's Medical Center -Honolulu (Open-label)</td>
<td>350 hospitalized participants</td>
<td>18-95 years</td>
<td>2</td>
<td>5 days</td>
<td>Usual Care + HCQ: Day 1 400 mg twice daily; Days 2-5 200 mg twice daily Usual care</td>
<td>BL, Days 3, 5, 8, 11, and 28</td>
<td>• Oxygen saturation of &gt;94% on room air with defined risk factors consistent with moderate disease OR oxygen saturation of &lt;94% on room air consistent with severe disease • Ability and willingness to comply with study procedures</td>
<td>• QTc greater than 450 milliseconds on screening EKG or telemetry • Pregnant or lactating women • Inability to take oral pills or inability to use a feeding tube • Inability to obtain informed consent either from the patient or from the next of kin if patient is incapacitated. For the purpose of this study obtaining a verbal consent from a family member on the phone with a witness will be considered acceptable since there is a “no visitor” policy in force at hospitals. • Patients requiring ICU level care • Use of azithromycin or hydroxychloroquine within 30 days prior to admission</td>
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**References**