**Supplementary file 3/Table 3:** Current clinical trials on hydroxychloroquine and azithromycin for COVID-19 treatment

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **SN** | **Trial identifier** | **Title/Location** | **Participants** | **Study type/ Year** | **Status** | **Primary outcome** |
| 1 | NCT04329832 | HCQ vs. Azithromycin for Hospitalized Patients With Suspected or Confirmed COVID-19 (HAHPS)/ US | 300 | CT/ 2020 | Recruiting | COVID ordinal outcomes scale at 14 d (TF: assessed once on d 14 after enrollment) |
| 2 | NCT04334382 | HCQ vs. Azithromycin for Outpatients in Utah With COVID-19 (HyAzOUT)/ US | 1550 | CT/ 2020 | Recruiting | Hospitalization within 14 d of enrollment (TF: from enrollment to 14 d after enrollment) |
| 3 | NCT04341207 | Epidemiology of  SARS-CoV-2 and Mortality to COVID-19 Disease in French Cancer Patients (ONCOVID)/ France | 1000 | CT/ 2020 | Recruiting | Prevalence and the 3-months incidence of SARS-CoV-2 in cancer patients (TF: up to 3 months)  Covid-19 disease-specific mortality rate in cancer patients treated by HCQ and azithromycin (TF: up to 12 months) |
| 4 | NCT04336332 | Randomized Comparison of Combination Azithromycin and HCQ vs. HCQ Alone for the Treatment of Confirmed COVID-19 / US | 160 | CT/ 2020 | Recruiting | Changes in patients viral load (TF: baseline, d 3 and d 6)  Second evaluation of changes in patients viral load (TF: d-6) |
| 5 | NCT04358068 | Evaluating the Efficacy of HCQ and Azithromycin to Prevent Hospitalization or Death in Persons With COVID-19/ US | 2000 | CT/ 2020 | Recruiting | Proportion of participants who died from any cause or were hospitalized (TF: 21-d) |
| 6 | NCT04335552 | Pragmatic Factorial Trial of HCQ, Azithromycin, or Both for Treatment of Severe  SARS-CoV-2 Infection/ US | 500 | CT/ 2020 | Recruiting | WHO ordinal scale measured at 14 d after enrollment (TF: d-14) |
| 7 | NCT04344379 | Prevention of SARS-CoV-2 in Hospital Workers s Exposed to the Virus (PREP-COVID)/ France | 900 | CT/ 2020 | Recruiting | To assess the impact of HCQ and azithromycin on the prevention of SARS-CoV-2 contamination in hospital workers exposed to 40 d of treatment.(TF: 3 months) |
| 8 | NCT04344444 | Treatment in Patients With Suspected or Confirmed COVID-19 With Early Moderate or Severe Disease (RCT)/ US | 600 | CT/ 2020 | Recruiting | Most severe outcome (TF: 5 d ) |
| 9 | NCT04358081 | HCQ Monotherapy and in Combination With Azithromycin in Patients With Moderate and Severe COVID-19 Disease/ US | 444 | CT/ 2020 | Recruiting | Percentage of participants who achieve clinical response (TF: 15 d ) |
| 10 | NCT04345861 | HCQ Plus Azithromycin Versus HCQ for COVID-19 Pneumonia (COVIDOC Trial) (COVIDOC)/ France | 150 | CT/ 2020 | Recruiting | Time to clinical improvement of at least 1 level on the ordinal scale between d-1 (d of the first administration of study drug) to d-11. (TF: up to d-11 ) |
| 11 | NCT04321278 | Safety and Efficacy of HCQ Associated With Azithromycin in SARS-CoV-2 Virus (Coalition COVID-19 Brasil II)/ Brazil | 440 | CT/ 2020 | Recruiting | Evaluation of the clinical status (TF: 15 d after randomization ) |
| 12 | NCT04322396 | Proactive Prophylaxis With Azithromycin and HCQ in Hospitalized Patients With COVID-19 (ProPAC-COVID)/ Denmark | 226 | CT/ 2020 | Recruiting | Number of d alive and discharged from hospital within 14 d (TF: 14 d ) |
| 13 | NCT04371744 | QT-Logs : Artificial Intelligence for QT Interval Analysis of ECG From Smartwatches in Patient Receiving Treatment for COVID-19 (QT-Logs)/ France | 100 | Observatonal / 2020 | Recruiting | Corrected QT (QTc) interval measurement (TF: 10 d ) |
| 14 | NCT04341727 | HCQ, HCQ,Azithromycin in the Treatment of SARS-CoV-2 Infection (WU352)/ US | 500 | CT/ 2020 | Recruiting | Hours to recovery (TF: 42 d ) |
| 15 | NCT04354428 | Treatment for COVID-19 in High-Risk Adult Outpatients/ US | 630 | CT/ 2020 | Recruiting | LRTI rates (TF: 28 d )  Incidence of hospitalization or mortality (TF: d-28)  Change in upper respiratory viral shedding (TF: d-1 through d-14) |
| 16 | NCT04366089 | Oxygen-Ozone as Adjuvant Treatment in Early Control of COVID-19 Progression and Modulation of the Gut Microbial Flora (PROBIOZOVID)/ Italy | 152 | CT/ 2020 | Recruiting | Delta in the number of patients requiring orotracheal intubation despite treatment (TF: 21 d ) |
| 17 | NCT04381936 | Randomized Evaluation of COVID-19 Therapy (RECOVERY)/ UK | 12000 | CT/ 2020 | Recruiting | All-cause mortality (TF: within 28 d) |
| 18 | NCT04324463 | Anti-Coronavirus Therapies to Prevent Progression of Coronavirus Disease 2019 (COVID-19) Trial (ACT COVID19)/ Canada | 1500 | CT/ 2020 | Recruiting | Outpatients: Hospital admission or death (TF: up to 6 wk post randomization )  Inpatients: Invasive mechanical ventilation or mortality (TF: up to 6 wk post randomization ) |
| 19 | NCT04366206 | Factors Associated With Clinical Outcomes in Patients Hospitalized for COVID-19 in GHT-93 Est/ France | 143 | Observational/ 2020 | Recruiting | Composite of death and mechanical ventilation (TF: at 14-d follow-up ) |
| 20 | NCT04365764 | Effect of Treatments in Patients Hospitalized for Severe COVID-19 Pneumonia: a Multicenter Cohort Study/ France | 400 | Observational/ 2020 | Recruiting | Composite of death and mechanical ventilation (TF: 14-d follow-up ) |
| 21 | NCT02735707 | Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community- Acquired Pneumonia (REMAP-CAP)/ New Zealand | 7100 | CT/ 2020 | Recruiting | All-cause mortality (TF: d-90 )  Day alive and outside of ICU (TF: d-21) |
| 22 | NCT04412746 | COVID-19 and Diabetes in West of Algeria (COVIDIAB-13)/ Algeria | 100 | Observational/ 2020 | Recruiting | Prevalence of diabetes among all hospitalized COVID-19 (TF: 3 months) |
| 23 | NCT04278404 | Pharmacokinetics, Pharmacodynamics, and Safety Profile of Understudied Drugs Administered to Children Per Standard of Care (POPS) (POPS or POP02)/ US | 5000 | Observational/ 2020 | Recruiting | Clearance, volume of distribution, half-life, elimination rate constant, absorption rate constant, AUC, peak plasma concentration, time for peak plasma concentration as measured by PK sampling (TF: up to 90 d from the time of consent/ for participants with Down Syndrome - up to 210 days) |
| 24 | NCT04328272 | Effectiveness of HCQ in COVID-19 Patients (Covid)/ Pakistan | 75 | CT/ 2020 | Not yet recruiting | National Early Warning Score equal to zero (TF: 3-5 d) |
| 25 | NCT04365231 | HCQ Azithromycin COVID-19 Pregnancy Trial (HASCOPT)/ France | 50 | CT/ 2020 | Not yet recruiting | Percentage of patients with a negative RT-PCR test result to COVID-19 (TF: 7 d ) |
| 26 | NCT04371406 | Efficacy of Azithromycin-associated HCQ Therapy Given in General Practice in Early-stage Disease in COVID-19 Patients (MG-COVID) / France | 2770 | CT/ 2020 | Not yet recruiting | Rate of patients with occurrence of an unfavorable outcome between randomization and d 14 (TF: between randomization and d14 )  Primary outcome of ancillary virological study : evolution of viral load between d-0 and d-14 (TF: between d-0 and d-14 ) |
| 27 | NCT04392128 | Study Evaluating the Efficacy of HCQ and Azithromycine in Patients With COVID-19 and Hematological Malignancies (HYACINTHE) (HYACINTHE)/ France | 114 | CT/ 2020 | Not yet recruiting | Evaluation of the efficacy of HCQ and azithromycin on the viral load drop at d 5. (TF: 5 d of treatment ) |
| 28 | NCT04405921 | HCQ, Azithromycin in the Treatment of COVID-19 (PACTT)/ Tunisia | 200 | CT / 2020 | Not yet recruiting | Clinical recovery at d-14, from the start of treatment. (TF: 14 d ) |
| 29 | NCT04347512 | Evaluation of the Efficacy of the HCQ-Azithromycin Combination in the Prevention of COVID-19 Related SDRA (TEACHCOVID)/ France | 405 | CT/ 2020 | Not yet recruiting | Rate of patients reaching a significant hypoxemia, in each arms. (TF: from d-0 to d-7 ) |
| 30 | NCT04354597 | HCQ and Azithromycin as Prophylaxis for Healthcare Workers Dealing With COVID-19 Patients (MOPHYDA)/ Jordan | 200 | CT/ 2020 | Not yet recruiting | Effect of HCQ and azithromycin in preventing infection with COVID-19 among healthcare workers working with COVID-19 patients (TF: 4 months ) |
| 31 | NCT04390594 | Efficacy and Safety Evaluation of Treatment Regimens in Adult COVID-19 Patients in Senegal (SEN-CoV-Fadj)/ Senegal | 258 | CT/ 2020 | Not yet recruiting | SARS-CoV-2 viral load level (TF: d-7 ) |
| 32 | NCT04374552 | Asymptomatic COVID-19 Trial (ACT)/ US | 140 | CT/ 2020 | Not yet recruiting | The primary outcome is the rate of decline in viral load over the 10 d after randomization (TF: 10 d ) |
| 33 | NCT04359316 | Azithromycin in Hospitalized COVID-19 Patients (AIC)/ Iran | 40 | CT/ 2020 | Not yet recruiting | Time to clinical improvement (TF: from date of randomization until 14 d later) |
| 34 | NCT04349592 | Qatar Prospective RCT Of Therapy Eliminating COVID-19 Transmission (Q-PROTECT)/ NP | 456 | CT/ 2020 | Not yet recruiting | Proportion of virologically cured (no virus detected) cases at d 6 (TF: d-6 ) |
| 35 | NCT04395768 | International ALLIANCE Study of Therapies to Prevent Progression of COVID-19 / Australia | 200 | CT/ 2020 | Not yet recruiting | Symptoms (TF: once daily for 15 d)  LOS (TF: at 15 and 45 d)  Invasive mechanical ventilation or mortality (TF: any time within 15 d) |
| 36 | NCT04361461 | Use of HCQ Alone or Associated for Inpatients With SARS-CoV-2 Virus (COVID-19)/ Brazil | 500 | CT/ 2020 | Not yet recruiting | Individual response rate (TF: 14d) |
| 37 | NCT04334512 | A Study of Quintuple Therapy to Treat COVID-19 Infection (HAZDpaC)/ US | 600 | CT/ 2020 | Not yet recruiting | The rate of recovery of mild or moderate COVID-19 in patients using quintuple therapy (TF: 12 wk )  Reduction or Progression of symptomatic day (TF: 12 wk )  Assess the safety of quintuple therapy, via pulse, oxygen saturation, and ECG (TF: 12 wk )  Assess tolerability of quintuple therapy (TF: 12 wk ) |
| 38 | NCT04339816 | Azithromycin Added to Hydrochloroquine in Patients Admitted to Intensive Care With COVID-19: Randomised Controlled Trial (AZIQUINE-ICU)/ NP | 240 | CT/ 2020 | Not yet recruiting | Proportion of alive patients free off mechanical ventilation (TF: 14 d after enrolment ) |
| 39 | NCT04365582 | OUTpatient Treatment of COVID-19 in Patients With Risk Factor for Poor Outcome (OUTCOV)/ France | 640 | CT/ 2020 | Not yet recruiting | Hospital admission (TF: d- 20 ) |
| 40 | NCT04363203 | VA Remote and Equitable Access to COVID-19 Healthcare Delivery (VA-REACH TRIAL) (VA-REACH)/ US | 300 | CT/ 2020 | Active, not recruiting | D to resolution of cough, fever and shortness of breath (TF: 30-d ) |
| 41 | NCT04322123 | Safety and Efficacy of HCQ Associated With Azithromycin in SARS-CoV-2 Virus (COVID-19) (Coalition-I)/ Brazil | 630 | CT/ 2020 | Active, not recruiting | Evaluation of the clinical status (TF: 15 d after randomization ) |
| 42 | NCT04368351 | Bacteriotherapy in the Treatment of COVID-19 (BACT-ovid)/ Italy | 70 | Observational/ 2020 | Active, not recruiting | Delta of time of disappearance of acute diarrhea (TF: 21 d ) |
| 43 | NCT04349410 | The Fleming [FMTVDM) Directed COVID-19 Treatment Protocol (FMTVDM)/ US | 500 | CT/ 2020 | Enrolling by invitation | Improvement in FMTVDM Measurement with nuclear imaging (TF: 72 hrs ) |

Abbreviations – AUC: Area under curve, D: Day, ECG: Electrocardiogram, FMTVDM: Fleming method for tissue and vascular differentiation and metabolism, HCQ: Hydroxychloroquine, Hr: Hour, ICU: Intensive care unit, IL: Interleukin, LOS: Length of stay, LRTI: Lower respiratory tract infection, NP: Not provided, RT-PCR: Reverse transcription polymerase chain reaction, TF: Time frame, US: United States, WHO: World Health Organization, Wk: Week