Hydroxychloroquine for Post-exposure Prophylaxis to Prevent Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Randomized Trial

Outline

- Background & Rationale
- Aims
- Methods
- Results
- Conclusions
Strategies to interrupt SARS-CoV-2 transmission: Vaccines, PEP, Treatment

Households – high incidence settings – observe transmission

Outside cluster

Cluster

Key
- Household
- Infected → Treatment
- Susceptible → PEP, PrEP
  - Close contact, Transmission
  - Close contact, No transmission

• Household transmission: 15%-35%\(^1\)
• HCQ hypothesized to decrease transmission\(^2\)

PEP for SARS-CoV-2

Hydroxychloroquine for Post-exposure Prophylaxis to Prevent Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Randomized Trial

- Using repurposed medication to prevent SARS-CoV-2 transmission
- Multi-site, double-blind, controlled, house-hold level randomized trial of HCQ PEP to prevent SARS-CoV-2 acquisition.
- Between 3/31/20 and 8/21/20, 829 participants were recruited from 41 states.
- >90% retention over the 14 days of follow-up with >90% of swabs returned and tested (PCR)

Barnabas, Brown, et. al., Trials, 2020
Barnabas, Brown, et. al., Ann Intern Med, 2020
HCQ COVID-19 PEP Study Design

Close Contacts of Index Cases

Household / Social Contacts
- Household member
- Contact in enclosed space

Health Care Workers
- Cared for COVID-19 patient without PPE

Randomized by Household

Hydroxychloroquine
- Daily Rx (HCQ) (Days 1-14)
- Daily swabs & surveys (Days 1-14 & 28)

Control
- Daily Rx (ascorbic acid) (Days 1-14)
- Daily swabs & surveys (Days 1-14 & 28)
Study procedures

• Remote study: Recruitment through health systems, social media recruitment focused on high incidence areas, website sign-up, eConsent, telehealth, self-collection, courier/mail transport
• Daily on-line survey: Symptoms screen and adherence monitoring
• Outcome ascertained by daily swabs for 14 days
Does hydroxychloroquine (HCQ) prevent SARS-CoV-2 infection after close contact with a person with diagnosed SARS-CoV-2 infection?

671 US households
829 adults with a close contact with SARS-CoV-2 infection

HCQ 337 households, 407 participants

53 infections

Daily nasal swabs
PCR testing × 14 days

HR 1.10 (95% CI 0.73-1.66)

Vitamin C 334 households, 422 participants

45 infections


http://annals.org/doi/10.7326/M20-6519

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Participant racial, ethnic, and geographical diversity

- Combined results with companion HCQ/Azithromycin treatment trial using the same methods
- A total of 307,632 unique online users clicked on online recruitment advertisements
- N=1,160 participants from 41 states
- Participants shipped 14,380 (90%) of expected nasal swabs and completed 17,129 (90%) of expected daily surveys over 14 days.
- Compared demographics to concurrent clinic-based Convalescent Plasma Study
Observational post-hoc comparison of demographics between entirely remote vs. clinic-based COVID-19 studies
(Lead: Jenell Stewart, University of Washington)

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Heat map of participant location by 3-digit zip codes relative to study site institutions across the United States.
Timeline

March
- 3/8 Idea Conceived
- 3/20 WIRB Approval
- 3/30 UW VRC Activated
- 3/31 1st Enrollment

April
- 4/3 NYU Activated
- 4/8 SUNY Upstate Activated
- 4/10 UMB and UCLA Activated
- 4/20 Tulane Activated
- 4/23 Protocol v1.2 Rollout
- 4/24 Index Enrollment
- 4/27 BMC Activated

May
- 5/1 Enrolled 200th Participant
- 5/9 Social Media Campaign Launch
- 5/27 Nationwide Recruitment
- 5/28 1st DSMB

June
- 6/16 SUNY and UCLA Close to Enrollment
- 6/29 Enrolled 600th Participant

July
- Facebook Boycott

August
- 8/7 2nd DSMB
- 8/21 Final DSMB
- Close enrollment

Sept
- Received specimens
- Data QCs
- Analysis

Oct
- Submitted abstract
- Submitted mss
- 10/24 Results public

Pandemic Clinical Trial Guidance
- Responsive
- Service
- Science
Discussion

> Remote trials – support diverse trial participants
> High fidelity to the protocol, procedures, and safety monitoring
> Limitations:
  – Post-hoc comparison with convalescent plasma study is limited
  – Did not capture change in personnel or participant time for study involvement
> Remote trial participation and recruitment may improve research equity and inclusion of participants from more diverse racial, ethnic, and geographic communities – additional trials will provide further evidence
> Participants

> Investigators, UW ICRC Coordinating Center, COVID-19 PEP Study Team


> Hydroxychloroquine COVID-19 PEP Study Team

> BMGF: INV-016204

> Sandoz donated hydroxychloroquine for this study

> REDCap (UL1 TR002319, KL2 TR002317, and TL1 TR002318 from NCATS/NIH)
HCQ COVID-19 PEP Study Team

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