Town Hall Agenda

• Updates on current research activity
• Outpatient Research Presentations:
  — RADx – Yukari Manabe, MD
  — Plasma – David Sullivan, MD
  — ACTIV-2 – Kelly Dooley, MD, PhD
  — PROTECT – Mark Sulkowski, MD
  — Astra-Zeneca Vaccine – Anna Durbin, MD
  — HOPE Registry – Cassie Lewis-Land, MS, CCRP
Updates on Current Research Activity
COVID-19 Research Updates: Recent completion of study enrollment

• A Randomized Placebo-Controlled Safety and Dose-Finding Study for the Use of the IL-6 Inhibitor Clazakizumab in Patients with Life-Threatening COVID-19 Infection
  — Investigators: Drs. Nada Alachkar, Russell Wesson and Mark Landrum
  — Johns Hopkins Hospital and Howard County General Hospital
  — Enrollment, 67 patients (180 overall)

• CRITICAL: CRIzanlizumab for Treating COVID-19 vAscuLopathy
  — Investigators: Drs. Charles Lowenstein and Thorsten Leucker
  — Johns Hopkins Hospital and Johns Hopkins Bayview Medical Center
  — Enrollment, 50 patients (JHU study)
Maryland COVID-19 Data Dashboard: Daily new cases of SARS-CoV-2 infection

December 9
MD daily COVID-19 positive: 2,692
7-day average: 7.74%
<table>
<thead>
<tr>
<th>COVID-19 Severity</th>
<th>Panel’s Recommendation</th>
</tr>
</thead>
</table>
| Non-hospitalized or hospitalized but not requiring supplemental oxygen | • At this time, there are insufficient data to recommend either for or against the use of bamlanivimab or casirivimab + imdevimab for the treatment of outpatients with mild to moderate COVID-19.  
• Do not use dexamethasone (AI) |

<table>
<thead>
<tr>
<th>Prevention and Prophylaxis of SARS-CoV-2 infection</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-exposure</td>
<td>The Panel recommends against the use of any agents for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pre-exposure prophylaxis (PrEP), except in a clinical trial (AIII).</td>
</tr>
<tr>
<td>Post-exposure</td>
<td>The Panel recommends against the use of any agents for SARS-CoV-2 post-exposure prophylaxis (PEP), except in a clinical trial (AIII).</td>
</tr>
</tbody>
</table>

Strength of recommendation: A, Strong; B, Moderate; C, Optional  
Quality of Evidence: I, One or more randomized trials with clinical outcomes and/or validated lab endpoints; II, One or more well-designed, nonrandomized trials or observational cohort studies; III, Expert opinion  

https://www.covid19treatmentguidelines.nih.gov; accessed December 9, 2020
Updates on Clinical Research for Ambulatory Patients with or at risk for SARS-CoV-2 infection
Outpatient Research: RADx
Yukari Manabe, MD
**Rapid Acceleration of Diagnostics (RADx) Projects Overview**

The NIH has launched several programs to accelerate innovation in, development and commercialization of, and implementation of COVID-19 testing. RADx-ATP is one of these programs.

<table>
<thead>
<tr>
<th>Project Description</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>RADx Tech (RADx-Tech)</td>
<td>Highly competitive, rapid three-phase challenge to identify the best candidates for at-home or point-of-care tests for COVID-19</td>
</tr>
<tr>
<td>RADx Underserved Populations (RADx-UP)</td>
<td>Interlinked community-engaged demonstration projects focused on implementation strategies to enable and enhance testing of COVID-19 in underserved and/or vulnerable populations</td>
</tr>
<tr>
<td>RADx-Radical (RADx-Rad)</td>
<td>Develop and advance novel, non-traditional approaches or new applications of existing approaches for testing</td>
</tr>
<tr>
<td>RADx Advanced Testing Program (RADx-ATP)</td>
<td>Rapid scale-up of advanced POC technologies to increase rapidity and enhance and validate throughput – and support of ultra-high throughput machines and facilities</td>
</tr>
<tr>
<td>Data Management Support</td>
<td>Build an infrastructure for and support coordination of the various data management needs of many of the COVID-19 efforts</td>
</tr>
</tbody>
</table>
# NIH Rapid Acceleration of Diagnostics (RADx) Initiative for COVID-19

### RADx Tech Projects by Phase

#### 11/25/20

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>April 29, 2020</td>
<td>698 reviewed 137 Deep Dive (1 active)</td>
<td>48 WP1 (12 active)</td>
<td>28 WP2 (22 contracted, 6 awaiting contract, 2 contracts terminated)</td>
<td>2.9M tests/week</td>
</tr>
<tr>
<td>2848 started 703 completed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**FAST TRACK FOR ADVANCED DIAGNOSTIC TECHNOLOGIES**

- **48 to WP1 (35%)**
- **17 directly to WP2 (8%, including 9 ATP)**
- **17 to WP2 (47% of completed WP1 projects)**
- **17 from WP1 (61%)**
- **11 from DD (39%, includes 9 ATP)**

**Deployment**

**DEPLOY MILLIONS of tests per week**
Study Rationale

• Demand for SARS-CoV-2 exceeds current testing capacity.
• Identify low cost and easily scalable diagnostic tests that directly detect SARS-CoV-2.
• Find suitable replacements for NP samples, such as: midturbinate or saliva.
• Bridge the evidence gap in performance of NAT and antigen test in different sample types: NP, MT and Saliva.
Research Goal

- Determine the accuracy of novel SARS-CoV-2 assays against a NP swab gold standard
- Compare the performance of antigen tests in saliva and nasal samples to the current standard RT-PCR test.
- Setup biorepository for future testing and research collaboration.
- Study findings will be shared with NIH-supported RADx Clinical Studies Core in their recommendation to device manufacturers and the NIH.
Recruitment

- Recruitment
  - Letters to Providers
  - Flyers
  - Phone call (Index pt provides study information to close contacts)
  - Partner study
  - HOPE Registry

- Participant (>18 years)
  - Symptomatic
  - Asymptomatic

- Study Location: ICTR-CRU
  - Bayview
  - Green Spring Station

*An asymptomatic close contact is defined as a person who has none of the above COVID-19 symptoms but who was within 6 feet of an infected person for at least 15 minutes starting from 2 days before illness onset or 2 days prior to specimen collection of a positive specimen.
Sample Collection

NP Swab
- Nares to the pharynx
- Swabs into VTM

MT
- Dry sample

Saliva
- Spit/passive drool (~ 2ml)
If you’re sick and think you might have COVID-19, or if you’re a close contact of someone who tested positive, you may qualify for a Johns Hopkins study on easier COVID-19 tests.

Get tested.

Call today to find out if you’re eligible: 443-301-8572

Researchers at Johns Hopkins are seeking volunteers to participate in a clinical research study to identify easier approaches for COVID-19 testing. The potential participants will be eligible for the study if they are either: A symptomatic person suspected of having COVID-19 or an asymptomatic close contact of a person diagnosed with COVID-19. Participation in the study requires phone screening, informed consent and visit to the testing site for samples collection. Benefits: 1) All study participants will undergo the gold standard testing for COVID-19. 2) Participant will receive test results within 48 hours. 3) Participants will be reimbursed for time and travel.

Principal Investigator: Yukari Manabe, M.D. IRB00264304
Outpatient Research: Plasma
David Sullivan, MD
Convalescent Plasma Randomized Clinical Trials for SARS-CoV-2 Prophylaxis and Early COVID-19 Treatment are Foundational for Subsequent Hyperimmune Globulin and Vaccines

• David Sullivan, Shmuel Shoham, Kelly Gebo
• Dan Hanley, Arturo Casadevall and Bryan Lau
• DoD OTA-W911QY2090012
• Bloomberg Philanthropy, NIAID, The Moriah Fund, The Mental Wellness Foundation, Octapharma
Study Rationale

- Antibodies work for the SARS-CoV-2 vaccine
- Antibodies decrease death in the hospital
- Infection prevention and outpatient early treatment has not been validated for FDA approval
- Drugs are not coming to the rescue. We have only antibodies for therapy.
- Passive immunization is an established approach to prevention and treatment of viral infections (e.g. rabies immune globulin (RIG), hepatitis B immune globulin (HBIG), RSV monoclonal antibody
- Convalescent plasma has now been used as TREATMENT for severe COVID-19 in over 250,000 hospital patients
- Convalescent plasma has proven success for hemorrhagic fevers, influenza, Ebola, bacterial and other viral diseases
How it Works

COVID-19 Patients

Recovery

Plasma Antibody Draw

Virus-neutralizing antibody

Convolsecent Plasma

Convalescent Plasma <7-9%

Single IV Dose

Randomized Therapy

Placebo Plasma (2019)

Double Blind-Patient and Study Team

Placebo Plasma 13-18%

~50-75% Reduction With Antibody Plasma

Negative or HIV, Hep B,C or Other TTI

And

CLIA Lab Viral Titer Greater Than 1:320
Recruitment

**Infection Prevention**  
**Subjects:** 500 subjects  
—**Inclusion:** ≥ 18 years old, high risk exposure to COVID+ person in past 120 hours at home at work at play.  
—30 minute screen day -1, 1 hour transfusion day 0, swab follow up day +1, 7, 14, 28 & 90 (15 minutes)

**Early Treatment**  
**Subjects:** 1344 subjects  
—**Inclusion:** ≥ 18 years old, COVID-19 infection, well enough to not require hospitalization, symptom onset <8 days  
—30 minute screen day -1, 1 hour transfusion day 0, follow up day 14, 28 and 90 (15 minutes)

—**Design:** blinded; 1:1 randomization; 1 unit of convalescent plasma (ELISA titer ≥ 1:320) vs. normal plasma
Randomizations are at 543, Transfusions 489, plasma dispensed at 505
Infection Prevention 109 (20% of 500) Early Treatment ~434 (72% of 600)
(33% of 1344)

Study recruitment over time
Dec 4   IP-109 ET-434=543 +45
Nov 28  IP-104 ET-394=498 +36
Nov 21  IP-98 ET-364=462 +75
Nov 14  IP-82 ET-305=387 +59
Nov 7   IP-75 ET-253=328 +34
Oct 31  IP-66 ET-228=294 +40
Oct 24  IP-58 ET-196=254 +23
Oct 17  IP-52 ET-179=231 +20
Oct 3   IP-45 ET-134 = 179 +27
Sept 19 IP-34 ET-102 = 136 +17
Sept 12 IP-30 ET-89 = 119 +12
Aug 29  IP-26 ET-65 = 91 +12
Aug 15  IP-23 ET-45 = 68 +11

Table 2: Cumulative Randomization by Trial and Site (As of 05 December 2020, 21:00 EDT)

<table>
<thead>
<tr>
<th>Site</th>
<th>CSSC-001 Post Exposure Prophylaxis</th>
<th>CSSC-004 Outpatient Early Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomized, N (%)</td>
<td>Transfused, N (%)</td>
</tr>
<tr>
<td>AAMC</td>
<td>4 (3.7)</td>
<td>3 (3.0)</td>
</tr>
<tr>
<td>BCM</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>JHSPH-Shiprock</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>JHSPH-Whitnriver</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>JHU</td>
<td>36 (33.0)</td>
<td>35 (35.0)</td>
</tr>
<tr>
<td>I/B: RIH</td>
<td>8 (7.3)</td>
<td>7 (7.0)</td>
</tr>
<tr>
<td>MS-Georgetown</td>
<td>10 (9.2)</td>
<td>10 (10.0)</td>
</tr>
<tr>
<td>MS-Washington</td>
<td>1 (0.9)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>NorthShore</td>
<td>2 (1.8)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>UAB</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>UCinci</td>
<td>2 (1.8)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>UC-Irvine</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>UCLA</td>
<td>7 (6.4)</td>
<td>5 (5.0)</td>
</tr>
<tr>
<td>UCSD</td>
<td>21 (19.3)</td>
<td>19 (19.0)</td>
</tr>
<tr>
<td>UMass</td>
<td>2 (1.8)</td>
<td>2 (2.0)</td>
</tr>
<tr>
<td>UR</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Utah</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>UTHealth</td>
<td>3 (2.8)</td>
<td>3 (3.0)</td>
</tr>
<tr>
<td>VBMC</td>
<td>2 (1.8)</td>
<td>2 (2.0)</td>
</tr>
<tr>
<td>WCHN-Danbury</td>
<td>1 (0.9)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>WCHN-Norwalk</td>
<td>12 (11.0)</td>
<td>11 (11.0)</td>
</tr>
<tr>
<td>Total</td>
<td>108 (100.0)</td>
<td>106 (100.0)</td>
</tr>
</tbody>
</table>

Note: Number of transfused is based on data entered in CSSC-001, and CSSC-004 system; number of blood dispensed is based on data from LOCATOR system; both may be subject to late data entry.

For CSSC-001, 3 randomized subjects was confirmed not getting transfusion; for CSSC-004, 11 subjects were confirmed not getting transfusion.
We Need Your Help

• If you have an infected or an exposed patient that you think would be interested in these trials- reach out to us.

—Early Treatment
  ▪ dsulliv7@jhmi.edu
  ▪ 443-690-2496 (David Sullivan cell phone)
  ▪ kgebo@jhmi.edu
  ▪ 443-794-6757 (Kelly Gebo cell phone)

—Infection Prevention
  ▪ sshoham1@jhmi.edu
  ▪ 202-215-6760 (Shmuel Shoham cell phone)
Outpatient Research: ACTIV-2
Kelly Dooley, MD, PhD
Adaptive Platform Treatment Trial for Outpatients with COVID-19

A Multicenter Trial of the AIDS Clinical Trials Group (ACTG) and the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership
Trial Design

- Randomized, blinded, controlled platform
- Allows agents to be added and dropped during study for efficient testing of new agents
- Begins with a phase II, followed by a transition into a larger phase III evaluation for promising agents.
- When two or more agents are being tested concurrently, the same placebo will be used, if feasible.
Study Eligibility

• Ambulatory Adult (≥18 years)
• Active CoV-2 infection ≤7 days prior to Entry
• At least one COVID-19 symptom for ≤10 days prior to Entry, plus one of the following symptoms present <48 hours of entry:
  — Fever or feeling feverish, cough, shortness of breath at rest or with activity, sore throat, body or muscle pain, fatigue, headache, chills
• Tailored per study agent
Phase II Objectives

• Determine safety and efficacy of an agent to reduce the duration of COVID-19 symptoms and nasopharyngeal SARS-CoV-2 RNA detection through 28 days after study entry.
<table>
<thead>
<tr>
<th>Virology: NP Swabs</th>
<th>Oxygen saturation: Pulse ox</th>
<th>Other considerations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Proportion negative by ≥20%</td>
<td>• Proportion oxygen saturation of ≥96%</td>
<td>• Safety</td>
</tr>
<tr>
<td>• Decrease of ≥1 log10 copies/mL</td>
<td></td>
<td>• Dynamics of virology and symptoms</td>
</tr>
<tr>
<td>• Reduction in median AUC</td>
<td></td>
<td>• Viral rebound</td>
</tr>
</tbody>
</table>
Phase III Objectives & Endpoint

• **Objective**: Determine if an agent will prevent the composite endpoint of either hospitalization or death through 28 days after study entry.

• **Endpoint**: Death from any cause or hospitalization through 28 days after study entry.
  —Hospitalization defined as requiring ≥24 hours of acute care in a hospital or similar acute care facility.
Thank you

More information:
www.riseabovecovid.org

Referrals:
Rennisse McKinley, MHSA
Health Educator II/Recruiter
410 955-7127 or
410 955-2898 - rmckinl2@jhmi.edu
Outpatient Research: PROTECT Study
Mark Sulkowski, MD
Lambda interferon for prevention and early treatment of SARS-CoV-2 infection

• Type 3 interferon
  — IFNs are antivirals
  — Lambda receptors are largely restricted to epithelial cells
  — Once weekly pegylated interferon lambda has been extensively studied for viral hepatitis B and C with less side effects than IFN alfa or beta
  — Not FDA approved for any indication

• Household contacts are at high risk for SARS-CoV-2 infection

• CDC MMWR 11/6/2020
  — Prospective study of household transmission of SARS-CoV-2 in Nashville, Tennessee and Marshfield, Wisconsin
  — April–September 2020
  — Rate of secondary from index patients (n=101):
    ▪ 53% (102/191 at risk persons)
Peginterferon lambda-1a for the prevention and treatment of SARS-CoV-2 infection: The PROTECT Study

- Household contacts of persons with confirmed COVID-19
  - ≥ 18 years old
  - ≤ 7 days of exposure and no symptoms
  - Oxygen saturation ≥ 95%

- PegIFN lambda or placebo – one SC injection
  - Participants dosed with pending NP swab results

- Location: Greenspring Station COVID-19 CRU
Peginterferon lambda-1a for the prevention and treatment of SARS-CoV-2 infection: The PROTECT Study

Phone 410-314-1142
Email PROTECT-study@jhmi.edu
https://www.covidprotectstudy.org/
Outpatient Research: Astra-Zeneca Vaccine
Anna Durbin, MD
Vaccine Platforms

• mRNA vaccines
  — Moderna & Pfizer
• Virus vectored vaccines
  — Astra Zeneca ChAdOx1
  — Janssen Ad26
  — Merck VSV-vectored
  — Merck measles virus-vectored
• Sub-Unit Protein
  — Novavax
  — Sanofi

Callaway Nature 30 April 2020
Pfizer mRNA vaccine (BNT162b2)

• Modified RNA to dampen innate immune sensing and increase mRNA translation

• Now in Phase 3 clinical trial (30 µg dose)
  — >30,000 randomized 1:1; 2 doses given 21 days apart
  — Fully enrolled at JHU

• *Interim efficacy results announced Nov. 9: >90% efficacy*

• EUA filed Nov. 20, 2020

• JHU will participate in pediatric trial to begin Q2 2021 (K. Talaat, PI)
AZD-1222

- ChAdOx1 vector expressing the Spike protein of SARS-CoV-2 protein
- Enroll 44,000 subjects ≥18 years of age
- Randomized 2:1 vaccine to placebo
- Goal is to enroll a diverse population of subjects; those who have borne the major burden of COVID
  - Persons living with HIV are eligible (CD4 ≥ 200)
- JHU currently enrolling (A. Durbin, PI)
  - Included JHU CRNs: Tidal Health, Anne Arundel, and Tower Health
  - Utilized the Hope registry, Fraility registry, and the CoVPN registry
  - Collaborated with Kathleen Page, Father Bruce at Sacred Heart for outreach to the Latinx com
• Sanofi Pasteur
  — Sub-unit protein vaccine given with GSK adjuvant
  — Projected enrollment to begin mid-late January 2021
• Merck & Co
  — Measles virus-vectored vaccine
  — Enrollment expected to begin April 2021
Outpatient Research: HOPE Registry
Cassie Lewis-Land, MS, CCRP
Recruitment Innovation Unit HOPE Registry

Cassie Lewis-Land, MS, CCRP
Program Administrator
Recruitment Innovation Unit
Objective of HOPE Registry and Outreach

The registry is designed to be patient centric allowing potential participants:

• to stay informed of study opportunities that they may be eligible to join related to COVID-19 research

• ability to choose a study or studies that best fits their personal preferences and gives them autonomy in choosing

• Ability to spread the word about research opportunities within their networks
How it HOPE Registry Works

1. Participant completes the HOPE Registry survey on REDCap.
2. Participant is provided opportunity to select studies they are interested in.
3. Study team determines the participant’s eligibility and recruits participant if applicable.

- We recruit participants via social media, online advertisements, phone calls, MyChart, emails and text messages.
- The survey uses branching logic to determine which studies the participant may be eligible for.
- Participant selection triggers email notification to appropriate study team.
HOPE Registry Enrollment

**Hope Registry Dashboard**

**Total Participants**

7246

**How Participants Heard About the Registry**

*Some participants may have been contacted via multiple methods*

**Race**

<table>
<thead>
<tr>
<th>Race</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Indian or Native Alaskan</td>
<td>18</td>
<td>0.50%</td>
</tr>
<tr>
<td>Asian</td>
<td>226</td>
<td>4.50%</td>
</tr>
<tr>
<td>Black or African American</td>
<td>441</td>
<td>8.80%</td>
</tr>
<tr>
<td>Native Hawaiian or Pacific Islander</td>
<td>6</td>
<td>0.10%</td>
</tr>
<tr>
<td>White</td>
<td>4404</td>
<td>81.10%</td>
</tr>
<tr>
<td>Other</td>
<td>244</td>
<td>5.00%</td>
</tr>
</tbody>
</table>

**Demographics**

**Mean Age**

53.53

**COVID Positive**

14.20%
How to join HOPE Registry

Study Teams wanting to join can contact RIU HOPE team:
• we can help you submit a Change in Research (CIR) to IRB to utilize the registry
• build branching logic to identify enrollees in registry whom meet study inclusion criteria

Interested in joining the registry as a participant:
• hoperegistry@jhu.edu
• Website johnshopkinshope.org
• Text “HOPKINSHOPE” to 474747
• Call 410-314-1334
COVID-19 Clinical Research Center
How to work with us

• Ask questions
  — COVID19ResearchCtr@jhmi.edu

• Start at the ICTR COVID-19 CRC website
  — https://ictr.johnshopkins.edu/covid-research-center
  — Re-design underway to provide step-by-step guidance for human subjects and non-human subject research

• Join our monthly Town Hall Meetings
Questions

COVID-19 Clinical Research Center