Operation Warp Speed/Therapeutics

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What is Operation Warp Speed (OWS)?

- Joint effort of DHHS and DOD
- Mission: do everything possible to make highly performing, thoroughly evaluated vaccines, drugs and diagnostics available in the US as soon as possible and ideally during this calendar year
- To that end, offer financial, manufacturing, logistical, scientific, medical and regulatory assistance to leading candidates

Criteria for Candidates

- Timeliness: availability by EOY 2020
  - For therapeutics, this mainly means repurposed drugs
  - Certain virus-specific products possible—neutralizing antibodies
- Scientific merit
  - Strong mechanistic rationale and
  - Successful animal model studies or
  - Early clinical signal
- Manufacturability and scale-up
  - Feasible to make at commercial scale by EOY 2020 or at the least 1st quarter 2021

Therapeutics Focus

- At OWS start—approximately May 15—hundreds of trials of immunomodulatory agents and a few putative antivirals ongoing worldwide
- *De novo* small molecule development timeline outside program parameters
- Repurposed antivirals (as was done with remdesivir) feasible—pick up from screening programs
- Virus neutralizing monoclonal or polyclonal antibodies feasible with acceleration of development
- Additional agents to manage disease complications considered

Therapeutic Efforts

- Rapid, comprehensive inventory of ongoing development programs, including monoclonal antibodies, worldwide
- Assessment of scientific merit and prioritization by cross-Agency group—this activity is ongoing
- Assessment of state of manufacturing for leading candidates
- Special emphasis on small molecule repurposed antivirals and monoclonal antibodies

Assembling a Program

- Lead candidates identified and developmental needs assessed—this is an iterative process
- Continuation of BARDA efforts, e.g. Regeneron monoclonal cocktail
- Creation of teams to work closely with selected manufacturers
- Research team to work on standardized assays and comparisons

Types of Interventions: Therapeutics

- Some (large) companies need no assistance but seek advance purchasing agreements with various conditions (e.g., should their product prove successful)
- Some companies need little clinical assistance but require funding for at risk manufacturing scale-up and/or advanced purchasing
- Some companies need logistical help with supply chain bottlenecks
- Many companies need assistance with clinical program

Clinical Program

- ACTIV: Dr. Francis Collins had started this public-private partnership in April run by the FNIH
  - Performed rapid survey of potential clinical trial networks
  - Screened many compounds for scientific merit
  - Selected 3 immunomodulators to test
  - Proposed study of anticoagulation in COVID19
- OWS/ACTIV
  - Developed 2 “Master Protocols”, one for outpatients (ACTIV 2) and one for hospitalized patients (ACTIV 3) and launched in August
  - Developed process and criteria for candidate entry
  - Currently studying Lilly’s neutralizing Ab in both trials; other agents in queue
  - OWS also supporting immunomodulator and anticoagulation trials as well as (non-ACTIV) trials of hyperimmune globulin and convalescent plasma

Challenges for Clinical Trials of COVID19 Patients

- Large number of ongoing trials—many underpowered, not randomized
- Competing platform trials and industry-sponsored trials in the US
- Difficulties in reaching infected outpatients
- Existing clinical trial networks based in academic medical centers—difficult to reach community sites who have most of the patients
- Monoclonal antibodies given by infusion are difficult in an outpatient setting
- In-hospital trials mostly facing competition issue

Other Master Protocols Ongoing

- RECOVERY (UK); SOLIDARITY (WHO); REMAP-CAP; I-SPY COVID; UNIFY
- Additional USG-sponsored MP or ongoing studies: ACTT, BET (ACTIV); ACTIV-1 (Immunomodulators); ACTIV-4 (three separate studies of anticoagulation in outpatients, hospitalized patients and discharged patients); INSIGHT 13 (hyperimmune globulin, NIAID)

Summary

- OWS hopes to assist developers to have treatment options available by the end of this year
- A few therapeutics contracts are public, some under negotiation
- Only able to support products in fairly late stage development
- Clinical evaluation proving very challenging
- New clinical signals may trigger OWS support for additional agents; rather late to utilize mechanistic plausibility alone or even promising animal data