

Search Results Project Details

[Share](#)[Back to Search Results](#)[Description](#)[Details](#)[Sub-Projects](#)[Publications](#)[Patents](#)[Outcomes](#)[Clinical Studies](#)[News and More](#)[History](#)[Similar Projects](#)

Influenza and Emerging Infectious Diseases

Project Number

1ZIAAI000984-14

Contact PI/Project Leader

DAVEY, RICHARD

Awardee Organization

**NATIONAL INSTITUTE OF
ALLERGY AND INFECTIOUS
DISEASES**

Description

Abstract Text

Novel means first to better characterize and then to treat infection with major respiratory pathogens using existing or newly developed strategies are a primary focus of this important project within the Clinical Research Section. In this regard, our Section has undertaken clinical research efforts to help better characterize and treat infection with both novel and seasonal subtypes of influenza. An initial treatment trial involving open-label administration of two units of hyperimmune plasma to 98 hospitalized patients with severe influenza suggested that investigational arm participants might have fewer days in the hospital, in the ICU, on mechanical ventilation, and may have improved disposition at Day 7. Based upon these highly suggestive trends, the CRS then launched a follow-up multicenter trial (called IRC005) enrolling patients with severe influenza A infection who were randomized in a double-blind manner to receive either high-titer (hyperimmune) plasma or a low-titer (control) plasma in addition to standard-of-care treatments. 140 subjects out of a desired goal of 150 were randomized in this trial, with the primary endpoint being an assessment of clinical status using an ordinal outcome score as measured at Day 7. The major finding of IRC005 was that the use of high-titer immune plasma did not confer a clinical benefit over non-immune plasma in patients hospitalized with influenza A, and thus this immunotherapy could not be recommended as a useful adjunctive treatment strategy for future patients. This outcome provides an important counterpoint to over 100 years of speculation and a series of anecdotal reports that convalescent plasma might be a powerful adjunct in the treatment of severe influenza A. As a separate trial launched through the INSIGHT clinical trials network, we also conducted an international multi-center randomized, double-blind, placebo-controlled study of hyperimmune intravenous immunoglobulin (IVIG) versus standard-of-care in hospitalized patients with severe influenza A or B. This clinical outcome trial was preceded by successful completion of a multi-center pilot trial in 31 patients through domestic US sites within the INSIGHT network that showed that administration of IVIG to hospitalized patients or outpatients was safe, significantly boosted HAI titers against the infecting influenza A subtypes, and could be conducted at clinical sites while maintaining the blind. By June, 2018, the trial reached and actually exceeded the accrual goal of the desired number (320) needed to power the endpoint of clinical improvement at Day 7 of illness. Similar to IRC005, however, no treatment benefit was found for IVIG in patients with influenza A. Surprisingly, however, a significant treatment benefit was found for patients hospitalized with influenza B infection despite the lower antibody titers present in IVIG against influenza B virus. In-depth antibody characterization of the IVIG product provided a potential explanation for this discrepancy by documenting the presence of up to 10-fold higher avidity antibody against both major lineages of influenza B than against the major influenza A subtypes in this plasma-derived product. The current plan is to explore this unexpected outcome through the launch of a new IVIG trial aimed at a larger number of patients hospitalized with influenza B. In addition to the completion of these interventional trials mentioned above, we continue to contribute to the management and oversight of a large international observational protocol for hospitalized patients with seasonal influenza infection, as well as a third protocol looking at the genomic host response, all administered under the auspices of the INSIGHT network. In the realm of ongoing biodefense-related initiatives, we continue to 1) monitor yearly the clinical and psychological status of a subset of patients previously exposed to anthrax as a result of the October 2001 anthrax attacks, and 2) continue to enroll and study patients on a protocol designed to permit diagnosis and in-depth characterization of individuals presenting elsewhere with unusual infectious or inflammatory conditions that have often defied diagnosis and treatment at other centers. The Special Clinical Studies Unit (SCSU) with the NIH Clinical Center is one of a small number of special high containment patient care units within the US called upon to hospitalize patients or staff suffering high-risk exposures to highly-infectious agents who require observation and/or care under conditions of high containment, such as the medically-evacuated HCWs exposed to or infected with Ebola virus in 2014-15. The section continues to provide the direct medical oversight to the SCSU. Most recently this has involved hospitalizing and providing care for patients with COVID-19 from the surrounding community who have been transferred to the NIH for access to investigational therapies. Through engagement with a large domestic and international network enterprise comprised of over 60 medical centers and coordinated through NIAID's Division of Microbiology and Infectious Diseases (DMID), the Section has participated in three separate phases of the Adaptive COVID-19 Treatment Trial (ACTT) studying investigational therapeutics in COVID-19 inpatients presenting with respiratory compromise. The first of these trials established that the use of remdesivir results in a statistically significant reduction in the time to recovery in patients hospitalized with an oxygen requirement. The second of these trials is studying whether the addition of an immunosuppressive medication such as a JAK-Stat inhibitor (baricitinib in this case) can dampen the potentially damaging cytokine response in severe COVID-19 and thereby improve the clinical outcome relative to remdesivir alone. That second phase has completed accrual and the data for the primary and secondary endpoints are presently being analyzed. Following the Sections lead role in helping orchestrate the only multicenter randomized controlled (RCT) safety and efficacy study (PREVAIL II) of putative MCMs in the treatment of patients with confirmed Ebola infection during the 2013-16 West African crisis, the outcomes of that trial were instrumental in helping design the next investigational RCT of MCMs implemented during the 10th Thank you for your feedback!

Democratic Republic of the Congo (DRC) that began in August 2018. NIAID collaborated with the Institut National pour la Recherche Biomedicale (INRB), the WHO, and several international partners to rapidly implement an RCT of 4 different promising investigational countermeasures against Ebola in that country. 693 patients were accrued in this landmark trial that ultimately established both the safety and efficacy of two different monoclonal antibody products (REGN-EB3 and Mab-114) in treating both adult and pediatric patients with Ebola virus disease (EVD), not only proving for the first time that effective treatment of EVD was possible but also establishing that important clinical research could be safely conducted in the midst of a public health crisis. The phase 1 randomized, double-blind dose-escalating safety and immunogenicity trial of (VSVG-ZEBOV) vaccine against EVD that the Section completed in early 2015 was the forerunner to an ongoing pre-exposure vaccination protocol called PREPARE that is using VSVG-ZEBOV vaccine to immunize HCWs, BSL-4 Laboratory staff, and other at-risk personnel against Ebola virus infection. The protocol features randomization to a homologous booster immunization at month 18 to determine whether the booster further augments antibody levels induced by the primary immunization as assessed at month 36. As of mid 2020 233 patients have been enrolled and will provide the basis for the primary endpoint determination.

Public Health Relevance Statement

Data not available.

NIH Spending Category

Anthrax	Biodefense	Biotechnology	Clinical Research	Clinical Trials and Supportive Activities
Comparative Effectiveness Research		Coronaviruses	Emerging Infectious Diseases	Health Disparities
Immunization	Immunotherapy	Infectious Diseases	Influenza	Lung
Orphan Drug	Patient Safety	Pneumonia & Influenza	Prevention	Rare Diseases
				Vaccine Related

Project Terms

2019-nCoV	Acute	Adult	Africa	African	Anthrax Attack	Anthrax disease	Antibodies
Antibody Avidity	Antibody titer measurement		Birds	COVID-19	Caring	Clinical	
Clinical Research	Clinical Trials Network		Clinical assessments		Collaborations		
Communicable Diseases	Communities		Consensus	Containment	Country	Data	
Democratic Republic of the Congo	Development		Diagnosis	Disease Outbreaks	Dose		
Double-Blind Method	Ebola		Ebola Hemorrhagic Fever	Ebola virus			
Emerging Communicable Diseases	Endpoint Determination		Enrollment	Epidemic	Exposure to		
Future	Genomics	Goals	Health Personnel	Healthcare	Hospitals	Human	

[Read More](#)

Details

Contact PI/ Project Leader

Name
[DAVEY, RICHARD](#)

Title

Contact
[Email not available](#)

Other PIs

Not Applicable

Program Official

Name
 Contact
[Email not available](#)

Organization

Name
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
 City
 Country

Department Type
Unavailable
 Organization Type
Unavailable

State Code
 Congressional District

Other Information

FOA

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Project Start

Study Section

Date

Fiscal Year

2020

Award Notice Date

DUNS Number CFDA Code

Project End Date

[Thank you for your feedback!](#)

Project Funding Information for 2020

Total Funding
\$3,504,680

Direct Costs
\$0

Indirect Costs
\$0

Year	Funding IC	FY Total Cost by IC
2020	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	\$3,504,680

NIH Categorical Spending

[Click here for more information on NIH Categorical Spending](#)

Funding IC	FY Total Cost by IC	NIH Spending Category
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	\$1,401,872	Health Disparities; Minority Health;
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	\$3,504,680	Anthrax; Biodefense; Biotechnology; Clinical Research; Clinical Trials and Supportive Activities; Comparative Effectiveness Research; Coronaviruses; Emerging Infectious Diseases; Immunization; Immunotherapy; Infectious Diseases; Influenza; Lung; Orphan Drug; Patient Safety; Pneumonia & Influenza; Prevention; Rare Diseases; Vaccine Related;

Sub Projects

No Sub Projects information available for 1ZIAAI000984-14

Publications

No Publications available for 1ZIAAI000984-14

Patents

No Patents information available for 1ZIAAI000984-14

Outcomes

The Project Outcomes shown here are displayed verbatim as submitted by the Principal Investigator (PI) for this award. Any opinions, findings, and conclusions or recommendations expressed are those of the PI and do not necessarily reflect the views of the National Institutes of Health. NIH has not endorsed the content below.

No Outcomes available for 1ZIAAI000984-14

Clinical Studies

No Clinical Studies information available for 1ZIAAI000984-14

News and More

Related News Releases

No news release information available for 1ZIAAI000984-14

 Thank you for your feedback!

 **History**

No Historical information available for 1ZIAAI000984-14

 **Similar Projects**

No Similar Projects information available for 1ZIAAI000984-14

Thank you for your feedback!