Supplemental materials

1 Protocol team structure

To oversee the implementation of this master protocol, a protocol team was formed including: Protocol co-chair(s)

- NIAID, Division of Clinical Research representatives
- INSIGHT University of Minnesota representatives
- INSIGHT International Coordinating Center representatives
- Representatives from collaborating trials networks (i.e. PETAL, CTSN and the VA)
- Representative from ACTIV-2 protocol team
- Representatives from the central specimen repository
- Representative from the drug distribution group
- Representatives from collaborating manufacturers of investigational agents
- Representatives from site investigators
- Community representative(s)

A core team consisting of the co-chair(s), ICC leaders, NIAID representatives, study statisticians, representatives from collaborating trials networks, and other representatives and the INSIGHT PI will also regularly convene to review study progress and address study conduct and administrative issues that arise.

2 Operationalisation of the primary endpoint

The TICO primary objective is to determine whether investigational agents are safe and efficacious compared with placebo when given with established standard of care (SOC). The primary efficacy endpoint is time to sustained recovery through day 90 i.e. when a participant is discharged from hospitalization to home and remains at home for at least 14 consecutive days. This patient-centred endpoint was chosen because of the extended duration of health impairment associated with COVID-19 [1-3]. The longer follow-up to capture this endpoint (compared to the common 28 days [4-6]) was designed to provide a more comprehensive assessment of the capacity of a therapeutic agent to speed recovery from COVID-19.

The TICO primary endpoint of sustained recovery is defined as 14 continuous days at home, where home is defined as the type or level of residence where the participant lived prior to their SARS-CoV-2 infection.

This approach avoids categorizing patients as recovered if they continue to have care needs beyond their pre-morbid state despite discharge from an acute care facility, or if they are re-admitted to hospital shortly after initial discharge. To operationalize the collection of this endpoint, a participant's 'home' is classified at enrolment (types of residences are defined below) and a participant's current location, and consecutive days spent at that location, is collected fortnightly during follow-up using a dedicated CRF.

There are seven possible categories for classifying home in the TICO study. They are:

Independent dwelling withOUT professional medical help - Participant is living in a house, apartment, flat, condominium independently (regardless whether alone or with family or friends; also regardless of any paid help such as housekeeping service, maid, gardener etc.).

Independent dwelling WITH professional medical help - Participant is living in a house of any form, apartment, flat, or condominium but is requiring visiting professional medical help (e.g., visiting nurse, physiotherapist, or other home healthcare personnel meant to provide medical or rehabilitation care in the home)

Community dwelling - Participant is homeless, living on the streets or undomiciled, or may be living in a shelter or hotel (including hotel stay for quarantine purposes).

Residential care facility - These are non-skilled nursing facilities where care and services are provided to assist with activities of daily living. If the nature of the services can be safely and effectively performed by a trained nonmedical person, the services will be considered residential care. Examples include assisted living facility, group home, low-level care facility, or other nonmedical institutional setting.

Other Healthcare facility - Skilled nursing facility (nursing homes), acute inpatient rehabilitation facilities (acute rehab), or other healthcare facility that provides onsite medical care above a residential care facility but with a lower intensity than provided in hospitals.

Long-term inpatient care hospital - Long-term acute care hospital (LTACH), long-term care hospital. Note: These are hospitals/facilities meant to provide longer term (typically >20-30 days) of acute-care services after discharge from the short-term acute care hospital. Services requiring this level of care may include mechanical ventilation, intensive wound care, intensive pain management. LTACHs are hospitals that specialize in the treatment of patients with serious medical conditions that require care on an ongoing basis but no longer require intensive care or extensive diagnostic procedures.

Short-term acute care hospital - Short-term acute care hospital (similar to the index/enrolling hospital). Most acute care hospitals fall into this category, regardless of the duration of hospital admission.

3 Sample size considerations for the initial futility assessment

The following assumptions were made in estimating the required sample size for the initial futility assessment, considering the marginal tests for each of the ordinal outcomes separately.

a. The primary analysis will be intention-to-treat.

b. A proportional odds model with indicators for the investigational agent group and baseline severity of illness as defined by the ordinal outcome will be used to estimate the odds ratio. The model will be stratified by study site pharmacy.

c. Type 1 error = 0.30 (1-sided) and power = 0.95.

d. The clinical status (% distribution for each pulmonary+ category) of participants in the placebo group at Day 5 is assumed as shown in the 3rd column Supplemental Table 3. Since both randomized treatment groups will receive remdesivir as standard of care (unless contraindicated), these percentages were estimated using Day 5 data from the ACTT1 trial for a subgroup of patients similar to the intended participants of this trial who were randomized to remdesivir.

e. We targeted an odds ratio (active/placebo) of 1.60 for a more favourable outcome. This corresponds to the % distribution of the clinical status of participants in the investigational agent group at Day 5 shown in the 2nd column in Supplemental Table 3. For example, the percentage of participants in the 2 most favourable categories would be increased to 56.7% in the group receiving the investigational agent from 45.0% in the placebo group (a 11.7% increase). Conversely, the percentage of participants in the 4 most severe categories would decrease to 22.7% from 32.0% in the placebo group. The same proportional improvement was assumed across the ordinal scale.

f. Based on the category percentages in Supplemental Table 3, the estimated initial futility sample size with a single comparison between an investigational treatment and placebo is 293. This was increased to 300 to allow for some missing data at Day 5.

4 Sample size considerations for final assessment of efficacy

The following assumptions were made in estimating the required sample size for the final assessment of efficacy.

a. The primary analysis will be intention to treat. Gray's test with rho=0 will be used [7], with stratification by disease severity at entry for comparing each investigational agent to control for the primary endpoint of time to sustained recovery. Gray's test with rho=0 is the analogue of the log-rank test in the presence of competing risks; it is used here to account for the competing risk of death when analysing time to sustained recovery.

b. Type 1 error will be set at 0.025 (1-sided). This type 1 error will not be adjusted for the number of investigational agents being compared with placebo as each of the agents is expected to impact the primary endpoint through different mechanisms. If this is not the case, a type 1 error adjustment may be considered.

c. Power is set at 90% to detect a 25% increase in the rate of sustained recovery for the investigational treatment compared to placebo. This moderate efficacy is assumed considering the findings from ACTT-1 [8],and the percentage of patients in each baseline risk category of the ordinal outcome. Based on the results from ACTT-1 [8], we expect approximately 50% of patients enrolled after the initial futility assessment to be in the more severe strata (5 and 6 in the ordinal categories shown in Supplemental Table 3). However, all patients who are enrolled prior to the initial futility assessment are in the less severe strata at entry (categories 3 and 4 in Supplemental Table 3). These patients will also be part of the primary analysis. Thus, we assume that 40% of patients in the final analysis will be in the more severe strata; mortality is expected to be higher for patients in the more severe strata. Among surviving patients, we assume most will have met the criteria for sustained recovery.

d. With these assumptions for type 1 and type 2 error and a sustained recovery rate ratio of 1.25 for the investigational agent versus control, 843 sustained recoveries are needed [9, 10].

e. Given the duration of follow-up, we estimate that the sample size is slightly larger than the number of recoveries (i.e., we expect a low rate of loss-to-follow-up or deaths). For 2 groups, we assume that the sample size is approximately 20% higher than the number of recoveries, to account for deaths, a small number of withdrawals of consent, and a small number of patients remaining in the hospital at Day 90. Total sample size for 2 groups is approximately 1,000 (500 per group).

f. In order to observe 843 sustained recoveries among 1000 participants, and assuming 3% withdrawal of consent, at least 87% of participants (pooled across the two treatment arms) would have to achieve sustained recovery by Day 90. Assuming a recovery rate ratio of

1.25, this corresponds to 89.9% with sustained recovery among those randomized to the investigational agent, compared with 84.1% in the control group.

5 Randomization application

In order to facilitate randomizations to multiple possible agents, a flexible web-based randomization application was developed. The flexibility is accomplished with a database-driven approach pulling information from three tables: (i) randomisation table, which contains stratum specific schedules (as randomisation is stratified by pharmacy and disease severity stratum) for one or multiple agents; (ii) drug table, which contains agent availability and allows stopping/restricting randomisation to selected agents, and information describing the agent, including number of doses of the agent available at the site study pharmacy; and (iii) constraint table, which contains contraindications and information used to modify inclusion/exclusion criteria. Randomisation assignments will be obtained in sequence from pre-generated schedules stratified by pharmacy and disease severity stratum. Allocation will be 1:1 Active:Placebo for one agent, 2:1:2:1 Active A:Placebo A:Active B:Placebo B for two agents (A and B), and so on. Using permuted blocks with k agents, every k placebo assignments will include one agent specific placebo assignment per agent, and every k active assignments will include one per agent. Using the mass-weighted urn scheme [11], the underlying Active:Placebo sequence is generated to ensure an approximate 1:1 balance for each active versus pooled placebo comparison within strata throughout the trial.

The application can also vary allocation according to stratum (i.e. pharmacy or disease severity). With 2 agents, allocation for the less severe stratum might be 2:1:2:1 as above but if agent B has not advanced to Disease Stratum 2 (and can therefore not recruit individuals with high disease severity), for the more severe stratum allocation would be 1:1 Active A: Placebo A. Furthermore, the application allows a limited number of sites to allocate patients 2:1:2:1: Active A:Placebo A:Active B:Placebo B or 1:1 Active B:Placebo B initially

to obtain safety data for DSMB review for agent B while other sites randomize participants to only Active A; Placebo A until the safety review is complete.

6 Pharmacy set-up options

A number of pharmacy options are available to participating sites.

1. A single study site pharmacy serving multiple clinical sites within a close geographical area (e.g. the same city). Local site's clinical staff screen and randomise patient before ordering relevant study provided standard of care and placebo/agent from the study site pharmacy. Study provided standard of care and placebo/agent are made up and the placebo/agent is blinded at the study site pharmacy before being distributed to the local site clinical staff for administration.
2. A single study site pharmacy serving multiple local site pharmacies within a close geographical area. Local site's clinical staff screen and randomise patient before ordering relevant SOC and placebo/agent from the study site pharmacy. The study site pharmacy selects the appropriate number of vials of both study provided standard of care and placebo/agent. The study site pharmacy then arranges transport of the appropriate number of vials to the local site pharmacy At the local site pharmacy, the study provided standard of care and placebo are made up and the placebo/agent is blinded before being distributed to clinical staff for administration.
3. A traditional pharmacy set-up where the study site pharmacy only serves a single clinical site

7 Supplemental tables

Supplemental Table 1 Participating International Coordinating Centres (ICC), Clinical Sites and Site Coordinating Centres

INSIGHT Copenhagen ICC Centre of Excellence for Health, Immunity, and Infections (CHIP), Department of Infectious Diseases, Rigshospitalet, Copenhagen, Denmark		
Site Name	**City**	**Country**
University Hospital Zurich	Zurich	Switzerland
Unité VIH/SIDA Genèva	Geneva	Switzerland
Johann Wolfgang Goethe Univ. Ho sp., Infektionsambulanz CRS	Frankfurt	Germany
Universitätsklinik Köln	Cologne	Germany
Universitätsklinikum Regensburg	Regensburg	Germany
Hvidovre University Hospital, Department of Infectious Diseases	Hvidovre	Denmark
Aarhus Universitetshospital, Skejby	Aarhus	Denmark
Odense University Hospital	Odense	Denmark
Aalborg Hospital	Aalborg	Denmark
Rigshospitalet, Department of Infectious Diseases	Copenhagen	Denmark
Nordsjællands Hospital, Hillerød	Hillerod	Denmark
Zealand University Hospital Roskilde	Roskilde	Denmark
Kolding Sygehus	Kolding	Denmark
Herlev-Gentofte Hospital	Hellerup	Denmark
Bispebjerg Hospital	Copenhagen	Denmark
Wojewodzki Szpital Zakazny	Warsaw	Poland
Hospital Universitari Germans Trias i Pujol (site and INSIGHT Site Coordinating Centre Spain)	Badalona	Spain
Hospital General Universitario Gregorio Marañón	Madrid	Spain

Hospital Clínic de Barcelona	Barcelona	Spain
Hospital Universitario La Paz	Madrid	Spain
Hospital Clínico San Carlos	Madrid	Spain
Hospital del Mar	Barcelona	Spain
Hospital Universitari Vall d'Hebron	Barcelona	Spain
Hospital Universitario de Bellvitge	Hospitalet de Llobregat	Spain
Hospital Universitario Arnau de Vilanova (Lleida)	Barcelona	Spain
AIDS and Clinical Immunology Research Center	Tbilisi	Georgia
Central City Clinical Hospital of Ivano-Frankivsk City	Ivano-Frankivsk	Ukraine
Karolinska University Hospital	Stockholm	Sweden
Capio Sankt Görans Sjukhus	Stockholm	Sweden
Uppsala University Hospital	Uppsala	Sweden
INSIGHT London ICC Medical Research Council Clinical Trials Unit at UCL, University College London, London, UK		
Site Name	**City**	**Country**
Hôpital Saint-Louis	Paris	France
Groupe Hospitalier Sud Île de France	Melun	France
Hopital Lariboisière	Paris	France
Ospedale San Raffaele S.r.l.	Milan	Italy
L. Sacco Hospital-Institue of Infectious and Tropical Diseases	Milan	Italy
INMI Lazzaro Spallanzani IRCSS	Rome	Italy
Bergamo Hospital	Bergamo	Italy
Royal Free Hospital	London	United Kingdom
Royal Victoria Infirmary	Newcastle upon Tyne	United Kingdom

Guy's & St. Thomas' NHS Foundation Trust	London	United Kingdom
MRC/UVRI Research Unit on AIDS (site and INSIGHT Site Coordinating Centre Uganda)	Entebbe	Uganda
St Francis Hospital, Nsambya	Kampala	Uganda
Gulu Regional Referral Hospital	Gulu	Uganda
Mulago Hospital Complex	Kampala	Uganda
Lira Regional Referral Hospital	Lira	Uganda
Masaka Regional Referral Hospital	Masaka	Uganda
CISPOC	Maputo	Mozambique
National & Kapodistrian University of Athens Medical School (INSIGHT Site Coordinating Centre Greece)	Athens	Greece
Attikon University General Hospital	Athens	Greece
1st Respiratory Medicine Dept, Athens University Medical School	Athens	Greece
AHEPA University Hospital	Thessaloniki	Greece
Dept of Critical Care and Pulmonary Medicine, Evangelismos General Hospital	Athens	Greece
Democritus University of Thrace	Alexandroupoli	Greece
3rd Dept of Medicine, Medical School, NKUA	Athens	Greece
St. Peters Tuberculosis Specialized Hospital	Addis Ababa	Ethiopia
INSIGHT Sydney ICC The Kirby Institute, University of New South Wales, Sydney, Australia		
Site Name	**City**	**Country**
Hospital General de Agudos JM Ramos Mejia	Buenos Aires	Argentina
CEMIC	Buenos Aires	Argentina
Hospital Italiano de Buenos Aires	Buenos Aires	Argentina
Hospital Profesor Bernardo Houssay	Buenos Aires	Argentina
NCGM	Tokyo	Japan

Fujita	Toyoake Aichi	Japan
Tan Tock Seng Hospital	Singapore	Singapore
Chennai Antiviral Research and Treatment Clinical Research Site (CART-CRS)	Chennai	India
Institute of Human Virology-Nigeria (IHVN)	Abuja	Nigeria
INSIGHT Washington ICC Veterans Affairs Medical Center and George Washington University, Washington, DC, USA.		
Site Name	**City**	**Country**
Washington DC VA Medical Center	Washington	United States
MedStar Health Research Institute	Washington	United States
Henry Ford Health System	Detroit	United States
Denver Public Health	Denver	United States
Cooper University Hospital	Camden	United States
West Haven VA Medical Center	West Haven	United States
Hennepin Healthcare Research Institute/HCMC	Minneapolis	United States
University of South Florida, Tampa General Hospital	Tampa	United States
SUNY Downstate Medical Center	Brooklyn	United States
Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center	Torrance	United States
Georgetown University	Washington	United States
UT Southwestern Medical Center	Dallas	United States
Parkland Health and Hospital Systems	Dallas	United States
Minneapolis VA Medical Center	Minneapolis	United States
University Hospitals Cleveland Medical Center	Cleveland	United States
University of Minnesota	Minneapolis	United States
Instituto de Infectologia Emílio Ribas - IIER	Sao Paulo	Brazil

Complexo Hospitalar Professor Edgard Santos	Salvador	Brazil
Instituto Nacional de Infectologia Evandro Chagas- INI	Rio de Janeiro	Brazil
Hospital Universitario Maria Aparecida Pedrossian	Campo Grande	Brazil
Socios En Salud Sucursal Peru	Lima	Peru
Hospital Nacional Hipolito Unanue	Lima	Peru
Instituto Nacional de Ciencias Medicas y Nutrición Salvador Zubiran (INCMNSZ)	Mexico City	Mexico
Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas (INER)	Mexico City	Mexico
Hospital General Dr. Manuel GEA Gonzalez	Mexico City	Mexico
Hospital General Dr. Aurelio Valdivieso	Oaxaca	Mexico
INSIGHT NIH-DCR ICC Department of Clinical Research, National Institute of Allergy and Infectious Diseases, Bethesda, MD, USA		
Country	**Country**	**Country**
Lincoln Medical Center	Bronx	United States
Maimonides Medical Center	Brooklyn	United States
CHRISTUS Spohn Shoreline Hospital	Corpus Christi	United States
Hendrick Medical Center	Abilene	United States
Hoag Memorial Hospital Presbyterian	Newport Beach	United States
Cotton O'Neil Clinical Research Center	Topeka	United States
CHRISTUS Good Shepherd Medical Center	Longview	United States
Velocity Chula Vista	Chula Vista	United States
Velocity San Diego	La Mesa	United States
Rhode Island Hospital	Providence	United States

The Miriam Hospital	Providence	United States
Memorial Healthcare System	Hollywood	United States
INSIGHT U.S. Department of Veterans Affairs (VA) research network ICC		
Site Name	**Site City**	**Country**
VA Greater Los Angeles Healthcare System	Los Angeles	United States
San Francisco VA Health Care System	San Francisco	United States
Miami VA Healthcare System	Miami	United States
Bay Pines VA Healthcare System	Bay Pines	United States
VA Palo Alto Healthcare System	Palo Alto	United States
Michael E. DeBakey VA Medical Center	Houston	United States
Southern Arizona VA Health Care System	Tucson	United States
North Florida/South Georgia Veterans Health Sysem	Gainesville	United States
Salem VA Medical Center	Salem	United States
VA San Diego Healthcare System	San Diego	United States
VA Loma Linda Healthcare System	Loma Linda	United States
Clement J. Zablocki Veterans Affairs Medical Center	Milwaukee	United States
Tennessee Valley Healthcare System	Nashville	United States
Sacramento VA Medical Center	Mather	United States
Portland VA Health Care System	Portland	United States
VA Providence Healthcare System	Providence	United States
VA Long Beach Healthcare System	Long Beach	United States
Saint Louis VAMC	Saint Louis	United States
Prevention and Early Treatment of Acute Lung Injury (PETAL) ICC		
Massachusetts General Hospital, Boston, USA		

Site Name	Site City	Country
Baystate Medical Center (site and ALIGNE Site Coordinating Center)	Springfield	United States
Beth Israel Deaconess Medical Center (site and Boston Site Coordinating Centre)	Boston	United States
Massachusetts General Hospital	Boston	United States
University of Mississippi Medical Center	Jackson	United States
UCSF San Francisco (site and California Site Coordinating Centre)	San Francisco	United States
Ronald Reagan UCLA Medical Center	Los Angeles	United States
Stanford University Hospital & Clinics	Stanford	United States
UC Davis	Davis	United States
UCSF Fresno	Fresno	United States
UCSF Medical Center at Mount Zion	San Francisco	United States
University of Colorado Hospital (site and Colorado Site Coordinating Centre)	Aurora	United States
National Jewish Health | St. Joseph Hospital	Denver	United States
University of Michigan Medical Center (site and Michigan Site Coordinating Centre)	Ann Arbor	United States
Montefiore Medical Center Moses Hospital (site and Montefiore-Sinai Site Coordinating Centre)	Bronx	United States
Montefiore Weiler	New York	United States
Banner University Medical Center Tucson	Tucson	United States
Cleveland Clinic Foundation	Cleveland	United States
University of Cincinnati Medical Center (site and Ohio Site Coordinating Centre)	Cincinnati	United States
Cleveland Clinic Fairview Campus	Cleveland	United States
Cleveland Clinic Marymount Campus	Cleveland	United States
Cedars-Sinai Medical Center	Los Angeles	United States
Oregon Health and Science University (site and Pacific Northwest Site Coordinating Centre)	Portland	United States

Swedish Hospital Cherry Hill	Seattle	United States
Swedish Hospital First Hill	Seattle	United States
UPMC Presbyterian	Pittsburgh	United States
UPMC Magee	Pittsburgh	United States
UPMC Shadyside	Pittsburgh	United States
Wake Forest Baptist Health (site and Southeast Site Coordinating Centre)	Winston-Salem	United States
Medical University of South Carolina	Charleston	United States
University of Kentucky	Lexington	United States
Virginia Commonwealth University Health System	Richmond	United States
Intermountain Medical Center (Site and Utah Site Coordinating Centre)	Murray	United States
University of Utah Hospital	Salt Lake City	United States
Utah Valley Regional Medical Center	Provo	United States
LDS Hospital	Salt Lake City	United States
Vanderbilt University Medical Center	Nashville	United States
Cardiothoracic Surgical Trials Network (CTSN) ICC Icahn School of Medicine at Mount Sinai, New York, USA		
Site Name	**City**	**Country**
Allegheny General Hospital	Pittsburgh	United States
Baylor College of Medicine	Houston	United States
Baylor, Scott and White Health	Dallas	United States
Cedars-Sinai Medical Center	Los Angeles	United States
CHI St. Vincent, Arkansas	Little Rock	United States
Duke University Hospital	Durham	United States
East Carolina Heart Institute	Greenville	United States

Emory University	Atlanta	United States
Inova Heart & Vascular Institute	Falls Church	United States
Lutheran Medical Group	Fort Wayne	United States
MH Mission Hospital	Asheville	United States
Mount Sinai Medical Center	New York	United States
New York University Langone Health	New York	United States
Northwell Health	Manhasset	United States
Ochsner Clinic	New Orleans	United States
Piedmont Healthcare	Atlanta	United States
Texas Heart Institute	Houston	United States
University of Louisville	Louisville	United States
University of Maryland	Baltimore	United States
University of Southern California	Los Angeles	United States
University of Virginia Health Systems	Charlottesville	United States
WakeMed Heart Center	Raleigh	United States
West Virginia University	Morgantown	United States
Dartmouth-Hitchcock Medical Center	Lebanon	United States
Hôpital Laval	Quebec	Canada

Supplemental Table 2 Agent specific information contained in separate appendices

Section	Key sub-sections
Introduction/Rationale for studying the agent	• Potential risks and benefits of agent • Motivation for agent selection with consideration of results from trials of other agents
Agent Specific Eligibility Criteria	n/a
Description of investigational agent	• Administration and duration

	• Formulation and preparation • Supply, distribution, and accountability • Contraindicated medications • Precautionary medications
Clinical and laboratory evaluations in addition to master protocol	• Timing • Special instructions
Clinical management issues	• Infusion-related reactions • Hypersensitivity • Pregnancy and breast-feeding considerations • Criteria for discontinuation of infusion

Supplemental Table 3 Safety Data Collection Schedule

	Infusion +2 hrs	Days 0-7	Day 14	Day 28	Day 90	Month 6, 12 and 18
Infusion-related reactions and symptoms	X					
Incident grade 3 and 4 clinical AEs			X[1]	X[1]		
Clinical AEs of any grade severity	X	X	X[2]	X[2]		
Targeted laboratory abnormalities of any grade		X (Day 5)				
Hospital admissions and deaths	Collected through to Month 18					
Serious AEs (including those reported as part of the pulmonary and pulmonary+ ordinal outcomes)	Collected through Day 90					
Unanticipated problems	Collected through Day 90					
Any serious adverse event related to study intervention	Collected through Day 90					

1. All grade 3 and 4 events since previous visit
2. All grade 1 and 2 events on the day of the visit only

Supplemental Table 4 Hypothesized percentage of participants in each category on Day 5 in the investigational agent and placebo groups based on aforementioned assumptions.

Pulmonary Plus Category	Investigational Agent + Standard of Care	Placebo + Standard of Care
1. No limiting symptoms due to COVID-19	3.2	2.0
2. Limiting symptoms due to COVID-19	53.5	43.0
3. Moderate end-organ dysfunction	20.6	23.0
4. Serious end-organ dysfunction	12.8	17.0
5. Life-threatening end-organ dysfunction	5.0	7.3
6. End-organ failure	4.5	7.0
7. Death	0.4	0.7
Total	100.0	100.0

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