

“Solidarity Trial”: A Feeling of Trust Towards COVID-19 Treatments

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Corona Virus Disease (COVID-19) drugs are not being developed at the pace in which the disease is spreading throughout the world. WHO and its partners have announced the worldwide clinical trial on 18th March 2020, known as “Solidarity Trial” for greater co-ordination of developments of drugs. [1]“*Solidarity Trial is an international clinical trial to help find an effective treatment for COVID-19*”. [1, 2] The trial is randomized, open-label and adaptive. This trial will analyze four treatment options against standard of care, after recruiting patients from various countries, and then will approach to their relative effectiveness against the disease. The aim of this trial is to rapidly explore if any of the administered drugs will slow progression of disease or improve survival.[2]

The rationale of conducting “Solidarity Trial” is to reduce time taken by the trials. Randomized clinical trials generally take years to conduct, while, “Solidarity Trial” will reduce the duration by 80%.[2] By enrolling patients from around the world, this trial might be able to provide result more rapidly than multiple small trials. Moreover, those small multiple trials will not be able to gather solid evidence required to determine the relative effectiveness of given unproven drugs. [2] Besides this, with involvement of multiple countries, the cost of trial will also reduce. Already, 100 countries including Norway, Canada, Spain,

Argentina, Thailand, South Africa, India, Indonesia, Switzerland and others have committed to join this trial. Norway is the first country to contribute its first patient for this important trial.[2] This trial will provide simplified procedure to enable hospitals to participate without any paperwork. The countries with least infrastructure can follow a main protocol, while those with better facility will launch “daughter trials” that will gather added data.[2,3]

Four treatment options are selected for this trial on the basis of evidence gathered from animal studies, clinical studies and laboratory results. They are Remdesivir, Lopinavir with Ritonavir, Lopinavir with Ritonavir + Interferon beta-1a and Chloroquine or Hydroxychloroquine.[2,3] Remdesivir, acts by inhibiting RNA-dependent RNA polymerase and stops viral replication, has provided encouraging outcome in Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS).[2,3] Lopinavir /Ritonavir, approved for treatment of HIV, are protease inhibitors. They block the aspartic protease enzyme that breaks down proteins into small pieces needed for viral replication. [3] These drugs were tried in China for treatment of COVID-19.[4] But, there was no significant clinical improvement and reduction in mortality among patients. However, there was reduction in median time to clinical improvement by one day comparing to standard-care group.[4] Interferon beta-1a is a class of protein called cytokines that are produced by host cells in response to virus. Then, they signal other cells around them to enhance anti-virus defense mechanism.[3] It has shown some effective results against COVID-19 in combination with Lopinavir/Ritonavir.[2,3] Furthermore, Chloroquine or hydroxychloroquine are believed to interfere with fusion of virus with host cell by increasing pH of viral endosome or to allow zinc influx to viral cell that inhibits RNA-dependent RNA polymerase.[3] They have shown possible beneficial effect against pneumonia caused by COVID-19 in small studies conducted in China and France.[2,3]

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Eligible patients for this trial are adults (age ≥ 18 years) with confirmed diagnosis of COVID-19 recently or already admitted to participant hospital. [2] Patients with any contraindication to the study treatments will be excluded from trial. The patients are asked to sign written consent which explains that they understand all the possible risks and beneficial effects of this trial. [2] There will be a medical team for each patient responsible to monitor if any of the study treatment would be definitely unsuitable to the patient. The severity of disease is assessed by recording clinical presentations like difficulty in breathing, patient on oxygen, patient on ventilator, and radiography of chest showing bilateral lung abnormalities. The underlying medical conditions are also recorded like chronic lung disease, chronic heart disease, chronic liver disease, chronic renal disease, tuberculosis and HIV. [2] Then, the patients are randomly allocated to treatment options. This may include local standard of treatment only OR local standard of treatment PLUS one of Remdesivir, Chloroquine or Hydroxychloroquine, Lopinavir with Ritonavir, Lopinavir with Ritonavir PLUS Interferon beta-1a. [2.3] This random allocation of treatment options is done by computer, not any medical staff. The critical information of trial is only collected at randomization stage and at the time patient is discharged or dead. This information includes which drugs were given, duration of therapy, date of discharges, date of death and cause of death. [2] This entire trial is monitored by Global Data and Safety Monitoring Committee, an independent group of experts. [2]

This clinical trial has brought the world to one stage for common goal related to health issue. The world may believe that this trial will soon bring good and positive result of treatment options for COVID-19 with the support of multiple countries under umbrella of WHO. Additionally, this trial will also create important basis for conducting new trials collaboratively if any new pandemics will occur unfortunately in the future.

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