Leveraging the capabilities of NWEH to simplify clinical evaluation of a potential COVID-19 antiviral

Driving a new potential antiviral

A leading pharmaceutical firm and a major clinical development and analytical service company partnered with NorthWest EHealth (NWEH) to support patient recruitment for a potential COVID-19 antiviral therapy.

Steven Hargreaves

Steven Hargreaves, Senior Research Nurse and Community Team Lead at NWEH, works with general practitioners (GPs), nurses, and study administrators across Greater Manchester to streamline clinical trials and patient experiences within trials. He has worked with NWEH for more than five years and acted as study lead on the MOONSONG trial.

Senior Clinical Team Manager

The Senior Clinical Team Manager (SCTM) who led the trial has 19 years of experience in clinical research and has overseen the running of more than 75 trials across a range of therapeutic areas. She has fulfilled various roles, including acting as a clinical trial manager and analytical chemist, and has spent the past four years leading large clinical teams around the globe.

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Conducting a clinical trial during the COVID-19 pandemic

We spoke to Steven Hargreaves and the SCTM at the clinical and development analytical service company about the rationale behind and challenges encountered while conducting a Phase II trial of a potential antiviral therapy for COVID-19 using ground-breaking methods.

Notable challenges included slow patient recruitment and the need for rapid patient processing. The NWEH tool FARSITE provided a pioneering new way to rapidly access appropriate patients at the earliest possible stage, allowing researchers to overcome recruiting difficulties, and offered a new approach in a real-time feasibility system to tackle the time constraints associated with efficacy testing for a new antiviral.

"Any updates were made immediately and NWEH was very open to receiving and responding to my questions, which is a fantastic quality in a working partnership of this kind. They are a great group of people to work with, and the presence of top-level group members in our meetings didn't go unnoticed. Another big plus is that they helped to source the principal investigators (PIs) for MOONSONG."

Steven Hargreaves

A whole new world

The world has been forever transformed by the COVID-19 pandemic. An estimated 645 million cases and 6.64 million deaths have been attributed to COVID-19[1] and, despite widespread vaccination efforts, these numbers continue to rise.

But the situation has improved in many ways. There are many more treatments available to us today than there were on 11 March 2020 – the date on which the World Health Organisation (WHO) officially declared the spread of SARS-CoV-2 a global pandemic.

Current treatments for patients in the UK with COVID-19 at risk of serious illness include antiviral medications (nirmatrelvir and ritonavir, remdesivir, or molnupiravir) and neutralising antibodies (sotrovimab). [2] Many of these treatments were repurposed to fight COVID-19 in the early days of the pandemic, when treatments were scarce and the need was urgent.

New drugs that act as potent antivirals against SARS-CoV-2 and which can be taken orally are still needed to improve outcomes for individuals who face the highest levels of risk.

NWEH has entered an exciting partnership for the clinical evaluation of AT-527, an orally available antiviral compound that has demonstrated activity against the SARS-CoV-2 virus in vitro.[3] The active metabolite of AT-527 cannot pass into human cells and is thought to be produced in substantial amounts in the respiratory tract. Thus, AT-527 may represent a promising weapon in the ongoing fight against COVID-19. The MOONSONG study was designed to assess this possibility.

Introducing MOONSONG

MOONSONG is a Phase II, randomised, double-blind study that evaluated AT-527 500 mg or 1100 mg versus placebo in adults with mild or moderate COVID-19.

The study was conducted across many countries, including Canada, Spain, and the UK, from July 2021 to December 2021.[4] Key endpoints included:

- Reduction in SARS-CoV-2 RNA
- Time to cessation of viral shedding and non-detectable virus
- The percentage of patients who were SARS-CoV-2-positive at pre-specified timepoints
- Time to improvement in symptoms, including duration of fever
- Complications of COVID-19
- Safety and tolerability
- Pharmacokinetic parameters.

Clinical trials in the age of COVID-19, however, are not without their challenges.

The SCTM summarised some of these challenges: *"The pressure associated with clinical studies of COVID-19 is extreme. The speed of the studies is much faster than in other therapy areas that I've worked in, because we need to capture patients in the five-day window following a positive test. Then there are the problems unique to COVID – for example, how do you see the patients during lockdowns?"*

In MOONSONG, study staff would travel to patient's homes to discuss aspects of the study and take samples. To ensure their safety, masks were fit-tested at a central location and other types of personal protective equipment – such as car seat covers – were provided. But sample collection also presented its own set of hurdles.

Steven explained: *"One of the biggest challenges was handling the samples. We had to collect saliva samples, nasopharyngeal swabs, and all sorts of bloods, including post-dose samples. Some had to be put on ice, some had to be spun within 30 minutes, some had to sit and clot – we even had to upgrade our centrifuge at one of the study sites so that we could seal the samples without risking airborne spread of the virus."*

FARSITE: accelerating clinical trials

The NWEH Feasibility Assessment and Recruitment System for Improving Trial Efficiency (FARSITE) – a feasibility tool designed to streamline the recruitment of patients into clinical trials from primary care – was used to support the MOONSONG study.

Steven describes the platform: *"FARSITE extracts data from registered GP surgeries and sends that data to a centralised repository in an anonymised form. Using FARSITE, clinical personnel can construct and carry out searches to identify patients matching the trial protocol, and the data is refreshed in real-time in daily feeds. They can include all sorts of factors, including age, smoking history, medications, blood results, and so on. When a researcher is ready to recruit for that trial, FARSITE can be used to connect them to the relevant GP. The GP will receive trial details via FARSITE and will decide whether they want to participate or not. The tool also has a feature that allows for literature and useful materials to be sent directly to patients, eliminating the need to visit practice sites, whilst adhering to the appropriate approvals processes."*

NWEH identified patients within the FARSITE system based on available COVID test data and GPs reviewed those choices twice each day, once in the morning and once in the afternoon. By doing so, investigators were able to access results for patients at the earliest possible stage. This speed is crucial for studies of antiviral compounds, which provide reduced benefit when given even a short time after infection. The NWEH team was also based at the surgery, which allowed them to contact patients on the practice's behalf.

This level of support was provided at two sites: Tower Family Healthcare in Bury, UK, and Chapel Street Medical Centre in Ashton-under-Lyne, UK. Steven added: *"Tower Family Healthcare represents around 50,000 patients and has been working with us since our earliest trials. NWEH is fortunate to hold a permanent research room on site. Chapel Street Medical Centre started working with us more recently, but they are active participants in trials and one of the principal investigators there has won several awards."*

Support beyond the software

In addition to recruiting patients through FARSITE, NWEH supported with many additional trial activities, including:

- Site set-up responsibilities
- Development of research documents
- Collection of samples
- Entering the data into relevant documents and systems
- Interaction with patients.

The SCTM described her experience working with NWEH as a positive one*: "NWEH has a wonderful system for creating process documents that is unlike anything I've seen elsewhere. They were very responsive when I raised potential concerns due to my experiences as a quality manager in the UK. Any updates were made immediately and the team was very open to receiving and responding to my questions, which is a welcome quality in a working partnership of this kind.*

A patient-focused approach

Many elements of the NWEH approach feed into the larger goal of anticipating and addressing patient needs.

Reasons for patient engagement in trials vary widely and include factors such as a desire for increased face-to-face contact with their GP, or wanting a more thorough health check, which may not be offered in everyday practice. This is also beneficial for GPs because it allows them to identify potential issues at an earlier stage than might otherwise be the case.

There is also an ongoing movement to open the doors of the research world to a broader range of patients. Although some patients are seen by physicians frequently, their opportunities to get involved in research are often limited. Steven explains: *"More often than not, we tend to recruit patients to trials who have never considered taking part in research before. An overwhelming majority then ask us what further clinical research opportunities are available to them when the trial ends. This is partly because these patients attend visits at their own GP practice. Many would otherwise assume that trial visits are hospital-based, which is a potential deterrent."*

Another component of NWEH's patient-centric approach is the compensation of patients for their time on studies. During MOONSONG, study visits sometimes extended beyond those associated with COVID symptoms and subsequent recovery. These visits may have interfered with the patient's home life and privacy during a pandemic. Steven added: *"Some other decentralised studies require patients to spend extended amounts of time at a specified location, which could mean losing salary or annual leave. Patients should be compensated for the impact on their time."*

Over the horizon

MOONSONG ended in December 2021. While AT-527 was safe and tolerated by patients, the primary endpoint of reduced viral load was not met in the overall study population.

Researchers did, however, identify a reduced viral load in high-risk patients with underlying health conditions who received AT-527 at the 1100 mg dose. The upcoming Phase III MORNINGSKY trial is being modified in response to this promising result.

Looking forward, it is hoped that the work conducted using FARSITE will lead to meaningful and more widespread change in accelerating patient recruitment and trial modelling. With plans for the tool to expand worldwide, it's safe to say that those hopes might soon be realised.

Best practice in patient recruitment

NWEH's Feasibility Assessment and Recruitment System for Improving Trial Efficiency (FARSITE) platform is an established feasibility tool to search, find, and recruit participants from primary care settings into clinical trials, whilst still preserving their confidentiality. FARSITE was used in the MOONSONG trial to identify and recruit patients from two GP practices in the North West of England.

NWEH:
true-to-life clinical trials

NWEH provides the pharmaceutical industry with a holistic approach to clinical trial design and delivery, helping bring drugs to market faster. FARSITE has the potential to streamline the complex processes associated with conducting trials in a regulated environment, affording the opportunity to bring life-saving therapeutics to the market quickly and efficiently.

NWEH is a leading figure in the field of electronic health record (EHR)-enabled randomised clinical trials. NWEH built the technology behind the success of the pioneering Salford Lung Study and is the only organisation in the world to have evaluated the safety and effectiveness of a pre-licence medicine in a real-world setting.

From feasibility studies and trial design to clinical delivery and data analysis, NWEH supports the success of pharmaceutical companies and contract research organisations across the globe.

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To find out more about the NWEH true-to-life approach to clinical trials and how the company's tools and expertise in recruitment, design and feasibility, clinical management and delivery, safety data reporting, and data analysis could be applied to future projects, visit nweh.co.uk.

NWEH WEBSITE

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This case study has been independently authored by NWEH.

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