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Dear participants in the ARCADIA study. We would like to thank you very much for taking part in this study and helping us to find out how to improve the treatment of diabetic patients hospitalized with COVID-19.

We are pleased to share the results of this study with you. In case you have any (medical) question after reading these results, please contact your treating physician.

Study title

A Phase II, randomised, double-blind, placebo-controlled clinical trial to assess the safety and efficacy of AZD1656 in diabetic patients hospitalised with suspected or confirmed COVID-19 (The ARCADIA Trial)

Who carried out the research? (including details of sponsor, funding and any competing interests)

This research was sponsored by St. George Street Capital (a U.K. charity) and was funded by the U.K. government and Excalibur Medicines Ltd.

What public involvement there was in the study (how many people, what their relevant lived experience was, and what they did)

The public were not involved in the planning and design of the study.
156 people took part in the study. Everyone had either type 1 or type 2 diabetes and were in hospital with COVID-19. Participants received either AZD1656 (an active drug) or placebo (a dummy pill that looks the same as AZD1656 but does not contain the active drug). Patients received one of these study treatments until they were discharged from hospital or until their illness worsened. The treatment lasted for a maximum of 21 days. Whilst in hospital, the health and well-being of the patients was assessed every day. One week after completing study treatment patients had a final visit to capture any new safety information or changes to medication.

Where and when the study took place

This study took place in 28 hospitals (14 hospitals in the United Kingdom, 7 hospitals in Romania and in 7 hospitals in Czech Republic) from August 2020 till May 2021.

Why was the research needed?

This research was needed to find out if patients with diabetes, who had been admitted to hospital with COVID-19, could benefit from a drug (a tablet) called AZD1656.

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What were the main questions studied?

The main questions studied were as follows:

1. Does AZD1656 help diabetic patients who are in hospital with COVID-19 to recover from this illness?
2. Is there a difference in the control of blood sugar levels of study patients treated with either AZD1656 or placebo?
3. Is AZD1656 safe to be given to study patients?
4. Does AZD1656 affect the length of hospital admission of study patients?
5. Does AZD1656 affect the need for mechanical ventilation (a machine that helps people breathe) of study patients?
6. Is there a difference in the number of deaths of study patients treated with either AZD1656 or placebo?

The study also explored the following questions;

a. Does AZD1656 affect the immune system of study patients?
b. Does the amount of vitamin D in blood at the start of the study have any effect on the recovery of study patients?
c. In those study patients with heart problems, does AZD1656 improve these heart problems?
d. Does patient ethnicity (race) have an impact on the health of study patients?

Who participated in the study?

In this study 156 patients (aged 18 years or over) with either type 1 or type 2 diabetes participated who had been admitted in the hospital with COVID-19.

What treatments or interventions did the participants take/receive?

All patients received the usual care provided to diabetic patients in hospital with COVID-19 (including oxygen therapy).

In addition, half of the patients received AZD1656 (the active study medication) and half of the patient received placebo (a dummy pill that looked the same as AZD1656 but did not contain the active drug).

What medical problems (adverse reactions) did the participants have?

Some patients who received AZD1656 experienced hypoglycaemia (lower than normal blood sugar level). This was an expected effect of the study drug and in all cases this was resolved quickly. One patient experienced a mild episode of hypokalaemia (lower than normal blood potassium level). There were no other adverse reactions during the trial.

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What happened during the study?

During the study all patients received the study treatment (AZD1656 or placebo) twice per day, whilst they were in hospital. If symptoms improved the study treatment was stopped and patients were discharged from hospital. If symptoms worsened the study treatment was also stopped and if needed patients were transferred to the intensive care for further treatment.

During the study daily blood tests and physical examinations were performed. The results of these tests were used to draw conclusions on the effect of the study treatment in these patients.

What were the results of the study?

The answers to the main study questions were as follows:

1. Most study patients recovered and were discharged well from the hospital. Overall, there was evidence that the health of the study patients treated with AZD1656 was slightly better than patients treated with placebo.
2. There was no difference in the control of blood sugar levels between patients receiving AZD1656 or placebo.
3. AZD1656 was safe to be given to study patients, with no unexpected side-effects seen.
4. AZD1656 had an effect on the length of hospital admission. Patients treated with AZD1656 tended to be discharged from hospital slightly earlier than those treated with placebo.
5. AZD1656 did not affect the need for mechanical ventilation (a machine that helps people breathe). There was no difference between treatment groups in the number of patients who required mechanical ventilation during their hospitalisation.
6. There was a difference in the number deaths in patients seen between treatment groups. Whilst the majority of patients in both groups survived, fewer deaths occurred in the AZD1656 group compared to the placebo group.

The study also found that:

a. AZD1656 affects the immune system (the body's defence system for protecting against disease) in a way that suggests a better immune response to COVID-19, as compared to placebo.
b. Patients with low Vitamin D levels at the beginning of the study, and who were treated with AZD1656, tended to be discharged from hospital earlier than patients with low Vitamin D levels treated with placebo.

c. AZD1656 had no detectable effect on the improvement of heart problems in study subjects.
d. The majority of the study patients were white. It was therefore not possible the determine if ethnicity (race) had an impact on the health of the patient.

It should be noted that these results are from a single trial. It is possible that new information or different results may be obtained from other studies of this drug in the future.

How has this study helped patients and researchers?

This study has helped provide valuable new information about the drug AZD1656. It has shown that AZD1656 was well-tolerated (safe) in patients with diabetes who have been admitted to hospital with COVID-19.

Researchers are also learning new information about how AZD1656 effects the immune system and also how COVID-19 effects the immune system. This information may be useful for treating other diseases.

Details of any further research planned

Not available.

Where can I learn more about this study?

Details of the trial protocol and design can be found in this publication: https://bmjopen.bmj.com/content/11/12/e049650

Further information on the trial can be found on ClinicalTrials.gov NCT04516759.

In addition, all updates including all future publications will be shared on the website of St George Street Capital: www.sgscapital.org