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GETAFIX (Glasgow Early Treatment Arm Favipiravir) – a study to compare the effectiveness of adding the antiviral drug favipiravir to standard care in COVID-19 patients, compared with standard care alone

Submission date
28/08/2020

Recruitment status
No longer recruiting

Registration date
07/09/2020

Overall study status
Completed

Last Edited
25/06/2025

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
COVID-19 is a new illness that can affect different parts of the body including the lungs and airways. The purpose of this study is to see if giving patients who have milder symptoms of COVID-19 (not requiring oxygen support) a drug called favipiravir will help with their symptoms and reduce the time it takes to recover. We are targeting patients who are at higher risk of going on to develop more severe COVID-19. Around 300 patients will take part in the study, and half will be given the drug along with the normal standard treatment, and the other half will receive normal standard treatment alone. We can then compare the two groups to see if the drug has a positive effect and if it may be useful in treating future patients with COVID-19.

Who can participate?
Adults aged 16 or over who have symptoms of COVID-19 and a positive COVID-19 test result, identified through Test and Protect/Safe Haven lists and self-presentation via the trial website. Participants should be in a higher risk category for severe disease according to the ISARIC4C risk index, as assessed by the treating doctor. Patients requiring oxygen therapy will not be included. All participants must be able to provide written informed consent, and be able to swallow tablets. The following are excluded: Pregnant or breastfeeding women, kidney disease requiring (or likely to require) dialysis or haemofiltration, history of hereditary xanthinuria, known allergy to the study drug or any ingredients, severe liver disease. Female participants of childbearing potential should not become pregnant within 3 months of completing the course of study drug.

What does the study involve?
If the patient is potentially eligible, a face-to-face screening visit will be arranged within 7 days. After informed consent has been given, patients will undergo screening tests to check they are suitable for the study. This will involve:
1. Routine clinical observations (temperature, pulse rate, oxygen saturation, blood pressure,

breathing rate)
2. Height and weight
3. Routine clinical blood tests
4. Pregnancy test (for people of childbearing potential)
5. Nose and throat swab to test for coronavirus (if not performed already)
6. Patients unable to return for a day 1 visit will also have blood samples for research purposes taken

Once confirmed as eligible, patients will be randomly allocated either to receive standard care alone or standard care and favipiravir – this will be decided randomly using a computer program. Patients receiving favipiravir will take the drug twice daily: 9 tablets 12 hours apart on the first day, and 4 tablets 12 hours apart on days 2-10. The tablet strength is 200 mg, and the tablets are round, coated and about 9 mm in diameter.

Patients will be assessed by telephone consultation on days 8, 15, 29 and 60 and any symptoms noted. If the patient is willing and able to attend a face-to-face visit on days 15, 29 and 60 then some additional assessments may be carried out at these visits, such as:

1. Routine clinical blood tests
2. Nose and throat swab test for COVID-19
3. Blood tests for immunological and epigenetic testing
4. End of treatment compliance check – return of any remaining study drug/empty containers and completed diary (favipiravir group only)
5. COVID-19 Health and Wellbeing Follow up Survey

Patients who are in the hospital will also have clinical observations performed daily, and blood tests on days 1, 3, and 8. Patients will also be asked to fill out a questionnaire about their health and wellbeing at these visits.

What are the possible benefits and risks of participating?

It is possible that favipiravir may help to reduce the symptoms of COVID-19 or reduce the time taken to recover. Even if patients do not benefit directly, information from this study will help improve our understanding of using favipiravir to treat COVID-19 for future patients.

Potential side effects of the treatment being used in the trial, and the percentage of people who experienced them, are summarised in the Patient Information Sheet. Patients taking favipiravir will be contacted daily by the study team while taking the drug, and if at any time the patient or their doctor felt the side effects were a problem, the drug would be stopped.

Where is the study run from?

The study is being coordinated by the Cancer Research UK Clinical Trials Unit in Glasgow. The study has no link to cancer, but the trials unit had the necessary resource and experience to run the trial, and CRUK were supportive of diverting resource to COVID-19 research during this time of need.

When is the study starting and how long is it expected to run for?

From May 2020 to November 2022

Who is funding the study?

Scottish Government Chief Scientist Office (CSO)

Who is the main contact?

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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2020-001904-41

Integrated Research Application System (IRAS)
283151

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 46289, IRAS 283151

Study information

Scientific Title
Glasgow Early Treatment Arm FavIpiravir: A randomized controlled study of favipiravir as an early treatment arm in COVID-19 patients

Acronym
GETAFIX

Study objectives
Favipiravir may be a more effective treatment for COVID 19 infection, compared to the current standard treatment of supportive care

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/05/2020, West of Scotland Research Ethics Committee 1 (Ward 11, Dykebar Hospital, Grahamston Road, Paisley PA2 7DE; +44 (0)141 314 0212; WoSRec1@ggc.scot.nhs.uk), ref: 20/WS/0073

Study design
Single centre, open-label randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions
Current interventions as of 11/10/2021:
On admission to the study (baseline) the following will be collected from patients:
1. Written informed consent
2. Assessment of eligibility criteria
3. Demographic details
4. Medical history including assessment of medical co-morbidities
5. Documentation of other medications the patient is taking
6. Clinical examination
7. Routine observations
8. Routine clinical blood tests
9. Height and weight to assess the current state of health, by calculation of a BMI which is required for eligibility, and to help understand the distribution of the drug in people of different sizes
10. Pre-morbid performance status as assessed by WHO criteria to give a longer-term indication of the state of health
11. WHO COVID 10 point ordinal severity scale assessment to measures the current severity of COVID-19
12. Assessment of adverse events
13. PK sampling (Favipiravir arm only)

Patients will be allocated to either standard care alone (control arm) or standard care + favipiravir (intervention arm) on a 1:1 basis using a minimisation algorithm incorporating a random component. Factors used in the minimisation will be:
1. Age (16 - 50 years; >50 – 70 years; >70 years)
2. <7 days duration of symptoms (yes; no; unknown)
3. Sex (male; female)
4. History of hypertension or currently obese (BMI >30 or obesity clinically evident)
5. COVID ordinal severity score at baseline (2/3; 4)
6. Treating hospital
7. Vaccination status

Patients receiving favipiravir will take the drug twice daily: 9 tablets, 12 hours apart on the first day, and 4 tablets, 12 hours apart on days 2-10. The tablet strength is 200 mg, and the tablets

are round, coated and about 9 mm in diameter. The following will be assessed on 8:
1. WHO COVID 10-point ordinal severity scale assessment (taken as the worst value on the previous day)
2. WHO COVID-19 10-point ordinal scale assessment (worst value days 2 – 8)
3. Documentation of concomitant medications
4. Assessment of adverse events
5. Routine clinical blood tests (as above)

Follow up will take place at 15, 29, and 60 days where the following will be assessed:
1. WHO COVID 10-point ordinal severity scale assessment
2. Assessment of AEs
3. Record of concomitant medications

The following assessments will be carried out, only if the patient is willing and able to attend a face-to-face visit:
1. Routine clinical blood tests
2. Nasopharyngeal swab for SARS-CoV-2 PCR
3. Nasopharyngeal swab for SARS-CoV-2 Viral Load
4. Blood tests for immunological and epigenetic testing
5. End of treatment compliance check - return of any remaining IMP/empty container, and completed diary (favipiravir arm only)
6. COVID-19 Health and Wellbeing Follow up Survey
7. Blood tests for immunological and epigenetic testing and routine clinical blood tests
8. Telephone or in-person assessment of concomitant medication and adverse events

Previous interventions:
On admission to the study (baseline) the following will be collected from patients:
1. Written informed consent
2. Assessment of eligibility criteria
3. Demographic details
4. Nasopharyngeal swab (a swab taken from the nose used for COVID-19 PCR assessment which gives either “postitive or negative” results, and is also used to measure the viral load which tells us how much virus a patient has)
5. Medical history including assessment of medical co-morbidities and suitability for potential entry to ICU
6. Documentation of other medications the patient is taking
7. Clinical examination
8. Human chorionic gonadotrophin (HCG) test to rule out pregnancy at trial entry. Results must be obtained and reviewed before randomisation for people of childbearing potential
9. Routine observations of respiratory rate, percentage of Oxygen in the blood, Blood pressure, and temperature, to gauge the current state of health
10. Routine clinical blood tests which will include those required to assess eligibility (full blood count, urea and electrolytes, renal function: creatinine and eGFR, liver function tests, c-reactive protein and an assessment of clotting)
11. Height and weight to assess the current state of health, by calculation of a BMI which is required for eligibility, and to help understand the distribution of the drug in people of different sizes
12. Pre-morbid performance status as assessed by WHO criteria to give a longer-term indication of the state of health
13. WHO COVID 10 point ordinal severity scale assessment to measures the current severity of COVID-19

Patients will be allocated to either standard care alone (control arm) or standard care + favipiravir (intervention arm) on a 1:1 basis using a minimisation algorithm incorporating a random component. Factors used in the minimisation will be:
1. Age (16 - 50 years; >50 – 70 years; >70 years)
2. <7 days duration of symptoms (yes; no; unknown)
3. Sex (male; female)
4. History of hypertension or currently obese (BMI >30 or obesity clinically evident)
6. COVID ordinal severity score at baseline (2/3; 4)
7. Treating Hospital

Patients receiving favipiravir will take the drug twice daily: 9 tablets, 12 hours apart on the first day, and 4 tablets, 12 hours apart on days 2-10. The tablet strength is 200 mg, and the tablets are round, coated and about 9 mm in diameter. The following will be assessed on days 1 to 10 unless indicated otherwise:
1. WHO COVID 10 point ordinal severity scale assessment (taken as the worst value on the previous day)
2. Documentation of concomitant medications
3. Assessment of adverse events
4. Routine clinical blood tests (as above)
5. Routine observations/vital signs (as above)
6. Routine clinical blood tests and blood tests for immunological and epigenetic testing on days 1, 3, 8, and 11 (as above)
7. Symptom directed clinical examination if clinically indicated
8. Nasopharyngeal swab (for COVID-19 SARS-CoV-2 PCR assessment and Viral Load) on days 1 (at time of first dose), 3, 7, 10, 13, and on discharge if before 15 days.
9. Pharmacokinetic samples according to the sample schedule to ascertain the concentration of blood circulating in the patient. Performed by The Pharmacy Department Uni of Strathclyde and Translational Pharmacology Lab, Uni of Glasgow.

For patients in the community or discharged from hospital before 14 days, telephone assessment of the WHO COVID 10 point ordinal severity scale assessment, concomitant medication, and adverse events, will be undertaken by an investigator with the patient.

Follow up will take place at 15, 29, and 60 days where the following will be assessed:
1. WHO COVID 10 point ordinal severity scale assessment
2. Blood tests for immunological and epigenetic testing and routine clinical blood tests
3. Telephone or in person assessment of concomitant medication and adverse events
4. Nasopharyngeal swab (for SARS-CoV-2 PCR assessment and viral load)
5. The COVID-19 Health and Wellbeing follow up survey

Records will also be kept of survival, duration of hospitalisation, and duration of pyrexia.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Favipiravir

Primary outcome(s)

Current primary outcome measure as of 21/03/2022:
Efficacy of favipiravir in addition to standard care in patients with COVID-19 in reducing the severity of disease compared to standard care alone measured using the WHO COVID 10-point ordinal scale score up to and including day 15

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Previous primary outcome measure:
Efficacy of favipiravir in addition to standard care in patients with COVID-19 in reducing the severity of disease compared to standard care alone measured using the WHO COVID 10-point ordinal scale at 15 days

Key secondary outcome(s))

Current secondary outcome measures as of 11/10/2021:
1. Effect of favipiravir on ICU admission rate measured by proportion of patients ≥level 7 on the WHO-COVID 10-point ordinal scale up to and including day 29
2. Overall survival, assessed up to and including 60 days
3. Safety and tolerability of favipiravir in the study population measured by assessment of adverse events using the Common Terminology Criteria for Adverse Events (CTCAE) v5 at up to and including day 60
4. Effect of favipiravir on SARS-CoV-2 viral clearance, measured by PCR test at day 15, 29 and 60.
5. Pharmacokinetics of favipiravir measured by blood sampling at day 1 pre-dose, and 30 and 90 mins post dose
6. Patient factors (immunological and biometric markers) contributing to clinical conditions in COVID-19 patients measured by blood sampling up to including day 60
7. Post COVID-19 health and psychosocial consequences measured by the COVID-19 Health and Wellbeing follow up survey up to and including day 60.

Previous secondary outcome measures:
1. Effect of favipiravir in addition to standard care in the study population compared to standard care alone measured using:
1.1. The WHO COVID 10 point ordinal scale, measured at baseline, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 29, and 60 days (measurements on days 1-10 by telephone in outpatients)
1.2. Viral clearance measured from nasopharyngeal swabs at baseline and 8 days
1.3. Overall survival, assessed up to and including 60 days
1.4. Duration of pyrexia by temperature measured in inpatients only, up to and including the day of discharge or 60 days
2. Safety and tolerability of favipiravir in the study population measured by assessment of adverse events using the Common Terminology Criteria for Adverse Events (CTCAE) v5 at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 29, and 60 days (measurements on days 1-10 by telephone in outpatients)
3. Effect of favipiravir on the duration of hospitalisation measured by assessment of patient status up to and including 60 days
4. Pharmacokinetics of favipiravir measured by blood sampling at baseline and 1 days (outpatients), or baseline, 1, 3, 5, 8 and 10 days (inpatients)
5. Mechanisms of resistance, immunological and biometric markers contributing to clinical conditions in COVID-19 patients measured by blood sampling at baseline (screening), 15, 29, and 60 days (outpatients), or baseline (day 1) and 3, 15, 29, and 60 days (inpatients)
6. Post COVID-19 health and psycho-social consequences measured by the COVID-19 Health and Wellbeing follow up survey at 15, 29, and 60 days

Completion date
30/11/2022

Eligibility

Key inclusion criteria
Current inclusion criteria as of 11/10/2021:
1. Aged ≥16 at time of consent
2. Exhibiting symptoms associated with COVID-19
3. Positive for SARS-CoV-2 on valid COVID-19 test
4. Point 2 or 3 on the WHO COVID-19 ordinal severity scale at the time of randomisation (symptomatic independent, symptomatic assistance needed)
5. Able to provide written informed consent
6. Negative pregnancy test if the participant is of childbearing potential
7. Able to swallow oral medication

Previous inclusion criteria:
1. Aged ≥16 at time of consent
2. Exhibiting symptoms associated with COVID-19
3. Positive for SARS-CoV-2 on valid COVID-19 test
4. Point 1, 2, 3, or 4 on the WHO COVID-19 ordinal severity scale at the time of randomisation (asymptomatic with positive valid COVID19 test, symptomatic independent, symptomatic assistance needed, or hospitalized, with no oxygen therapy)
5. Have ≥10% risk of death should they be admitted to hospital as defined by the ISARIC4C risk index (https://isaric4c.net/risk)
6. Able to provide written informed consent
7. Negative pregnancy test if the participant is of childbearing potential
8. Able to swallow oral medication

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
302

Key exclusion criteria
Current exclusion criteria as of 21/03/2022:
1. Renal impairment requiring, or likely to require, dialysis or haemofiltration
2. Pregnant or breastfeeding
3. Childbearing potential, or, with partners of childbearing potential, who do not agree to the use adequate contraceptive measures for the duration of the study and for 3 months after the

completion of study treatment
4. History of acute or chronic gout, or hereditary xanthinuria
5. Judged to be ineligible by the principal investigator or sub-investigator
6. Known hypersensitivity to favipiravir, its metabolites, or its excipients
7. Severe hepatic impairment, defined as > Child-Pugh grade A, AST or ALT >5 x ULN or AST or ALT >3 x ULN and Total Bilirubin >2 x ULN
8. More than 7 days since onset of COVID-19 symptoms
9. Unable to discontinue contra-indicated concomitant medications
10. Eligible to directly access anti-viral or neutralising monoclonal antibody therapies for COVID19, as defined by UK clinical commissioning guidance at the point of assessment

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Previous exclusion criteria as of 11/10/2021:
1. Renal impairment requiring, or likely to require, dialysis or haemofiltration
2. Pregnant or breastfeeding
3. Childbearing potential, or, with partners of childbearing potential, who do not agree to the use adequate contraceptive measures for the duration of the study and for 3 months after the completion of study treatment.
4. History of hereditary xanthinuria
5. Judged to be ineligible by the principal investigator or sub-investigator
6. Known hypersensitivity to favipiravir, its metabolites, or its excipients
7. Severe hepatic impairment, defined as > Child-Pugh grade A, AST or ALT >5 x ULN or AST or ALT >3 x ULN and Total Bilirubin >2 x ULN
8. More than 7 days since onset of COVID-19 symptoms
9. Unable to discontinue contra-indicated concomitant medications (section 6.7)

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Previous exclusion criteria:
1. Renal impairment requiring, or likely to require, dialysis or haemofiltration
2. Pregnant or breastfeeding
3. Childbearing potential, or, with partners of childbearing potential, who do not agree to the use adequate contraceptive measures for the duration of the study and for 3 months after the completion of study treatment.
4. History of hereditary xanthinuria
5. Judged to be ineligible by the principal investigator or sub-investigator
6. Known hypersensitivity to favipiravir, its metabolites, or its excipients
7. Severe co-morbidities including patients with severe hepatic impairment, defined as: greater than Child-Pugh grade A, AST or ALT >5 x ULN, or AST or ALT >3 x ULN and Total Bilirubin >2 x ULN
8. >96 h since first positive COVID19 test sample was taken
9. Unable to discontinue contra-indicated concomitant medications

Date of first enrolment
14/09/2020

Date of final enrolment
07/07/2022

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
NHS Greater Glasgow and Clyde
J B Russell House
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
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G12 0XH

Sponsor information

Organisation
NHS Greater Glasgow and Clyde

ROR
https://ror.org/05kdz4d87

Funder(s)

Funder type
Government

Funder Name
Chief Scientist Office, Scottish Government Health and Social Care Directorate

Alternative Name(s)
Chief Scientist Office, Scottish Government Health Directorate CSO, Chief Scientist Office, Scottish Government Health Directorates, Chief Scientist Office of the Scottish Government Health Directorates, Scottish Government Health and Social Care Directorate of the Chief Scientist Office, Scottish Government Health Directorate Chief Scientist Office, The Chief Scientist Office, CSO

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
National Institute for Health Research (NIHR) (UK)

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		24/06/2025	25/06/2025	Yes	No
Protocol article	protocol	19/11/2020	23/11/2020	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Inpatients version v1.0	14/07/2020	07/09/2020	No	Yes
Participant information sheet	version 6	15/06/2021	11/10/2021	No	Yes
Participant information sheet	version 4	15/06/2021	11/10/2021	No	Yes
Participant information sheet	Outpatients version 1.0	14/07/2020	11/10/2021	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 6	11/06/2021	11/10/2021	No	No