SUMMARY OF CLINICAL TRIAL RESULTS FOR LAYPERSONS

1 CLINICAL TRIAL IDENTIFICATION

Researchers look at the results of many studies to decide if a drug works, and if it is safe for patients. It takes participants in many studies all around the world to advance medical science. This summary shows the results from only one study. The results of this study might be different to other studies.

1.1 Title of the Trial

Lay Title: Flurpiridaz (^{18}F) myocardial perfusion for the diagnosis of coronary artery disease

Full title: A Phase 3, Open-Label, Multicentre Study of Flurpiridaz (^{18}F) Injection for Positron Emission Tomography (PET) Imaging for Assessment of Myocardial Perfusion in Patients Referred for Invasive Coronary Angiography Because of Suspected Coronary Artery Disease

1.2 Protocol Number

GE-265-303

1.3 EU Trial Number

2017-005011-14

1.4 Other Identifiers

ClinicalTrials.gov Identifier: NCT03354273

2 NAME AND CONTACT OF SPONSOR

GE HealthCare
Pollards Wood
Nightingales Lane
Chalfont St Giles
Buckinghamshire
HP8 4SP
United Kingdom

Contact: https://www.gehealthcare.co.uk/about/contact-us

3 GENERAL INFORMATION ABOUT THE CLINICAL TRIAL

3.1 Where the Trial was Conducted

This study took place in the following countries:

- USA
- Canada
- The Netherlands
- France
- Finland
- Germany

3.2 When the Trial was Conducted

This trial started in June 2018 and ended in May 2022.

3.3 Main Objectives of the Trial and an Explanation of the Reasons for Conducting It

Coronary artery disease is a common cardiac condition and a leading cause of death worldwide. It is also known as coronary heart disease or ischaemic heart disease. Coronary artery disease happens when there is a narrowing of a blood vessel (artery) that delivers blood, oxygen and nutrients to the heart muscle (myocardium). This narrowing can be caused by a build-up of fatty deposits. When a complete blockage occurs, this is called a heart attack. 'Significant' coronary disease means that one of the major blood vessels in the heart has narrowed by at least half.

Researchers are looking for ways to better diagnose coronary artery disease. Flurpiridaz (^{18}F) Injection is a radioactive substance known as a radiotracer. It is used in a type of imaging scanner called PET (positron emission tomography). This type of scan shows distribution of the radiotracer to the myocardium, and it can help show where arterial blockages exist. Flurpiridaz (^{18}F) Injection is injected into a blood vessel in the arm, just before the PET scan is carried out. Flurpiridaz (^{18}F) then travels through the blood stream to the heart.

When this study was started, Flurpiridaz (^{18}F) Injection was not approved for use. Before a drug can be approved for use, researchers need to find out how safe it is and how effective it is. They do this by carrying out clinical trials, and they are allowed to use the drug in this setting.

The main goal of this study was to understand how well Flurpiridaz (^{18}F) Injection PET could help diagnose significant coronary artery disease. To do this, researchers compared how well PET performed against a test that is known to be very accurate for large arteries, called invasive coronary angiography. In invasive coronary angiography, a catheter (a long, thin, flexible tube) is inserted into a blood vessel in the arm or leg and threaded up into the coronary arteries of the heart. A dye (contrast medium) is then injected into the coronary arteries and x-ray images are taken. The dye makes the blood vessels more clearly visible on x-ray.

The researchers also compared Flurpiridaz (^{18}F) Injection PET with another type of cardiac scan called SPECT (single positron emission tomography). Like PET, SPECT involves the injection of a radiotracer just before the scan. The SPECT radiotracers used in this study are already widely used in hospitals and clinics. The researchers wanted to know if Flurpiridaz (^{18}F) Injection PET was better at identifying significant coronary artery disease than SPECT.

The researchers also recorded any side effects or medical problems that people experienced during the study.

4 POPULATION OF PARTICIPANTS

4.1 Number of Participants Included in the Trial

A total of 730 people with suspected coronary artery disease agreed to take part in this study. Of this total, 604 people received a dose of the study drug (Flurpiridaz (^{18}F) Injection), and 578 people completed all the procedures in the study.

The study enrolled 412 people in the United States, 129 in Canada and 189 in Europe. A breakdown of enrolment by country is shown in Table 1.

Table 1 Summary of enrolled participants by country

Country	Number of participants enrolled (percentage)
United States	412 (56%)
Canada	129 (18%)
The Netherlands	79 (11%)
France	71 (10%)
Finland	36 (5%)
Germany	3 (less than 1%)

4.2 Age Group and Gender Breakdown

Figure 1 summarises the ages of the people who completed the study.

Figure 1 Baseline demographics by age group

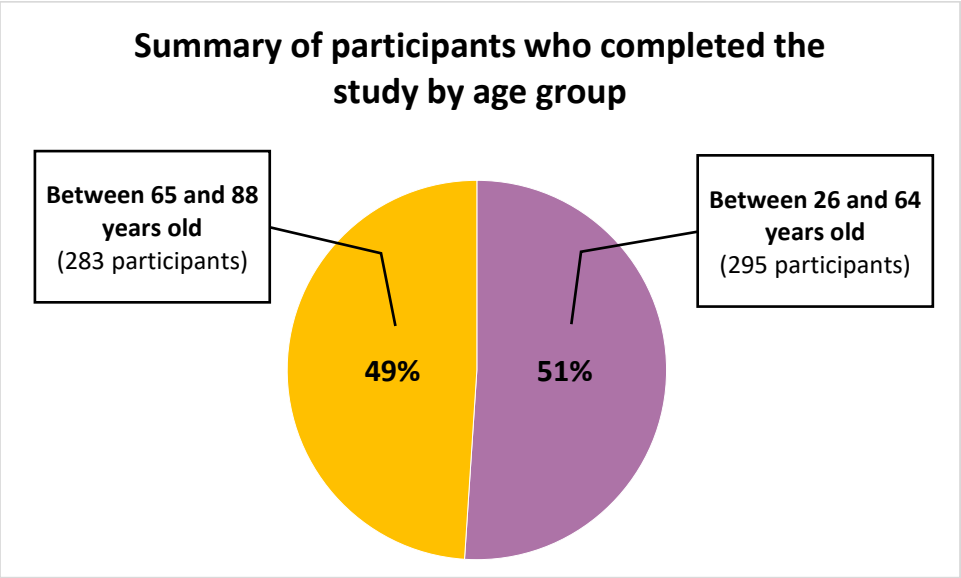
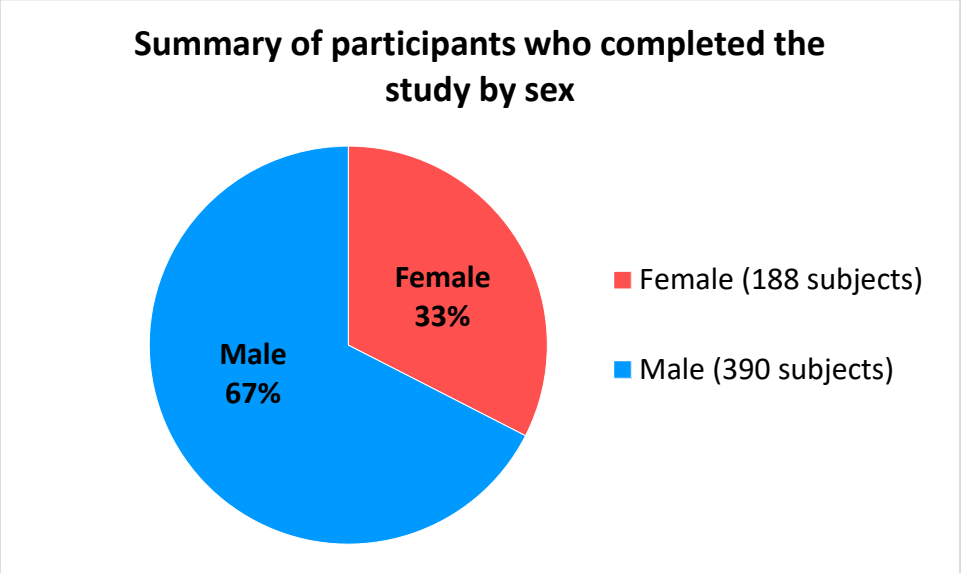


Figure 2 summarises how many men and women completed the study.

Figure 2 Baseline demographics by sex



4.3 Inclusion and Exclusion Criteria

People who were scheduled to have an invasive coronary angiography because of suspected coronary artery disease were asked to take part in this study.

There were a number of conditions that had to be met for a person to be considered suitable for this study. People who already had a diagnosis of coronary artery disease were not allowed to take part in the study.

People who lived with some other conditions were also excluded from the study. These included:

- Unstable angina, within 6 months before enrolment
- Stroke, within 3 months before enrolment
- Significant congenital heart disease
- Uncontrolled hypertension
- Uncontrolled tachycardia
- Previous heart failure or cardiomyopathy.

If the doctor decided that it was safer for the participant that they did not take part in the study, that person was excluded.

5 INVESTIGATIONAL MEDICINAL PRODUCTS USED

The drug being tested in this study was the radiotracer Flurpiridaz (^{18}F) Injection. This is a liquid that is given by intravenous injection (a needle into a vein), just before someone has a PET scan.

There were other drugs that were used as a part of this study, but that were not being studied. These are listed below:

- A radiotracer injection that was given as part of the SPECT scan. Either [^{99m}Tc]tetrofosmin or [^{99m}Tc]sestamibi was used.
- Participants either exercised or they received a stress agent as part of this study. A stress agent can be used to imitate the effects of exercise by increasing blood flow to the heart muscle. One of the following was used: adenosine, dipyridamole, or regadenoson.
- A dye, also known as a contrast agent, that was given as part of the invasive coronary angiography test.

5.1 What Happened During the Study?

Before beginning the study, all participants were evaluated by the study doctor to make sure that they met all the criteria to take part.

Then, each participant had a series of heart scans. These included:

- Two consecutive Flurpiridaz (^{18}F) Injection PET scans for rest and stress
- Two consecutive SPECT scans for rest and stress

- An invasive coronary angiography test.

These different types of cardiac scans were done on separate days. Invasive coronary angiography was carried out only after the other scans had been done.

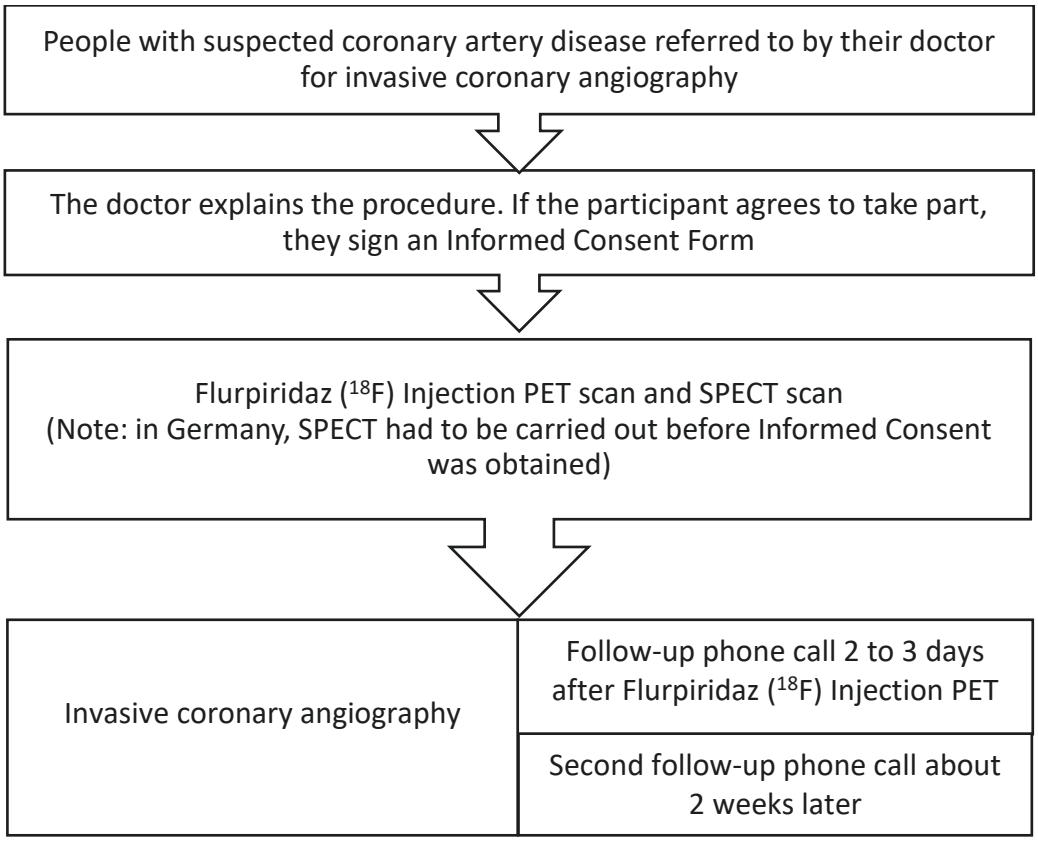
For the Flurpiridaz (^{18}F) Injection PET scans, one scan was done while the participant was resting. Then a second scan was done under stress. 'Under stress' in this case means that the person was asked to exercise (e.g., on a treadmill), or was given a drug that has a similar effect of increasing blood flow to the heart muscle.

On a separate day, each participant had a SPECT scan while resting and a second scan under stress. The SPECT scan involves the injection of a radiotracer just before the person is scanned.

After completing these two scans, participants then had an invasive coronary angiography test on a separate day.

Any medical problems were recorded throughout the study. The researchers also phoned each participant 2 days after the Flurpiridaz (^{18}F) Injection PET scan, and again about 2 weeks later, to check for any medical problems.

The flowchart below shows the different steps in the study.



6 DESCRIPTION OF ADVERSE REACTIONS AND THEIR FREQUENCY

This section discusses adverse reactions, also known as side effects. Side effects are unwanted medical problems (e.g., headache) that happen during the study and are thought to be related to the treatment being given in the study. The researchers recorded any medical problem that people had during the study, including any changes that were found from blood tests or urine tests.

Not all the people in this study experienced side effects. Out of the total of 604 people who received a Flurpiridaz (^{18}F) Injection, 19 experienced a side effect that the doctor thought might be related to it. This is equivalent to 3% of all participants who received the drug.

None of the participants experienced any serious side effects related to Flurpiridaz (^{18}F) Injection. A side effect is thought of as serious if it results in death, is life threatening, needs hospital care, or causes lasting problems.

Table 2 lists all the side effects that occurred in this study that were related to Flurpiridaz (^{18}F) Injection, for the 604 participants who received it.

Table 2 Summary of all side effects that were related to Flurpiridaz (^{18}F) Injection

Side effect	Number and percentage of participants (604 participants treated)
Imaging procedure artifact (extra imaging finding outside the heart)	4 (0.7%)
Palpitations (fluttering or pounding heartbeat)	3 (0.5%)
Headache	3 (0.5%)
Abdominal pain (stomach pain)	2 (0.3%)
Dizziness	2 (0.3%)
Sinus bradycardia (slow heartbeat)	1 (0.2%)
Vertigo (sensation that everything around you is spinning)	1 (0.2%)
Diarrhoea	1 (0.2%)
Fatigue (tiredness)	1 (0.2%)
Injection site pain	1 (0.2%)
Malaise (feeling generally unwell)	1 (0.2%)
Administration related reaction (a reaction related to the injection itself)	1 (0.2%)
Dysgeusia (odd taste in the mouth)	1 (0.2%)
Taste disorder	1 (0.2%)

The researchers also found that people in the study received a lower dose of radiation from the Flurpiridaz (^{18}F) Injection, compared to the SPECT radiotracer injection.

7 OVERALL RESULTS OF THE CLINICAL TRIAL

Some of the main findings from this study are described below. More information may be available in the websites listed at the end of this summary.

7.1 What was the sensitivity and specificity of the Flurpiridaz (^{18}F) Injection PET scan?

This question was the main goal of the study. Researchers compared how well Flurpiridaz (^{18}F) Injection PET performed against a test that is known to be very accurate, called invasive coronary angiography. The researchers first asked three independent experts to study the Flurpiridaz (^{18}F) Injection PET scans and to assess whether or not there was significant coronary artery disease present. These experts categorised scans as either 'healthy' or 'diseased'.

The researchers then compared these assessments to the results of invasive coronary angiography, to see how well Flurpiridaz (^{18}F) Injection PET performed. To do this the researchers used two measures, 'sensitivity' and 'specificity'.

Sensitivity and specificity are commonly used measures that can help us understand the performance of any test that has either a positive or a negative result. They are important measures, because no test is 100% accurate. A certain proportion of people will have a positive test result when in reality they are negative. Similarly, some will have a negative test result when in reality they are positive. In this study, sensitivity and specificity are defined as:

- **Sensitivity:** The proportion of people who are correctly identified as having significant coronary artery disease by PET assessment, out of all those who truly have the condition.
- **Specificity:** The proportion of people who are correctly identified as having healthy coronary arteries by PET, out of all people who truly have healthy coronary arteries.

The researchers decided that if both the sensitivity and specificity of Flurpiridaz (^{18}F) Injection PET were greater than 60%, then this test could be said to perform adequately.

The researchers found that Flurpiridaz (^{18}F) Injection PET exceeded this 60% threshold and had a good agreement with invasive coronary angiography. They found that:

Sensitivity: 80% of people (8 out of 10) with significant coronary artery disease were correctly identified as such by experts using Flurpiridaz (^{18}F) Injection PET.
Specificity: 64% of people (roughly 6 out of 10) with healthy coronary arteries were correctly identified as such by experts using Flurpiridaz (^{18}F) Injection PET.

7.2 How did the sensitivity and specificity of the Flurpiridaz (^{18}F) Injection PET scan compare to SPECT?

The researchers wanted to address this question because SPECT scans are already used in hospitals and clinics to assess people for coronary artery disease. They wanted to know if Flurpiridaz (^{18}F) Injection PET could be a more accurate tool than SPECT.

To answer this question, the researchers asked the same three independent experts to assess the SPECT scans, and categorise them as either 'healthy' or 'diseased'.

The researchers then compared these assessments to the results of invasive coronary angiography to see how well SPECT performed, in the same way that they had already done for Flurpiridaz (^{18}F) Injection PET.

They could then compare the sensitivity and specificity results of SPECT to those of Flurpiridaz (^{18}F) Injection PET. They found that:

The sensitivity of Flurpiridaz (^{18}F) Injection PET was better than SPECT The experts were able to correctly identify significant coronary artery disease more often using Flurpiridaz (^{18}F) Injection PET scans than they were able to with SPECT.
The specificity of Flurpiridaz (^{18}F) Injection PET was equal to SPECT The experts were able to correctly identify healthy coronary arteries equally well with both Flurpiridaz (^{18}F) Injection PET and SPECT.
Flurpiridaz (^{18}F) Injection PET was also shown to perform better than SPECT at correctly identifying significant coronary artery disease in women and in people with a body mass index (BMI) of at least 30 kg/m^2. It is known that these groups of people tend to be under-diagnosed compared to others.

8 COMMENTS ON THE OUTCOME OF THE CLINICAL TRIAL

This was a study of Flurpiridaz (^{18}F) Injection PET in adults who were scheduled to have an invasive coronary angiography because of suspected coronary artery disease.

The researchers showed that:

- Flurpiridaz (^{18}F) Injection PET was an accurate tool to detect both significant coronary artery disease and healthy coronary arteries, when compared with invasive coronary angiography.
- Flurpiridaz (^{18}F) Injection PET performed better than SPECT at detecting coronary artery disease, and about the same as SPECT at detecting healthy coronary arteries. It

was also found that Flurpiridaz (^{18}F) Injection PET performed better than SPECT at detecting disease in women and in people with a high BMI.

- The quality of images generated from Flurpiridaz (^{18}F) Injection PET scans was better than those from SPECT. The experts reported that they were more certain in the diagnoses they made with Flurpiridaz (^{18}F) Injection PET, because of the better image quality.
- Side effects related to Flurpiridaz (^{18}F) Injection were experienced by 19 out of 604 people who received the drug. None of these side effects were serious.

Overall, this study showed that Flurpiridaz (^{18}F) Injection PET performed well in diagnosing significant coronary artery disease, and it was generally well tolerated by the participants.

This study had certain limitations. Certain groups of people were excluded from the study, whereas in real world practice they might in fact undergo an assessment for suspected coronary artery disease. The outcome of this study reflects only one single study – other studies may show something different, and this includes either already done or future studies.

Findings from this study will be used to seek approval for the use of Flurpiridaz (^{18}F) Injection in PET heart scans.

9 INDICATION IF FOLLOW UP CLINICAL TRIALS ARE FORESEEN

No other trials of Flurpiridaz (^{18}F) Injection are currently ongoing or planned.

10 INDICATION WHERE ADDITIONAL INFORMATION COULD BE FOUND

You can find more detailed information about this study on this website:
https://www.gehealthcare.com/about/newsroom/press-releases/ge-healthcare-and-lantheus-phase-iii-clinical-trial-finds-18fflurpiridaz-pet

More information may also be available by looking up the official number or title of the study, or by going to https://clinicaltrials.gov/ct2/show/study/NCT03354273

For general information about clinical trials, go to:

http://www.testingtreatments.org/

https://www.clinicaltrials.gov/ct2/about-studies/learn

http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143534.htm

http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000489.jsp&mid=WC0b01ac058060676f

http://www.nhs.uk/conditions/clinical-trials/pages/introduction.aspx

http://www.ukcrc.org/wp-content/uploads/2014/03/iCT_Booklet.pdf

SIGNATURE PAGE

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