Oxford University Hospitals

OXFORD CENTRE FOR DIABETES, ENDOCRINOLOGY AND METABOLISM (OCDEM)
Radcliffe Department of Medicine, Churchill Hospital, Oxford. OX3 7LJ
Tel: 01865 857 359; www.ocdem.ox.ac.uk

Chief Investigator (Oxford): Prof Jeremy Tomlinson (Jeremy.tomlinson@ocdem.ox.ac.uk)

Local Principal investigator (Sheffield): Prof John Newell-Price (j.newellprice@sheffield.ac.uk)

PARTICIPANT INFORMATION SHEET

Dissecting the Contribution of glucocorticoid metabolism in Mild Autonomous Cortisol Secretion: a randomised controlled trial of the 11β-HSD1 inhibitor SPI-62

We'd like to invite you to take part in our research study. Before you decide, it is important that you understand why the research is being done and what it would involve for you. Please take time to read this information and discuss it with others if you wish. If there is anything that is not clear, or if you *would like more information, please ask us.*

1. What is the purpose of the study?

Benign nodules of the adrenal gland are common and can frequently produce too much of the stress hormone, cortisol (a condition called *mild autonomous cortisol secretion*, MACS) and this is associated with increased risks of frailty, development of diabetes, heart attacks and strokes. Currently there is no specific treatments to limit the effects of the excess cortisol in patients with MACS.

We have shown that within tissues such as bone, liver, fat and muscle, there is further generation of cortisol by a substance called 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) and this worsens many of the problems faced by patients with MACS. We want to see if a drug that can block the action of this enzyme, a so-called 11β-HSD1 inhibitor called SPI-62, can improve the health of patients with MACS.

2. Why have I been invited?

You have been invited to take part as you have been diagnosed with MACS. We aim to enrol 40 patients with MACS into the study.

3. Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of any medical care that you may need in the future.

4. What will happen to me if I decide to take part?

Visit 1 (screening & consent) – 1 hour

The first time we meet you it will either be in outpatients clinic or in our clinical research unit. The visit will be a screening visit where we will ask you some questions to check whether you are eligible for the study. We will

be able to answer any of your questions and if you are happy, we will ask you to sign a consent form. With your permission we would like to inform your GP of your involvement in the study.

At the screening visit we will measure your height, weight, and blood pressure, perform a physical examination as well as an electrical tracing of the heart, take some blood tests and perform pregnancy test where appropriate. We will also ask you to perform some memory tests using a computer or tablet device. We will also provide you with a sensor that sticks to the skin and is about the size of a 50 pence piece. You will wear this for up to 2-weeks and it allows us to measure blood sugar levels throughout the day (continuous glucose monitoring).

You will be required to attend 6 further visits over the next 16-weeks.

Visit 2 (baseline 1) – 3 hours

For us to see the benefits of SPI-62, a small sample of fat tissue from underneath the skin of your tummy will be taken; this is called an adipose tissue biopsy. We will use local anaesthetic to numb the area before inserting a needle under the skin. A small handheld device is then used to suck up some fat inside the needle. Less than 1 gram of fat tissue is removed (about the size of a couple of grains of rice). The procedure will take about 15 minutes and after the biopsy an adhesive dressing will be applied that can be removed the next day. Taking a fat sample may leave a bruise that could be quite large and possibly become hard underneath, but that should disappear after a couple of weeks.

We will also perform a special scan called a DXA scan that can accurately assess the amount of fat and muscle in your body. To perform the scan, you lie on a bed and a scanner passes over your body. The scan is not claustrophobic and uses only very low dose x-rays (approximately $1/10^{th}$ of a single chest x-ray).

We will also arrange for you to have a CT scan of the tummy. This is not a claustrophobic scan and involves going through a large donut-shaped scanner. It is an x-ray scan, but the dose is minimized (equivalent to about 2 years natural background radiation in the environment) as we only look at a small area to work out how much fat there is around your internal organs.

We will also repeat the memory tests using a computer or tablet that you did at the screening and consent visit as well as ask questions about your general health and quality of life.

We will attach a blood pressure monitor that automatically measures your blood pressure every 30 minutes during the day and every hour overnight. We will remove this when you return to the Clinical Research Unit (visit 3) Within 2-weeks of visit 2. We will give you instructions on how to remove the monitor in case you find this uncomfortable.

We will also provide you with a urine container to collect an overnight urine sample. We will ask you to flush away the urine you pass immediately before you go to bed. Any urine you pass overnight and first thing in the morning before returning to the Clinical Research Unit will go into the container. You will bring the urine collection with you to the Clinical Research Unit the following day (visit 3).

Finally, we will provide you with some container to collect samples your saliva every 2-hours over the course of a whole day and evening. You will be able to bring these back with you on visit 3.

Specifically before visit 3, for the night preceding the visit, we will ask you to avoid excessive exercise and alcohol (no more than 2 pints of beer or 5 small glasses (125ml) of wine (less than 12% alcohol), equating, in total to less than 6 units of alcohol), factors which we know significantly alter your metabolism. You should also avoid certain foods which are those naturally high in ^{13}C, the stable-isotope to be used on the study day and include cornflakes, popcorn, corn, foods rich in corn-starch such as shortbreads and rich in fructose corn syrup such as sweetened breakfast cereals. We would ask you not to eat any food from 8.00pm the night before you attend for visit 3 and drink only plain water. If you are on regular medications, these can be taken in the morning with a small amount

of plain water or during the procedure if you need to take them at specific times of day. If tablets need to be taken with food, you can discuss this with the research team

Visit 3 (baseline 2) – 7 hours

Within 2-weeks of visit 2, we will ask you to attend our research facility at approximately 08:00 in the morning (we will arrange a taxi for you) and the investigations and procedures that we would like to perform are numbered below. You will need to have had nothing to eat or drink except plain water from midnight the preceding evening. If it is more convenient for you, we can try and schedule investigations performed as part of visit 2 and 3 to be on the same day

Two cannulas (fine plastic tubes) will be placed into veins in your arms, and a third cannula will be placed into the back of one of your hands. The cannulas in your arms will be used to give infusions (drips) and the cannula in your hand will be used to take all blood samples. Inserting cannulas can be uncomfortable but will always be performed by an experienced practitioner. There is a very small risk of infection, but to minimize this risk, the skin is cleaned thoroughly.

To see how your fat tissue is functioning, a cannula (microdialysis catheter) will be placed into the superficial fat overlying the tummy. We use local anaesthetic that is given as an injection and this can cause some stinging for a few seconds, but after that there should be no discomfort. The cannula is very short (5cm in length) and fine (less than 0.1cm) and is attached to a pump that is approximately the size of a credit card. This device pumps fluid at a very slow rate into and out of the fat tissue and therefore allows us to sample hormones produced by the fat tissue. Samples will be collected from the pump every 30 minutes. This can be done without the need to disturb you. The fluid within the pump is identical to that which patients occasionally receive intravenously when admitted to hospital.

Starting at around 09.00, we will perform an insulin clamp test to see how insulin acts in your body. Infusions (drips) of insulin and glucose (sugar) will run through the cannulas in each of your arms and blood samples will be taken initially every 15 minutes and then every 5 minutes from the cannula in your hand. The glucose infusion will be adjusted according to your blood sugar levels. At 10 time points throughout the day, we will also take blood samples from the same cannula to be stored for laboratory analysis. We will also intermittently take samples of your breath which involves giving one short breath through a mouthpiece into an inflatable bag. The whole clamp test lasts 6 hours and you can sleep, read or use laptops/tablets throughout. After 6-hours you can eat and drink as normal and we will provide you with lunch. The total amount of blood taken in this test is less than a unit given at blood donation (approximately 220ml or 1.5 cups).

After the clamp test you will be prescribed either SPI-62 (6mg (3 tablets) to be taken once daily by mouth at approximately 09.00 or a dummy treatment (3 placebo tablets) that looks identical. Neither you, nor the doctors looking after you will know if you are taking the placebo or the SPI-62. Half of the participants will receive SPI-62 and half will receive the placebo. Only after the study is completed will the code be broken to determine if you were taking SPI-62 or placebo. We will provide you with enough medication for the first 4 weeks. More mediation will be provided at visits 4 and 5.

We will schedule your visits 4 to 7 and provide you with a date to start your treatment. You should take the prescribed study medication (SPI-62/placebo) at approximately 09.00 each morning. If you forget to take your medication in the morning, you can take it later in the day.

After the clamp has finished, we will provide you with a meal and arrange for a taxi to take you back home. For the 24-48h after the clamp, we would advise you to maintain a good non-alcoholic fluid intake (at least 1-2 litres per day) and to avoid strenuous exercise.

Telephone call 1 (2-weeks after starting treatment) – 15 minutes

We will call you to make sure that you are tolerating the tablets and not suffering any side effects.

Visit 4 (approximately 4-weeks after starting treatment) – 1 hour

We will undertake a brief physical examination and fasting (from 08.00pm the preceding evening) blood tests, provide you with a sensor for continuous glucose monitoring (as in visit 1) as well as ask you to do a timed urine collection and the salivary collections (identical to those performed in visit 2). We will ask if there has been any change to your current medication and also provide you with more study medication for the next 4-weeks.

Visit 5 (approximately 8-weeks after starting treatment) – 1 hour

This visit will be identical to visit 4 (but without the need for the glucose sensor) and will occur once you have been taking SPI-62/placebo for approximately 8-weeks. We will ask if there has been any change to your current medication and also provide you with more study medication for the final 4-weeks of the study.

Visit 6 (approximately 12-weeks after starting treatment) – 3 hours

This visit will be almost identical to visit 2 and will occur once you have been taking the SPI-62/placebo for 11-weeks. In addition to the tests we did at visit 2, we will take measurements of your height and weight, review you medications and ask about possible side effects and perform pregnancy test where appropriate. You should continue take the tablets with small volume of water the morning you are due to attend the clinical research unit for the investigations.

Visit 7 (approximately 12-weeks after starting treatment) – 7 hours

This visit will be almost identical to visit 3 and will occur once you have been taking the SPI-62/placebo for 12-weeks. In addition to the tests we did at visit 3, we will review your medications and ask about possible side effects and check how many tablets you have taken over the course of the study. You should continue to take the tablets with a small volume of water the morning you are due to attend the clinical research unit for the investigations. You should bring any remaining tablets with you. After these investigations are completed, we will stop all the study medication, but you will continue to take your usual medications (as you have been throughout the duration of the study).

Telephone call 2 (approximately 4-weeks after stopping treatment) – 15 minutes

We will call you to make sure you have not suffered any side effects since stopping the medication. If required, we will schedule an appointment for you to be reviewed in person on our clinical research unit

Once you have completed telephone call 2, your involvement in the study will finish.

A summary table describing your time commitment for the study is included at the end of this leaflet.

The total amount of blood that you will give over the 16-week duration of the study is 555ml or approximately 1.5x that which would be given at a typical blood donation. As a precaution, we would advise you to refrain from blood donation for 3 months after the study.

5. What should I consider?

If you have diabetes or have taken steroid medication by mouth within the last 3 months or are taking any other types of medication to control inflammation, strengthen your bones, lower your cholesterol or other fats in the blood, reduce your blood pressure, if you have had a vaccination within the last 4 weeks, or if you undertake

regular night-shift work, then you may not be eligible to take part in the study. The investigators on the study will discuss this with you. If you consume more alcohol than would be safe for this study or if your blood pressure is very poorly controlled, then you also may not be eligible to take part in the study.

If you are eligible to take part, you will be able to continue your usual prescribed medications and anything that you buy over the counter.

There is currently no evidence to suggest that the drugs used in this study can impact upon fertility or harm an unborn child conceived whilst taking them. However, as a precaution, if you are sexually active with the possibility of you or your partner conceiving, we would ask you either to be abstinent (when this is your preferred and usual lifestyle) for the duration of, and for up to 3-months after you finish taking the trial drugs. Alternatively, you should use an effective method of contraception. This may include using a contraceptive pill or the use of a condom.

You will be able to take part in other research studies at the same time if they are not trialling drugs or interventions that might influence the outcome of this study. If you have taken part in a clinical study that involved a treatment or intervention, there needs to be a gap of at least 12-weeks before we could consider including you in the DC-MACS study. If you are uncertain, then you should discuss this with the DC-MACS study team.

6. Are there any possible disadvantages or risks from taking part?

SPI-62 has been used in clinical studies in healthy volunteers and in patients with diabetes (over 150 individuals in total) in doses up to 10-times that which we are using in this study, for periods up to 6-weeks.

SPI-62 is not licenced in the UK but there are currently 4 completed trials, 1 trial awaiting results and 3 ongoing trials. So far, these trials have shown SPI-62 is safe, with the majority of participants experiencing only mild symptoms such as headache, nausea and vomiting. It is not clear whether these are actually side effects of SPI-62 at this stage. There may be side effects of the study medication that have not been seen in the other studies so far. Precautions will be taken, and you are encouraged to report anything that is troubling you.

During the insulin infusion part of the study, there is the risk that your blood sugar may go low. We will be monitoring your blood sugar every 5 minutes (measured by the bedside) and if your sugar does drop there will be doctors and nurses immediately at hand to correct things without delay. The protocols are specifically designed to keep your blood sugar stable throughout the duration of the procedure.

During the insulin clamp part of the study, we will infuse a glucose tracer into the bloodstream. This is specially labeled molecule called a stable isotope. It is NOT radioactive and is completely safe and not harmful. Any molecule that we introduce directly into the blood will have been tested before purchase for purity and to ensure it contains no harmful materials. All solutions that are introduced into the blood are prepared in a sterile cabinet and are filtered and sterilized.

In the unlikely event that you become unwell during the study period, in a medical emergency we would advise that you call for an ambulance without delay. You will be provided with contact numbers that you can give to the medical team treating you and they will be able to contact the study team. If it is not a medical emergency and you become unwell, then you can contact the study team and we will review you and offer advice and treatment where appropriate.

Some participants find, inserting the cannula for taking blood uncomfortable. These procedures will be performed by experienced nurses and medical staff and local anaesthetic creams can be used to minimize any discomfort. Taking a fat sample can cause some mild discomfort may leave a bruise that could be quite large and possibly become hard underneath, but that should disappear after a couple of weeks. Insertion of microdialysis catheters into the tummy can cause pain but we use local anaesthetic to numb the area and all staff are experienced. Care is taken to clean the skin before any needles are inserted and before the fat biopsy.

We reduce the risk of bleeding and bruising by pressing firmly on the site for 5 minutes after the procedure has been performed.

If you take part in this study you will have CT scans and Bone Densitometry scans. All of these will be extra to those that you would have if you did not take part in the trial. These procedures use ionising radiation to form images of your body and provide your doctor with other clinical information. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous.

We are all at risk of developing cancer during our lifetime. The normal risk is that this will happen to about 50% of people at some point in their life. Taking part in this study will increase the chances of this happening to you from 50% to 50.18 %.

7. What are the possible benefits of taking part?

As part of the study, you will receive checks of liver, kidneys, cholesterol, blood pressure and blood sugar levels and you will be informed of these results. We believe that SPI-62 may improve the signs and symptoms of MACS and therefore this may be of benefit to you. However, only 50% of participants will receive SPI-62 and the other 50% will receive the placebo. Our aim is to show that SPI-62 can be used as a treatment for MACS where currently there are no licensed drugs. As we don't know if SPI-62 will be beneficial, we will not provide you with medication after the study has ended, so any benefits may be temporary. However, there may be opportunities to take part in additional studies with this medication and the research team will talk to you about this.

8. Will my General Practitioner/family doctor (GP) be informed of my participation?

With your permission, we will inform your GP that you are taking part in this study. Should we identify any medical problems that would need medical investigation or treatment, then we would either notify your GP or arrange for the appropriate NHS referral.

9. Will my taking part in the study be kept confidential?

All the information about your participation in this study will be kept confidential. None of the research data stored on computers will be directly identifiable and we will replace your name, initials and date of birth with a participant code that includes a unique number and your initials. All the information will be coded. We will keep your personal details stored securely and separately from the research data to contact you about your participation in the study. Any identifiable data will be stored on computers in accordance with University and NHS guidelines, including on encrypted and password protected systems. No identifiable information will be stored on laptops. Access to the clinical research units and laboratories) where the data and samples are stored is *via* multiple point secured swipe access. Any paper information collected will be kept securely in appropriate secured environments.

Responsible members of the Universities of Oxford and Sheffield and the [local NHS Trust] may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.

10. Will I be reimbursed for taking part?

Yes. Participants will be offered £470 for completion of the study (£40 for visits 1, 4 and 5, £75 for visits 2 and 6, £100 for visits 3 and 7). We will also arrange and pay for taxi transport to and from your study days.

11. What will happen to the samples I give?

The research blood and urine samples you provide will be kept secure and labelled only with your study number, in freezers at the OCDEM, University of Oxford and University of Sheffield. Only investigators who are part of the study will have access to the samples. They will be analysed for hormones and other metabolites at laboratories in Universities of Oxford and Sheffield. If you agree to your samples being used in future research,

your anonymised samples will be used mainly by local researchers, but ethically approved research projects may take place in hospitals, universities, non-profit institutions or commercial laboratories worldwide.

Although it is not the primary purpose of the study, some of the data generated by the analysis of the samples may be used by a student gain a PhD or other educational qualification.

12. What will happen to my data?

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford is the sponsor for this study. It is the data controller and is responsible for looking after your information and using it properly.

We will be using information from you and your medical records in order to undertake this study and will use the minimum personally-identifiable information possible.

We will store any research documents with personal information, such as consent forms, securely at the Diabetes Trials Unit for 25 years after the end of the study as part of the research record. If you agree to your samples being used in future research, then your consent form will be held securely until the samples have been used up.

If you agree to your details being held to be contacted regarding future research, we will retain a copy of your consent form securely until such time as your details are removed from our database. We will keep the consent form and your details separate from one another and any research data.

We will keep any other identifiable information about you for 12-months after the study has finished

The local NHS Trust will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. A copy of the consent form from this study will be kept in your medical records for as long as those records are retained.

They will keep any other identifiable information about you from this study for 12 months after the study has finished.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at https://compliance.web.ox.ac.uk/individual-rights .

You can find out more about how we use your information by contacting:

Diabetes Trials Unit: DC-MACS@dtu.ox.ac.uk

Chief Investigator: Prof. Jeremy Tomlinson, E-mail: jeremy.tomlinson@ocdem.ox.ac.uk; Tel. 01865 857359

13. What will happen if I don't want to carry on with the study?

You can withdraw from the study at any point, you can do so by contacting the local study team (see section 21). If you do decide to leave the study, your current or future clinical care will not be affected in any way. If you withdraw from the study, unless you state otherwise, any samples and data collected whilst you have been in the study will be used for research as detailed above. You may choose to stop the study treatment and not undergo further assessments but remain on study follow-up. You can discuss this with the study team.

14. What will happen to the results of this study?

At the end of the study, the results will be presented at regional, national, and international meetings and published in medical journals. You will not be identified from any report or publication placed in the public domain. Once the study has been published, a copy of the final report will be available through the University

of Oxford website. Research findings will also be disseminated through dedicated departmental public engagement events and through patient support groups. Some of the research being undertaken may also contribute to the fulfilment of an educational requirement (e.g. a doctoral thesis).

15. What if we find something unexpected?

In the unlikely event of seeing abnormal results from the scans, urine, or blood tests, these will be checked by a clinical specialist. If the specialist judges that the abnormality is medically important, they will discuss the implications with you and arrange for further investigations as necessary. You will not be informed of findings that have no impact on your current or future health. It is important to note that scans and tests are not carried out for diagnostic purposes, and therefore they are not a substitute for a clinical appointment. The scans and tests are intended for research purposes only.

16. What if there is a problem?

The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of the clinical treatment which is provided.

If you wish to complain about any aspect of the way in which you have been approached or treated during the study, then please do contact the research team directly.

Chief Investigator: Professor Jeremy Tomlinson

Email. jeremy.tomlinson@ocdem.ox.ac.uk ; Tel. 01865 857359

Alternatively, you may contact the University of Oxford Research Governance, Ethics & Assurance Team (RGEA) office on 01865616480, or the head of CTRG, email ctrg@admin.ox.ac.uk.

The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study. If you wish to contact the PALS team (Oxford: Tel. 01865 235855; Email. PALSCH@ouh.nhs.uk

17. How have patients and the public been involved in this study?

This information sheet has been reviewed by potential participants in the study.

18. Who is organising and funding the study?

Research is organised by OCDEM, University of Oxford, in collaboration with University of Sheffield and is funded by the Medical Research Council, UK.

19. Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee. This study has been reviewed and given a favourable opinion by the London – Central Research Ethics Committee.

20. Participation in future research:

With your consent, we may contact you thereafter about ethically approved research studies for which you may be suitable. You would not be obliged to participate in any such further studies. You can request to be removed from this register at any time. Your consent form would be held for as long as you are on the register.

21. Further information and contact details:

Thank you for taking the time to read this leaflet. If you would like to be part of this study, or if you would like more information then please get in contact with:

Oxford
Prof. Jeremy Tomlinson (Chief Investigator); jeremy.tomlinson@ocdem.ox.ac.uk
Dr Riccardo Pofi (clinical research fellow); riccardo.pofi@ocdem.ox.ac.uk
Siobhan Gardiner (Lead Research Nurse): tel. 01865-857202; siobhan.gardiner@ocdem.ox.ac.uk

Sheffield
Prof. John Newell-Price (Principal Investigator); j.newellprice@sheffield.ac.uk
Dr Alan Kelsall (clinical research fellow); tel. +44 114 215 9075; a.kelsall@sheffield.ac.uk
Sharon Caunt (Lead Research Nurse): tel. +44 (0) 114 226 5976; sharon.caunt@nhs.net

DC-MACS Study summary:

The aim of the DC-MACS study is to see in a drug called SPI-62 may improve the symptoms or signs associated with mild autonomous cortisol secretion (MACS) from a benign adrenal nodule. The study treatment is for 12-weeks and half of the participants will receive the active medication (SPI-62) and half will receive a dummy pill (placebo). The table below summarizes the time commitment for each visit and which investigations will be performed at each visit. There is the possibility that some visits could be combined at your convenience (see footnotes below the table).

In total, we estimate that you might need 4.5 days off work (half a day for visits 1, 2, 4, 5 and 6 and a full day for visits 3 and 7) to complete the study. After the 24-hour blood pressure measurements, this may disturb your sleep, so in addition, this could require a day off work after this has been performed (2 extra days in total). In recognition of this time commitment, remuneration for taking part in the study is described in section 10 of the information leaflet.

	Before treatment			***Treatment with either SPI-62 or placebo***					***After treatment***
	Visit 1	**Visit 2**	**Visit 3**	**Phone call 1**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Phone call 2**
Duration of visit	***1h***	***3h [1]***	***7h [1]***	***15 mins***	***1h***	***1h***	***3h [2]***	***7h [2]***	***15 mins***
Blood tests, medical history and brief examination	X	X	X		X	X	X	X	
Continuous glucose monitoring	X				X				
Adipose tissue biopsy		X					X		
DXA body composition scan		X					X		
Abdomen CT scan		X					X		
Cognitive function testing	X	X					X		
Quality of life questionnaire		X					X		
24-hour blood pressure readings		X					X		
Timed overnight urine collection		X			X	X	X		
Hyperinsulinaemic-euglycaemic clamp			X					X	

[1] These visits may be combined if it is more convenient for you, although it is likely that a separate, dedicated visit for the abdomen CT scan will be required.

[2] These visits may be combined if it is more convenient for you, although it is likely that a separate dedicated visit for the abdomen CT scan will be required