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Randomised treatment of Acute Pancreatitis with Infliximab: Double-blind multi-centre trial (RAPID-I)

Patient that regains capacity information sheet

Contents

You have been taking part in RAPID-I and we would like to invite you to continue

RAPID-I is a study testing a medicine called infliximab to treat acute pancreatitis (a disease of your pancreas).

When you were admitted into hospital and diagnosed with acute pancreatitis, your relative/friend or doctor, provided consent on your behalf, to take part in the study when you were unable to make this decision for yourself. It is now your decision if you wish to continue to take part or not and what happens to the data we have collected from you so far.

Before you decide whether or not you wish to continue taking part, it is important for you to understand why the research is being done, what has happened so far in the study and what it will involve for you, if you decide to continue. Please take time to read this information sheet carefully and discuss it with relatives or friends if you wish.

Taking part is up to you. If you do not want to continue to take part then you do not have to and do not need to give a reason.

Please ask a member of the team looking after you if there is anything that is not clear, or if you would like more information.

Thank you for taking the time to read this information sheet. We hope you will find it helpful.

Important things to know

In this study we are testing a medicine called infliximab to treat acute pancreatitis. We are comparing two different doses of infliximab (in a solution of salt water) with a placebo (salt water containing no infliximab) to find out if infliximab is effective and safe for acute pancreatitis. We also wish to see how genes (which you were born with) work in acute pancreatitis, and if there is a link between the way genes work and the way infliximab works. Patients in the study are put into one of the three following groups:

- 5 milligrams of infliximab per kilogram body weight
- 10 milligrams of infliximab per kilogram body weight
- Placebo (saline)

You were assigned to one of the three groups and the study medicine was given through a tube into one of your veins.

All participants that are recruited into this study are aged between 18-85.

Why are we doing the RAPID-I study?

Acute pancreatitis is a common and serious disease that needs emergency admission to hospital, but there are no medicines to cure the illness or speed up recovery. Acute pancreatitis causes severe pain in the stomach area, loss of hunger, sickness and vomiting. In one out of every three or four patients part of the pancreas may die and become infected. Usually infection has to be drained away through the skin or by endoscopy (camera passed through the mouth) or by surgery.

In one out of every ten patients the lungs, heart or kidneys may stop working well and if this happens patients may need to spend time on the intensive care ward. Patients with very bad acute pancreatitis may need to stay in hospital for three months or more and a number of patients die from acute pancreatitis (three to five out of every one hundred patients).

Infliximab is a medicine that may help patients with acute pancreatitis by stopping swelling and soreness (inflammation) in the pancreas and other parts of the body. If infliximab is given early, as in this study, it is possible that infliximab may stop more serious acute pancreatitis with all its problems and may help patients with acute pancreatitis get home and back to normal more quickly. On the other hand, infliximab may have no effect on acute pancreatitis, so we wish to test it to find out if it works or not. Several million people in the world have been treated with infliximab and medicines like it for bowel and joint disease, but it has not been tried in acute pancreatitis.

This study is called RAPID-I because we are testing the medicine as soon as possible (rapidly) after patients have come to hospital with acute pancreatitis, and because it is the first study (number one) to do so.

The results of this study will be used to develop new treatments for patients with acute pancreatitis.

Why have I been asked to continue to take part?

We are inviting you to continue to take part in this study because you were diagnosed with acute pancreatitis at one of the hospitals in the study. As your relative/friend or doctor provided consent on your behalf, you have already received the study medicine.

The study aims to recruit 290 patients.

What will I have to do if I continue to take part?

You will be able to ask any questions that you have. If you have all of your questions answered and are willing to continue to take part, you will be asked to sign a consent form to confirm your continued participation in the study. You will be given a copy of the consent form and the information sheet to keep.

You will have already been put into one of the three possible groups. The study medicine was given within 36 hours from onset of your abdominal pain. The study medicine needed to be given quickly to give it the best chance of working. You were also given antibiotics into one of your veins. Patients treated with infliximab have a slightly increased risk of developing infection so antibiotics were given to reduce the risk of infection.

So far, and if you continue in the study, the research team have recorded and will record the following details about you that are part of standard care:

- How bad your pain is
- How your heart, lungs and kidneys are working
- The ward you are on (normal or intensive care)
- Blood, urine and other tests you have
- The cause of your acute pancreatitis
- Any treatment you have

Depending on how far through the study you are, we may wish to collect more blood samples during the study (you will already have had some blood samples taken for the study). Your study blood samples will be used to find out if infliximab is helping to treat acute pancreatitis or not. For this we will measure a protein in the blood that is linked with acute pancreatitis, up to 28 days after the study medicine has been given. Whenever possible blood will have been and will continue to be taken at the same time that routine samples are taken. All study blood samples that have been taken and will be taken amount

to about 1 ½ tablespoons of blood at each assessment. We will have also checked to see whether you may have had hepatitis B virus before starting the study. If you are discovered to have hepatitis B during the study, you may need to receive treatment for this. The study blood samples will also be used to check the levels of study drug in your blood, to check if you develop resistance to infliximab, to see how acute pancreatitis has affected your immune system (parts of the body that fight infection) and to see if there are any links between the way genes work in acute pancreatitis and the way infliximab works. On two occasions we will ask you to provide stool samples to help tell us how well your pancreas is working.

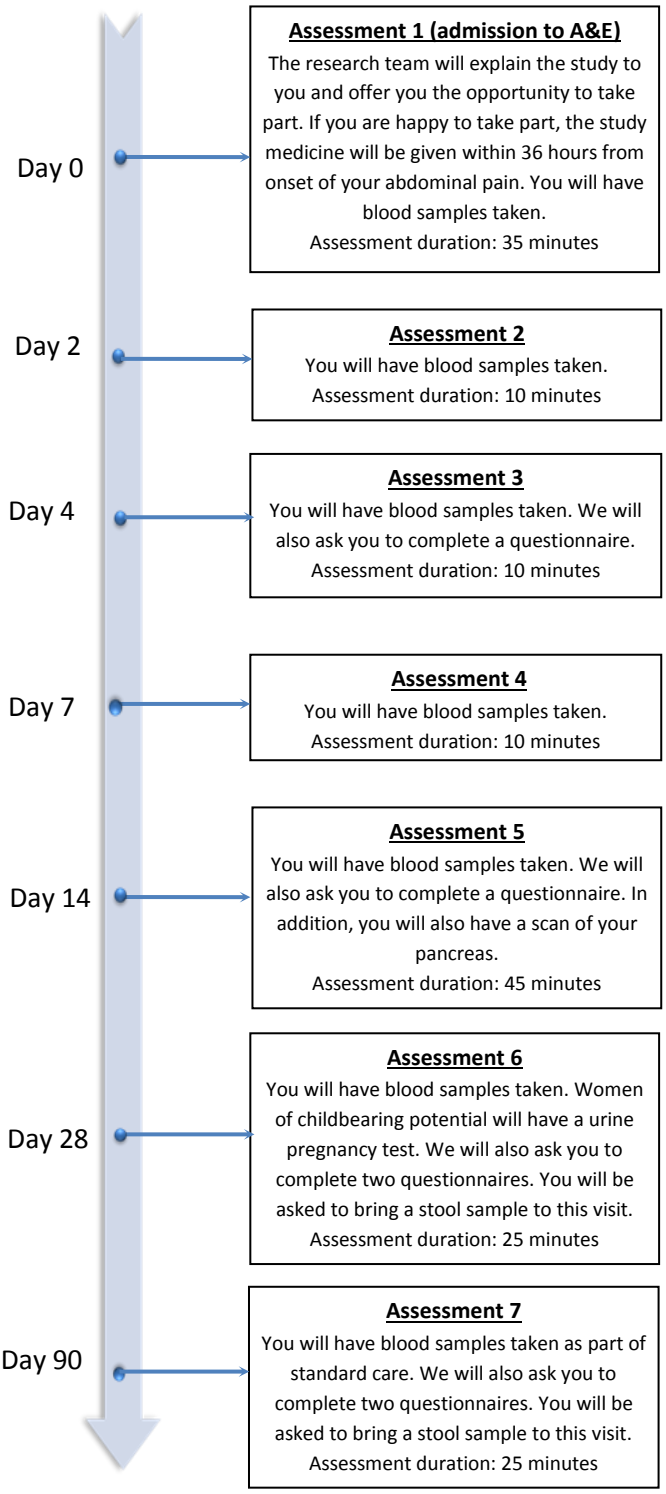
On one occasion in the study you will have a CT scan of your pancreas (you may have already had this), which is something patients may have as part of standard care for acute pancreatitis.

You will be asked to complete questionnaires about how you are, and what treatment you have (up to a maximum of 6 questionnaires over 90 days).

The study will run for 90 days from when you were given the study medicine. If you are sent home from hospital while you are in the study you will be asked to come back to the hospital for the study assessments. You would usually have to attend hospital once more than normal in standard care (Assessment 5 at Day 14). If you are still in hospital at the time of the study assessments, you will have these in hospital.

The timeline of assessments shows what assessments will take place throughout the duration of the study. Please ask a member of your research team if you are unsure at what point in the study you currently are.

Timeline of assessments



How will I know which treatment I have been given?

In research we often split patients up into groups to study how different treatments work. Patients in one group get a different treatment from patients in another group. In the RAPID-I study there are three groups:

- 5 milligrams of infliximab per kilogram body weight
- 10 milligrams of infliximab per kilogram body weight
- Placebo (saline with no infliximab)

It is very important that each group in the RAPID-I study has a similar mix of patients, so we know that if one group of patients does better than the others, it is very likely because of the treatment and not because this group has a different mix of patients. A single injection of hydrocortisone and chlorpheniramine will have been given to reduce the chance of any reaction from infliximab, as well as a course of antibiotics to reduce the chance of infection. These extra medicines will have also been given to you if you received placebo so we can be sure that any difference in outcome between infliximab and placebo is due to infliximab and not the extra medicines.

We use a computer programme that puts patients 'at random' into one of the groups – you might hear this described as 'randomisation' or 'random allocation', but they all mean the same thing. Neither you nor your doctor chose which group you were put in.

In the RAPID-I study, patients are randomised equally to each of the three groups, so this means you had the same chance of being put into each group.

This study is also a "blinded trial", which means that neither you nor the research team know which treatment you were given. Only the pharmacist who prepared the study medicine will know which group you are in and this information will be available to your research team if needed in an emergency.

What are the benefits and risks of continuing to take part?

By having taken part in this study, your symptoms of acute pancreatitis may have already have improved, although it is also possible that infliximab may have had little or no effect at all. Infliximab helps in bowel and joint disease and early research shows that infliximab may help patients with acute pancreatitis, but we do not know so we wish to find out by doing this study.

The results of this study may help others with acute pancreatitis and will be valuable in developing new medicines to treat acute pancreatitis.

Millions of patients in the world have been treated with infliximab for various diseases. Infliximab is a safe medicine and usually very well tolerated. Side effects from infliximab are uncommon. Most side effects occur when infliximab is given more than once, unlike in this study that tests a single dose of infliximab.

The two side effects that could occur with a single dose of infliximab, although unlikely, are allergic reactions (also known as infusion reactions) and infection.

Some patients (fewer than 5%) develop an infusion reaction while the medicine is given. This may cause headache, muscle ache, dizziness, low or high blood pressure, itching, fever, rash, flushing, sneezing, shortness of breath, stomach problems with nausea and vomiting, chest tightness, redness of the skin, sweating, shivers, light-headedness, sleepiness or racing of the heart. These side effects are usually mild to moderate and can usually be treated with drugs. All patients in the RAPID-I study will receive a single injection of hydrocortisone and chlorpheniramine before the trial medicine is given, to reduce the chance of an infusion reaction. If you experienced these side effects and they were serious, you or your research doctor may have considered stopping the study treatment. Infusion reactions occur in up to one in 20 patients having their first infliximab infusion. No deaths have been reported.

Another rare event that may occur one to 14 days after the infusion is a reaction that takes a while to develop (known as a delayed hypersensitivity reaction). This may or may have already caused fever, rash, headache, sore throat, muscle or joint pain, hand and face swelling or difficulty swallowing.

Infliximab is a medicine made of proteins from humans and mice. It is possible that your body could react against the medicine. Then if you have other medicines in the future that contain mouse proteins your body might react again. You should tell doctors in the future that you may have been treated with mouse proteins in this study. Your GP may have already been told by letter you are taking part in this study, via consent from your legal representative. The letter will have contained details of the study medicine you may have received.

Some patients given infliximab have simple infections such as the common cold, while other patients get more severe infections such as pneumonia or infection of the blood. About 1 in 100 patients treated with infliximab could develop a serious infection, so all patients in the RAPID-I study will be given antibiotics to help stop infection, as well as medicines to reduce reactions. You should let your research team know if you have a history of infection and discuss with them immediately if you develop an infection during the study.

Some patients have had tuberculosis (also called TB, a lung infection) during a course of infliximab, and a few have died from this. Although the risk from one dose is unknown, it is possible that you may have more of a chance to get tuberculosis if you receive infliximab. If you or any of your close family members have had tuberculosis, or you have any reason to suspect that you may have been exposed to tuberculosis in the past, you should inform your research team as soon as possible.

Other side effects after a single dose are rare. Side effects such as skin, joint and heart problems usually occur after infliximab has been given more than once.

Patients who are pregnant or breastfeeding cannot take part in the study. If you are a woman who could become pregnant you will be asked to have a pregnancy test during the study and must use contraception throughout the study and for a short time afterwards (until 6 months after receiving the study medicine). If you become pregnant while you are in the study you should immediately tell the research team. Women who become pregnant during the study will be closely monitored and expected to return for all study visits. Medical information about any pregnancies or breastfeeding during in the study will be collected.

As part of the study you will have one CT scan 14 days after coming into hospital (you may have already had this scan). Your doctors will be able to use this CT scan for your standard care, and may request that you have further CT scans for your standard care if your illness is more severe. The radiation from a single CT scan is low, but with repeated CT scans a small increase in the risk of cancer has been found. By taking part in this study it is estimated that over your lifetime the increase in your risk of cancer is roughly 1 in 1100.Your research team will ask you about any side effects you have had at every visit and will record them for the study. If you suffer from any of the side effects, or any other problems that you feel are not normal during the study, you should let the research team know at once.

What were the alternatives for treatment?

There is no other medicine available to stop damage in the pancreas and other parts of the body, or to help patients with acute pancreatitis (such as yourself) get home and back to normal more quickly. There is no other medicine to stop more serious acute pancreatitis. Feeding may have to be given in cartons of liquid (supplements) or through a tube in your nose or into a vein. If parts of your pancreas died and became infected then removal by endoscopy (camera passed through the mouth) or surgery may have been needed. If your lungs, heart or kidneys stop/stopped working well, then you may have/had to go to intensive care.

Do I have to continue to take part?

No, taking part is voluntary. It is up to you to decide whether or not you want to continue to take part. If you choose to continue you can also choose to stop at any time without giving a reason. The standard of care you receive now or in the future will be the same whether you continue your participation or not. If you decide you do not wish to continue taking part, you can also choose what happens to your samples and data that we have already collected.

What happens if I change my mind?

If at any point you decide to stop taking part in the study you will receive the treatment and follow up usually offered by your hospital. If you do decide to stop taking part we will ask you if you would like to:

- Complete the follow up visits for the study
  OR
- Stop taking part with no more study visits

The research team may be required to collect some limited information about any side effects you may have as a result of taking part in this study. This will only be collected if required by the regulatory authorities.

Will my participation be kept confidential?

Yes. All information collected about you during the study will be handled according to all applicable ethical and legal requirements.

Your NHS hospital will collect information from you and your medical records for this research study, in accordance with our instructions.

Your NHS hospital 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. Individuals from the University of Liverpool (the research team and representatives of the study Sponsor) and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Your NHS hospital will pass these details to the University of Liverpool along with the information collected from you and your medical records. The only people in the University of Liverpool who will have access to information that identifies you will be people who need to contact you and/or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details. Your NHS hospital will keep identifiable information about you from this study for up to a maximum of 25 years after the study has finished.

You will be given a study number, which will be used on each paper form that records details about your care and participation in the RAPID-I study. Your full name will be included on your consent form and a copy of this will be sent to the coordinating centre for the study, the Clinical Trials Research Centre (CTRC), which is part of the University of Liverpool. Every effort will be made to remove your name from any further information about you that leaves the hospital, so that you cannot be recognised from it. Your name will usually be removed by one of the study team at your hospital, but may be removed by the CTRC upon receipt.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government. Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance. Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee.

Details about the use of health services (health economics) will be collected in this study. The study team will retrieve information from your electronic hospitalisation records held by your hospital finance department. The collected data will only have your RAPID-I study number attached to it and no other personal identifiable information. Researchers at Bangor University, who are part of the RAPID-I research team, will use these data to calculate the overall costs of care. The data will be securely transferred from the hospital to the CTRC, then from the CTRC to Health Economics researchers at Bangor University using an encrypted electronic transfer system. These data will be collected for the period that you are in the study only, and stored securely for no longer than 12 months at Bangor University following the completion of the RAPID-I study, it will then be returned to the University of Liverpool for long-term storage. Bangor University will act as a joint data controller, with the University of Liverpool.

Safety and pregnancy information will be provided confidentially and securely to the company who supply infliximab (Merck, Sharp and Dohme). Information on patients who are breastfeeding will also be provided confidentially and securely to the company.

What has happened to the blood samples I have given?

All samples will have had your personal details removed and will have been sent to the National Institute for Health Research National Biosample Centre in Milton Keynes for processing and storage. A unique study number was attached and this is the only way of identifying your samples. Only the research team will be able to link this unique study number to you.

During the study the samples will be transported from the NIHR Biosample Centre to Liverpool Clinical Laboratories, and other UK laboratories approved by the University of Liverpool, for analysis of the results of the study.

Once the samples for this study have been analysed, there may be some sample remaining. Optionally, and with your consent, we wish to keep this for use in future research studies to advance the care and treatment of patients with acute pancreatitis, including for future studies we undertake with researchers in other countries. Any future research will be handled according to all applicable ethical and legal requirements of the UK. The samples will be labelled using your unique study number and securely held for an unlimited time by the NIHR National Biosample Centre.

Limited data collected from this study will be given to future researchers to help them study the samples, including data on your genes. You will not be identified and your clinical information will not be transported or stored in the same place as the samples. Your inherited genes are yours and belong to no one else, so if you or anyone else made public your inherited genes then it could be possible for you to be identified from samples obtained in this study. We will not share your identity with any other researchers and we will remove all links to your identity from any data on your genes we share with other researchers, making it very unlikely that you could be identified by taking part in this study.

Any results from future research will not be added to your notes and we will not be able to tell you the results of future studies carried out on these samples.

What will happen to the results of the study?

The results of the study will be presented at medical conferences and published in medical journals so that we can explain what the results show. The results of the study will also be made available to participants. Confidentiality will be ensured at all times and you will not be identified in any publication.

What if there is a problem?

If you have any concerns about this study, you should ask to speak with one of your research team who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from your treating hospital.

Every care will be taken in the course of this research study. In the unlikely event that you are injured as a result of the organisation (University of Liverpool) managing the trial, compensation may be available, but you may have to pay own legal costs. Your treating hospital has a duty of care to you whether or not you agree to participate in the trial and the University of Liverpool accepts no liability for negligence on the part of your hospital's employees. If you are harmed and this is due to someone's negligence, then you may have grounds for a legal action for compensation against the NHS Trust where you are being treated, but you may have to pay for your legal costs in connection with this matter.

Additional information

The University of Liverpool is the sponsor for this study in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as a joint data controller for this study, with Bangor University. This means that we are responsible for looking after your information and using it properly. The University of Liverpool will keep identifiable information about you for up to 25 years after the study has finished. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. You can find out more about how we use your information at www.rapid-one.org.uk.

The University of Liverpool is responsible for managing this study; the University of Liverpool has asked that the day-to-day running of the study is carried out by the Clinical Trials Research Centre (CTRC), which is part of the University of Liverpool.

The RAPID-I study has been reviewed for scientific content by the Medicines and Healthcare Products Regulatory Agency (MHRA), the Health Research Authority (HRA) and the National Research Ethics Service Committee. The South Central - Oxford C Research Ethics Committee has reviewed the study and given approval for it to take place.

This project is funded by the Efficacy and Mechanism Evaluation (EME) Programme, a Medical Research Council (MRC) and National Institute for Health Research (NIHR) partnership.

MRC Medical Research Council

NHS National Institute for Health Research

Thank you for reading this information sheet

Contacts for further information

If you would like more information or have any questions about the RAPID-I study please talk to:
Principal Investigator: **<PI NAME>**
Research Nurse: **<RN NAME>**
Telephone: **<number>**

Or visit the website: www.rapid-one.org.uk
If you wish to talk about the study with someone who is not part of the research team you can contact the local NHS Patient Advice and Liaison Service (PALS) or equivalent on: **<telephone number>**

RAPID-I

Randomised treatment of Acute Pancreatitis with Infliximab: Double-blind multi-centre trial

Trust headed paper
<Trust/Site address 1>
<Trust/Site address 2>
<Trust/Site address 3>
<Postcode>
Tel: <telephone number>

Consent Form

To be completed by the Researcher:

Centre Name:		Patient Initials:			

Once you have read and understood each statement please initial each box	Initial
Example: I confirm that I have read and understand the patient that regains capacity participant Information Sheet.	JS
1. I have read and understood the information sheet for this study. I have had the opportunity to ask questions and have had these answered satisfactorily.	
2. I understand that my continued participation is voluntary and that I am free to withdraw from the study at any time, without giving a reason, and without my care or legal rights being affected. I understand that in some cases further information about any unwanted effects of my treatment may need to be collected by the study team.	
3. I understand that my data will be held securely for a maximum of 25 years by the Clinical Trials Research Centre (CTRC) of the University of Liverpool and that they will be stored in a confidential manner.	
4. I give permission for a copy of my consent form, which will include my name, to be sent to the CTRC (where it will be kept in a secure location), to allow confirmation that my consent was given.	
5. I understand that relevant sections of my medical notes and any data collected during the study may be looked at by authorised individuals from the research team and those listed in 'Will my participation be kept confidential' (above, including NHS Trust and Regulatory Authorities). I give permission for these individuals to have access to my records.	
6. I give permission for blood and faecal samples to be collected and analysed for the study including analysis of my genes.	
7. I acknowledge that my safety, pregnancy and lactation data (if applicable) has been sent to Merck Sharp and Dohme, and agree to this being sent in the future (if applicable) during the study.	
8. I agree to my health economics (overall cost of care) data being securely transferred from my hospital to the CTRC, who will then securely transfer this to the research team at the University of Bangor for analysis.	
9. I acknowledge that my GP has been informed of my participation in the study.	
10. I acknowledge my participation in the above study so far and wish to continue to take part in the study.	
For women of childbearing potential only: N/A *(Please tick if not applicable)* ☐	
11. I agree to use adequate contraception for 6 months after I received the trial medicine.	
Below are optional statements:	
12. I agree to allow information or results arising from this study to be used in for future healthcare and/or medical research.	
13. I agree to gift any remaining samples and required data to the University of Liverpool (to be stored at the NIHR National Biosample Centre) for use in any future ethically approved research for acute pancreatitis.	

Your **full** name (please print):			
Your signature:		Date:	dd / mm / yyyy

To be completed by the Researcher:

Researcher **full** name (please print):			
Researcher signature:		Date:	dd / mm / yyyy